Question 1 of 220

A 34-year-old woman is admitted to the Emergency Department following a collapse. An ECG shows a polymorphic ventricular tachycardia. Which one of the following is not associated with an increased risk of developing torsade de pointes?

- A. Tricyclic antidepressants
- B. Subarachnoid haemorrhage
- C. Hypercalcaemia
- D. Romano-Ward syndrome
- E. Hypothermia

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- E. Hypothermia

Hypocalcaemia, not hypercalcaemia, causes prolongation of the QT interval and hence may predispose to the development of torsade de pointes

Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than marked left axis deviation in males and 450 ms in females.

Causes of a prolonged QT interval

Congenital	**Drugs**	**Other**
• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel) • Romano-Ward syndrome (no deafness)	• amiodarone, sotalol, class 1a antiarrhythmic drugs • tricyclic antidepressants, fluoxetine • chloroquine • terfenadine* • erythromycin	• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia • acute myocardial infarction • myocarditis • hypothermia • subarachnoid hemorrhage

Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 2 of 220

A 65-year-old man with a history of paroxysmal atrial fibrillation presents with palpitations. He has no other history of note and a recent echocardiogram was normal. An ECG confirms fast atrial fibrillation. Which one of the following agents is most likely to cardiovert him into sinus rhythm?

- A. Sotalol
- B. Procainamide
- C. Flecainide
- D. Disopyramide
- E. Digoxin

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Atrial fibrillation - cardioversion: amiodarone + flecainide

Atrial fibrillation: pharmacological cardioversion

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents with proven efficacy in the pharmacological cardioversion of atrial fibrillation

- amiodarone
- flecainide (if no structural heart disease)
- others (less commonly used in UK): quinidine, dofetilide, ibutilide, propafenone

Less effective agents

- beta-blockers (including sotalol)
- calcium channel blocks
- digoxin
- disopyramide
- procainamide

Question 3 of 220

A 17-year-old girl is brought into resus in cardiac arrest. On admission she is in asystole and attempts to resuscitate are unsuccessful. She collapsed whilst competing in a 1,500m race at college. The only past medical of note was asthma for which she occasionally used a salbutamol inhaler. There is no relevant family history. What is the most likely underlying cause of death?

- A. Long QT syndrome
- B. Hypertrophic obstructive cardiomyopathy
- C. Catecholaminergic polymorphic ventricular tachycardia
- D. Brugada syndrome
- E. Arrhythmogenic right ventricular dysplasia

Question 3 of 220

A 17-year-old girl is brought into resus in cardiac arrest. On admission she is in asystole and attempts to resuscitate are unsuccessful. She collapsed whilst competing in a 1,500m race at college. The only past medical of note was asthma for which she occasionally used a salbutamol inhaler. There is no relevant family history. What is the most likely underlying cause of death?

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- C. Catecholaminergic polymorphic ventricular tachycardia
- D. Brugada syndrome
- E. Arrhythmogenic right ventricular dysplasia

HOCM is the most common cause of sudden cardiac death in the young

Hypertrophic obstructive cardiomyopathy (HOCM) is a more common cause of sudden cardiac death than arrhythmogenic right ventricular dysplasia (ARVD).

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a form of inherited cardiac disease which is also associated with sudden cardiac death. It is inherited in an autosomal dominant fashion and has a prevalence of around 1:10,000.

Brugada syndrome is a form of inherited cardiovascular disease which again may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Features
- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

Associations
- Friedreich's ataxia
- Wolff-Parkinson White

Echo
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)
- mitral regurgitation

ECG
- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Question 4 of 220

A 26-year-old female is admitted to hospital with palpitations. ECG shows a shortened PR interval and wide QRS complexes associated with a slurred upstroke seen in lead II. What is the definitive management of this condition?

- A. Accessory pathway ablation
- B. Lifelong aspirin
- C. AV node ablation
- D. Lifelong amiodarone
- E. Permanent pacemaker

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✓ A. Accessory pathway ablation

B. Lifelong aspirin

C. AV node ablation

D. Lifelong amiodarone

E. Permanent pacemaker

This patient has Wolff-Parkinson White syndrome, with accessory pathway ablation being the definitive treatment

Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:
- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway*
- right axis deviation if left-sided accessory pathway*

Differentiating between type A and type B
- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW
- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management
- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol**, amiodarone, flecainide

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

**sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Question 5 of 220

A 54-year-old man is admitted following a myocardial infarction associated with ST elevation. He is treated with thrombolysis and does not undergo angioplasty. What advice should he be given regarding driving?

- A. Can continue driving but must inform DVLA
- B. Cannot drive until an angiogram has been performed and reviewed by a cardiologist
- C. Cannot drive for 1 week
- D. Cannot drive for 4 weeks
- E. Cannot drive for 12 weeks

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- ✓ D. Cannot drive for 4 weeks
- E. Cannot drive for 12 weeks

DVLA advice post MI - cannot drive for 4 weeks

DVLA: cardiovascular disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- angioplasty (elective) - 1 week off driving
- CABG - 4 weeks off driving
- acute coronary syndrome- 4 weeks off driving, 1 week if successfully treated by angioplasty
- angina - driving must cease if symptoms occur at rest/at the wheel
- pacemaker insertion - 1 week off driving
- implantable cardioverter-defibrillator: if implanted for sustained ventricular arrhythmia: cease driving for 6 months. If implanted prophylatically then cease driving for 1 month
- successful catheter ablation - 2 days off driving
- aortic aneurysm of 6cm or more - notify DVLA. Licensing will be permitted subject to annual review. An aortic diameter of 6.5 cm or more disqualifies patients from driving
- heart transplant: DVLA do not need to be notified

Question 6 of 220

A 62-year-old man is admitted with to the cardiology ward with infective endocarditis. Blood cultures grow *Streptococcus bovis*. What is the most appropriate investigation given the blood culture findings?

- A. Small bowel meal
- B. Bronchoscopy
- C. Cystoscopy
- D. Gastroscopy
- E. Colonoscopy

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Streptococcus bovis endocarditis is associated with colorectal cancer

Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. Other factors include:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- Bartonella
- Brucella
- HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in Staph aureus infections

Question 7 of 220

A 54-year-old male with no past medical history is found to be in atrial fibrillation during a consultation regarding a sprained ankle. He reports no history of palpitations or dyspnoea. After discussing treatment options he elects not to be cardioverted. If the patient remains in chronic atrial fibrillation what is the most suitable treatment to offer?

- A. Aspirin
- B. Warfarin, target INR 2-3
- C. No anticoagulation
- D. Warfarin, target INR 3-4
- E. Warfarin, target INR 2-3 for six months then aspirin

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- E. Warfarin, target INR 2-3 for six months then aspirin

Young AF, no TIA or risk factors, just give aspirin

Atrial fibrillation: anticoagulation

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006

The guidelines suggest a stroke risk stratification approach when determining how to anticoagulate a patient, as detailed below:

Low risk	**Moderate risk**	**High risk**
- annual risk of stroke = 1% • age < 65 years with no moderate or high risk factors • use aspirin	- annual risk of stroke = 4% • age > 65 years with no high risk factors, or: • age < 75 years with diabetes, hypertension or cardiovascular disease • use aspirin or warfarin depending on individual circumstances	- annual risk of stroke = 8-12% • age > 75 years with diabetes, hypertension or cardiovascular disease • previous TIA, ischaemic stroke or thromboembolic event • valve disease, heart failure or impaired left ventricular function • use warfarin

An alternative approach is the **CHADS2** score:

	Condition	**Points**
C	Congestive heart failure	1
H	Hypertension (or treated hypertension)	1
A	Age > 75 years	1
D	Diabetes	1
S2	Prior Stroke or TIA	2

The table below shows a suggested anticoagulation strategy based on the score:

Score	**Anticoagulation**
0	Aspirin
1	Aspirin or warfarin, depending on patient preference and individual factors
2-6	Warfarin if not contraindicated

Question 8 of 220

A 54-year-old man is admitted to the Emergency Department with a 15 minute history of crushing central chest pain. Which one of the following rises first following a myocardial infarction?

- A. AST
- B. Troponin I
- C. CK
- D. CK-MB
- E. Myoglobin

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Myoglobin rises first following a myocardial infarction

Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superceded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	Peak value	Returns to normal
Myoglobin	1-2 hours	6-8 hours	1-2 days
CK-MB	2-6 hours	16-20 hours	2-3 days
CK	4-8 hours	16-24 hours	3-4 days
Trop T	4-6 hours	12-24 hours	7-10 days
AST	12-24 hours	36-48 hours	3-4 days
LDH	24-48 hours	72 hours	8-10 days

Question 9 of 220

A 2-day-old baby girl is noted to become cyanotic whilst feeding and crying. A diagnosis of congenital heart disease is suspected. What is the most likely cause?

- A. Transposition of the great arteries
- B. Coarctation of the aorta
- C. Patent ductus arteriosus
- D. Tetralogy of Fallot
- E. Ventricular septal defect

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Congenital heart disease
- cyanotic: TGA most common at birth, Fallot's most common overall
- acyanotic: VSD most common cause

The key point to this question is that whilst tetralogy of Fallot is more common than transposition of the great arteries (TGA), Fallot's doesn't usually present until 1-2 months following the identification of a murmur or cyanosis. In the neonate, TGA is the most common presenting cause of cyanotic congenital heart disease

The other 3 options are causes of acyanotic congenital heart disease

Congenital heart disease: types

Acyanotic - most common causes
- ventricular septal defects (VSD) - most common, accounts for 30%
- atrial septal defect (ASD)
- patent ductus arteriosus (PDA)
- coarctation of the aorta
- aortic valve stenosis

VSDs are more common than ASDs. However, in adult patients ASDs are the more common new diagnosis as they generally presents later

Cyanotic - most common causes
- tetralogy of Fallot
- transposition of the great arteries (TGA)
- tricuspid atresia
- pulmonary valve stenosis

Fallot's is more common than TGA. However, at birth TGA is the more common lesion as patients with Fallot's generally presenting at around 1-2 months

Question 10 of 220

A 24-year-old male is diagnosed as having hypertrophic obstructive cardiomyopathy. Which one of the following markers is most useful in assessing risk of sudden death?

- A. Abnormal blood pressure changes on exercise
- B. Left ventricular outflow tract gradient
- C. QT interval
- D. Right atrial diameter
- E. QRS duration

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HOCM: prognostic factors

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

Question 11 of 220

Which one of the following features would indicate cardiac tamponade rather than constrictive pericarditis?

- A. Raised JVP
- B. Muffled heart sounds
- C. No Y descent on JVP
- D. Hypotension
- E. Tachycardia

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In cardiac tamponade there is characteristically no Y descent on the JVP. The other four features are seen in both cardiac tamponade and constrictive pericarditis

Cardiac tamponade

Features

- raised JVP, with an absent Y descent - this is due to the limited right ventricular filling
- tachycardia
- hypotension
- muffled heart sounds
- pulsus paradoxus
- Kussmaul's sign (much debate about this)
- ECG: electrical alternans

The key differences between constrictive pericarditis and cardiac tamponade are summarised in the table below:

	Cardiac tamponade	**Constrictive pericarditis**
JVP	Absent Y descent	X + Y present
Pulsus paradoxus	Present	Absent
Kussmaul's sign	Rare	Present
Characteristic features		Pericardial calcification on CXR

A commonly used mnemonic to remember the absent Y descent in cardiac tamponade is
TAMponade = TAMpaX

Question 12 of 220

Six weeks after having a prosthetic heart valve a patient develops infective endocarditis. What is the most likely causative organism?

- A. *Streptococcus viridans*
- B. *Staphylococcus epidermidis*
- C. *Staphylococcus aureus*
- D. *Streptococcus bovis*
- E. One of the HACEK group

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Most common cause of endocarditis:
- *Streptococcus viridans*
- *Staphylococcus epidermidis* if < 2 months post valve surgery

In the first two months following surgery for a prosthetic valve the most likely causative organism is *Staphylococcus epidermidis*

Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. Other factors include:
- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

Causes
- *Streptococcus viridans* (most common cause - 40-50%)
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Question 13 of 220

An 18-year-old female who is known to have Turner's syndrome is referred to cardiology as she has a murmur. On examination a soft ejection systolic murmur is heard. What is the most likely cause of this finding?

- A. Coarctation of the aorta
- B. Ventricular septal defect
- C. Pulmonary stenosis
- D. Supravalvular aortic stenosis
- E. Bicuspid aortic valve

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Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 14 of 220

A 71-year-old man is reviewed in the coronary care unit. He was admitted with an anterior ST-elevation myocardial infarction and received thrombolysis with alteplase. Ninety minutes following this an ECG shows a 30-40% resolution in the ST elevation. What is the most appropriate management?

- A. Percutaneous coronary intervention
- B. Repeat ECG in 4 hours, if still not a 50% resolution in ST elevation then proceed to percutaneous coronary intervention
- C. Repeat thrombolysis with alteplase
- D. Start a nitrate infusion
- E. Inform his relatives that further intervention is futile and ensure adequate pain relief

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Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Question 15 of 220

Each one of the following is associated with right axis deviation on ECG, except:

- A. Right ventricular hypertrophy
- B. Pulmonary embolism
- C. Wolf-Parkinson-White syndrome with right-sided accessory pathway
- D. Chronic lung disease
- E. Left posterior hemiblock

Question 15 of 220

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- ✓ C. Wolf-Parkinson-White syndrome with right-sided accessory pathway
- D. Chronic lung disease
- E. Left posterior hemiblock

Wolff-Parkinson-White syndrome is associated with a short PR interval and a wide QRS complex with a slurred upstroke, termed a delta wave. Axis deviation depends on the position of the accessory pathway

ECG: axis deviation

Causes of left axis deviation (LAD)
- left anterior hemiblock
- left bundle branch block
- Wolff-Parkinson-White syndrome* - right-sided accessory pathway
- hyperkalaemia
- congenital: ostium primum ASD, tricuspid atresia
- minor LAD in obese people

Causes of right axis deviation (RAD)
- right ventricular hypertrophy
- left posterior hemiblock
- chronic lung disease
- pulmonary embolism
- ostium secundum ASD
- Wolff-Parkinson-White syndrome* - left-sided accessory pathway
- normal in infant < 1 years old
- minor RAD in tall people

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

Question 16 of 220

Which one of the following is not an indication for insertion of a temporary pacemaker?

- A. Complete heart block following an inferior MI - blood pressure normal
- B. Complete heart block following an anterior MI - blood pressure normal
- C. Trifascicular block prior to surgery
- D. Mobitz type II heart block following an anterior MI - blood pressure normal
- E. Symptomatic bradycardia not responding to drug treatment

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- E. Symptomatic bradycardia not responding to drug treatment

Complete heart block following an inferior MI is NOT an indication for pacing, unlike with an anterior MI

Post-inferior MI complete heart block is common and can be managed conservatively if the patient is asymptomatic and haemodynamically stable

Pacemakers: temporary

Indications for a temporary pacemaker
- symptomatic/haemodynamically unstable bradycardia, not responding to atropine
- post-ANTERIOR MI: type 2 or complete heart block*
- trifascicular block prior to surgery

*post-INFERIOR MI complete heart block is common and can be managed conservatively if asymptomatic and haemodynamically stable

Question 17 of 220

Which one of the following treatments have not been shown to improve mortality in patients with chronic heart failure?

- A. Beta-blockers
- B. Spironolactone
- C. Frusemide
- D. Nitrates and hydralazine
- E. Enalapril

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- ✓ C. Frusemide
- D. Nitrates and hydralazine
- E. Enalapril

Whilst useful in managing the symptoms of acute and chronic heart failure frusemide offers no prognostic benefits.

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:
- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:
- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off** pneumococcal vaccine

*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

**adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Question 18 of 220

A 74-year-old man with symptomatic aortic stenosis is reviewed in the cardiology clinic. He is otherwise fit and well and keen for intervention if possible. What type of intervention is he most likely to be offered?

- A. Annual echocardiography, intervention when valve gradient > 75 mmHg
- B. Aortic bypass graft
- C. Bioprosthetic aortic valve replacement
- D. Balloon valvuloplasty
- E. Mechanical aortic valve replacement

Question 18 of 220

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Prosthetic heart valves - mechanical valves last longer and tend to be given to younger patients

Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	**Mechanical valves**
Usually bovine or porcine in origin Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays Mechanical valves have a low failure rate Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication. Target INR • aortic: 2.0-3.0 • mitral: 2.5-3.5

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Question 19 of 220

A 74-year-old man presents for a medication review. Blood pressure is recorded as 184/72 mmHg. This is confirmed on two further occasions. What is the most appropriate first line therapy?

- A. Ramipril
- B. Losartan
- C. Frusemide
- D. Bendroflumethiazide
- E. Atenolol

Question 19 of 220

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- ✓ D. Bendroflumethiazide
- E. Atenolol

The 2006 NICE guidelines recommended treating isolated systolic hypertension the same way as standard hypertension. In this age group thiazides or calcium channel blockers would be first-line agents

Isolated systolic hypertension

Isolated systolic hypertension (ISH) is common in the elderly, affecting around 50% of people older than 70 years old. The Systolic Hypertension in the Elderly Program (SHEP) back in 1991 established that treating ISH reduced both strokes and ischaemic heart disease. Drugs such as thiazides were recommended as first line agents. This approach is not contraindicated by the 2006 NICE guidelines which recommends treating ISH in the same stepwise fashion as standard hypertension

Question 20 of 220

A 58-year-old man with no past medical history of note is admitted to hospital with crushing central chest pain. ECG on arrival shows anterior ST elevation and he is subsequently thrombolysed with a good resolution of symptoms and ECG changes. Two months following discharge from hospital, which combination of drugs should he be taking?

- A. ACE inhibitor + beta-blocker + statin + aspirin
- B. Spironolactone + beta-blocker + statin + aspirin
- C. ACE inhibitor + beta-blocker + statin + aspirin + clopidogrel
- D. ACE inhibitor + statin + aspirin + clopidogrel
- E. Beta-blocker + statin + aspirin + clopidogrel

Question 20 of 220

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- D. ACE inhibitor + statin + aspirin + clopidogrel
- E. Beta-blocker + statin + aspirin + clopidogrel

The current guidance is to continue clopidogrel for 4 weeks following a ST-elevation myocardial infarction

Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

Clopidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk is > 1.5%

Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

Question 21 of 220

A 72-year-old man presents with lethargy and palpitations for the past four or five days. On examination his pulse is 123 bpm irregularly irregular, blood pressure is 118/70 mmHg and his chest is clear. An ECG confirms atrial fibrillation. What is the appropriate drug to control his heart rate?

- A. Amiodarone
- B. Atenolol
- C. Digoxin
- D. Amlodipine
- E. Flecainide

Question 21 of 220

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Atrial fibrillation: rate control - beta blockers preferable to digoxin

A number of factors including age and symptoms would favour a rate control strategy. The NICE guidelines suggest either a beta-blocker or a rate limiting calcium channel blocker (i.e. Not amlodipine) in this situation. Some clinicians would prefer to use a more cardio-selective beta-blocker such as bisoprolol, although this is not stipulated in current guidelines

Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents used to control rate in patients with atrial fibrillation
- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation
- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
• Older than 65 years • History of ischaemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 22 of 220

A 52-year-old female with a known history of systemic sclerosis presents for annual review to the rheumatology clinic. Which one of the following symptoms is most characteristic in patients who have developed pulmonary arterial hypertension?

- A. Exertional dyspnoea
- B. Paroxysmal nocturnal dyspnoea
- C. Cough
- D. Early morning dyspnoea
- E. Orthopnoea

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- C. Cough
- D. Early morning dyspnoea
- E. Orthopnoea

Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

Features
- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing
- oral calcium channel blockers

If there is a negative response to acute vasodilator testing
- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Question 23 of 220

You review a patient who has been admitted with a non-ST elevation myocardial infarction in the Emergency Department. Following recent NICE guidance, which patients should receive clopidogrel?

- A. Those who have a predicted 6 month mortality > 1.5%
- B. Patients who have a history of hypertension, ischaemic heart disease or diabetes mellitus
- C. Those who have a predicted 12 month mortality > 10%
- D. Those who have a predicted 6 month mortality < 10%
- E. All patients

Question 23 of 220

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B. Patients who have a history of hypertension, ischaemic heart disease or diabetes mellitus

C. Those who have a predicted 12 month mortality > 10%

D. Those who have a predicted 6 month mortality < 10%

E. All patients

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:
- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

The 6 month mortality may be calculated using a validated risk model such as GRACE.

Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive
- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

Antithrombin treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

Clopidogrel 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

Coronary angiography should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

Aspirin	Antiplatelet - inhibits the production of thromboxane A2
Clopidogrel	Antiplatelet - inhibits ADP binding to its platelet receptor
Enoxaparin	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Fondaparinux	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Bivalirudin	Reversible direct thrombin inhibitor

Question 24 of 220

A 55-year-old smoker with a past history of hypertension presents to the Emergency Department with shortness-of-breath since the morning. Examination reveals bibasal crackles whilst the CXR shows upper lobe diversion and perihilar shadowing. The ECG and cardiac enzymes are normal. What is the likely cause of his breathlessness?

- A. Infective endocarditis
- B. Phaeochromocytoma
- C. Fibromuscular dysplasia
- D. Renal artery stenosis
- E. Anterior myocardial infarction

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- ✓ D. Renal artery stenosis
- E. Anterior myocardial infarction

Flash pulmonary oedema, U&Es worse on ACE inhibitor, asymmetrical kidneys --> renal artery stenosis - do MR angiography

Renal artery stenosis may cause sudden onset or 'flash' pulmonary oedema. A myocardial infarction is unlikely given the normal ECG and cardiac enzymes. Chest pain would also be expected in a 55-year-old patient with no history of diabetes. Fibromuscular dysplasia is generally seen in young woman

Renal vascular disease

Renal vascular disease is most commonly due to atherosclerosis (> 95% of patients). It is associated with risk factors such as smoking and hypertension that cause atheroma elsewhere in the body. It may present as hypertension, chronic renal failure or 'flash' pulmonary oedema. In younger patients however fibromuscular dysplasia (FMD) needs to be considered. FMD is more common in young women and characteristically has a 'string of beads' appearance on angiography. Patients respond well to balloon angioplasty

Investigation

- MR angiography is now the investigation of choice
- CT angiography
- conventional renal angiography is less commonly performed used nowadays, but may still have a role when planning surgery

Question 25 of 220

A 65-year-old man is found to have an ejection systolic murmur and narrow pulse pressure on examination. He has experienced no chest pain, breathlessness or syncope. An echo confirms aortic stenosis and shows an aortic valve gradient of 40 mmHg. How should this patient be managed?

- A. Routine aortic valve replacement
- B. Urgent aortic valve replacement
- C. Anticoagulation
- D. Aortic valvuloplasty
- E. Regular cardiology outpatient review

Question 25 of 220

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- B. Urgent aortic valve replacement
- C. Anticoagulation
- D. Aortic valvuloplasty
- ✓ E. Regular cardiology outpatient review

Aortic stenosis management: AVR if symptomatic, otherwise cut-off is gradient of 50 mmHg

No action should be taken at present as he is currently asymptomatic. If the aortic valve gradient > 50 mmHg or there is evidence of significant left ventricular dysfunction then surgery is sometimes considered in selected asymptomatic patients

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 26 of 220

A 59-year-old female is admitted to the Emergency Department with a 30 minute history of central chest pain radiating to her left arm. An ECG shows ST elevation in leads II, III, aVF. Which coronary artery is most likely to be affected?

- A. Right coronary
- B. Left anterior descending
- C. Left main stem
- D. Left circumflex
- E. Anterior interventricular

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Inferior MI - right coronary artery lesion

ECG: coronary territories

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	**Coronary artery**
Anteroseptal	V1-V4	Left anterior descending
Inferior	II, III, aVF	Right coronary
Anterolateral	V4-6, I, aVL	Left anterior descending or left circumflex
Lateral	I, aVL +/- V5-6	Left circumflex
Posterior	Tall R waves V1-2	Usually left circumflex, also right coronary

Question 27 of 220

A 55-year-old man is admitted to the Emergency Department with 'tearing' chest pain radiating through to his back. Examination reveals a pulse of 96 / min regular, blood pressure of 130/85 mmHg and oxygen saturations of 97% on room air. A chest x-ray shows mediastinal widening. A CT shows dissection of the ascending aorta. What is the most suitable initial management?

- A. IV sodium nitroprusside
- B. Oral verapamil
- C. Observe only
- D. IV labetalol
- E. Surgical repair

Question 27 of 220

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- B. Oral verapamil
- C. Observe only
- ✓ D. IV labetalol
- E. Surgical repair

Aortic dissection • type A - ascending aorta - control BP(IV labetalol) + surgery • type B - descending aorta - control BP(IV labetalol)

The question tests ability to apply textbook knowledge to real world situations. Whilst surgical referral should be made as soon as possible definite surgery will inevitably take time and the blood pressure should be controlled in the meantime

Aortic dissection: management

Classification
- type A - ascending aorta (2/3 of cases)
- type B - descending aorta, distal to left subclavian origin (1/3 of cases)

Type A
- surgical management, but blood pressure should be controlled to a target systolic of 100-120 mmHg whilst awaiting intervention

Type B*
- conservative management
- bed rest
- reduce blood pressure IV labetalol to prevent progression

*endovascular repair of type B aortic dissection may have a role in the future

Question 28 of 220

A 17-year-old female presents with recurrent attacks of collapse. These episodes typically occur without warning and have occurred whilst she was running for a bus. There is no significant past medical history and the only family history of note is that her father died suddenly when he was 38-years-old. What is the likely cause?

- A. Vaso-vagal attacks
- B. Anxiety
- C. Epilepsy
- D. Cardiac syncope
- E. Malingering

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- B. Anxiety
- C. Epilepsy
- ✓ D. Cardiac syncope
- E. Malingering

Sudden death, unusual collapse in young person - ? HOCM

This is a rather vague question. However, a family history of sudden death should make you think of conditions such as hypertrophic obstructive cardiomyopathy

HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Features
- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

Associations
- Friedreich's ataxia
- Wolff-Parkinson White

Echo
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)
- mitral regurgitation

ECG
- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Question 29 of 220

A 72-year-old man is investigated for exertional chest pain and has a positive exercise tolerance test. He declines an angiogram and is discharged on a combination of aspirin 75mg od, simvastatin 40mg on, atenolol 50mg od and a GTN spray prn. Examination reveals a pulse of 72 bpm and a blood pressure of 130/80 mmHg. On review he is still regularly using his GTN spray. What is the most appropriate next step in management?

- A. Add nifedipine MR 30mg od
- B. Add isosorbide mononitrate 30mg bd
- C. Increase atenolol to 100mg od
- D. Add nicorandil 10mg bd
- E. Add verapamil 80mg tds

Question 29 of 220

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- ✓ C. Increase atenolol to 100mg od
- D. Add nicorandil 10mg bd
- E. Add verapamil 80mg tds

The BNF recommends an atenolol dose of 100mg daily in 1 or 2 doses for angina. The starting dose of isosorbide mononitrate is 10mg bd.

Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery.

Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- beta-blocker is the preferred initial treatment. For patients unable to take a beta-blocker there is no clear guidelines on the best alternative. Options include a rate-limiting calcium-channel blocker (verapamil or diltiazem); a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine); a nitrate; or a potassium-channel activator
- if there is a poor response to initial treatment then the beta-blocker should be increased to the maximum tolerated dose (e.g. atenolol 100mg od)
- again, there is no clear guidelines on the next step treatment. CKS advise adding a long-acting dihydropyridine (e.g. nifedipine) although other options include isosorbide mononitrate and nicorandil

Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Question 30 of 220

A 37-year-old woman who was investigated for progressive shortness-of-breath is diagnosed with primary pulmonary hypertension and started on bosentan. What is the mechanism of action of bosentan?

- A. Activator of soluble guanylate cyclase
- B. Phosphodiesterase type 5 inhibitors
- C. Endothelin receptor antagonist
- D. Prostanoid
- E. Slow calcium channel blocker

Question 30 of 220

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- B. Phosphodiesterase type 5 inhibitors
- ✓ C. Endothelin receptor antagonist
- D. Prostanoid
- E. Slow calcium channel blocker

Bosentan - endothelin-1 receptor antagonist

Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)
- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

Features
- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

Management
- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

Question 31 of 220

A 45-year-old man is diagnosed with endocarditis of the aortic valve. He is treated with intravenous benzylpenicillin and gentamicin. What is the most important ECG change to monitor for?

- A. Left ventricular hypertrophy (by voltage criteria)
- B. Reflex tachycardia
- C. ST segment depression
- D. Prolonged QT interval
- E. Prolonged PR interval

Question 31 of 220

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- A. Left ventricular hypertrophy (by voltage criteria)
- B. Reflex tachycardia
- C. ST segment depression
- D. Prolonged QT interval
- ✓ E. Prolonged PR interval

A prolonged PR interval could indicate the development of an aortic abscess, an indication for surgery

ECG: PR interval

Causes of a prolonged PR interval

- idiopathic
- ischaemic heart disease
- digoxin toxicity
- hypokalaemia*
- rheumatic fever
- aortic root pathology e.g. abscess secondary to endocarditis
- Lyme disease
- sarcoidosis
- myotonic dystrophy

A prolonged PR interval may also be seen in athletes

*hyperkalaemia can rarely cause a prolonged PR interval, but this is a much less common association than hypokalaemia

Question 32 of 220

Which one of the following drugs causes shortening of the QT interval?

- A. Digoxin
- B. Sotalol
- C. Amiodarone
- D. Tricyclic antidepressants
- E. Chloroquine

Question 32 of 220

Which one of the following drugs causes shortening of the QT interval?

- ✓ A. Digoxin
- B. Sotalol
- C. Amiodarone
- D. Tricyclic antidepressants
- E. Chloroquine

Digoxin causes shortening of the QT interval whilst the other four drugs cause QT prolongation

Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

Mechanism of action
- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the Na^+/K^+ ATPase pump

Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

Features
- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors
- classically: hypokalaemia*
- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion)

Management
- Digibind
- correct arrhythmias
- monitor potassium

*hyperkalaemia may also worsen digoxin toxicity, although this is very small print

Question 33 of 220

A 65-year-old female with a known history of heart failure presents for an annual check-up. She is found to have a blood pressure of 170/100 mmHg. Her current medications are furosemide and aspirin. What is the most appropriate medication to add?

- A. Bendroflumethiazide
- B. Spironolactone
- C. Bisoprolol
- D. Verapamil
- E. Enalapril

Question 33 of 220

A 65-year-old female with a known history of heart failure presents for an annual check-up. She is found to have a blood pressure of 170/100 mmHg. Her current medications are furosemide and aspirin. What is the most appropriate medication to add?

- A. Bendroflumethiazide
- B. Spironolactone
- C. Bisoprolol
- D. Verapamil
- ✓ E. Enalapril

Both enalapril and spironolactone have been shown to improve prognosis in patients with heart failure. Enalapril however would also treat the hypertension. The SOLVD and CONSENSUS studies have demonstrated the benefit of enalapril in patients with heart failure. NICE guidelines recommend the introduction of an ACE inhibitor prior to a beta-blocker in patients with chronic heart failure

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:
- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:
- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off** pneumococcal vaccine

*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

**adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Question 34 of 220

A 60-year-old man is admitted with palpitations to the Emergency Department. An ECG on admission shows a broad complex tachycardia at a rate of 150 bpm. His blood pressure is 124/82 mmHg and there is no evidence of heart failure. Which one of the following is it least appropriate to give?

- A. Procainamide
- B. Lidocaine
- C. Synchronised DC shock
- D. Adenosine
- E. Verapamil

Question 34 of 220

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- D. Adenosine
- ✓ E. Verapamil

Ventricular tachycardia - verapamil is contraindicated

Verapamil should never be given to a patient with a broad complex tachycardia as it may precipitate ventricular fibrillation in patients with ventricular tachycardia. Adenosine is sometimes given in this situation as a 'trial' if there is a strong suspicion the underlying rhythm is a supraventricular tachycardia with aberrant conduction

Ventricular tachycardia: management

Whilst a broad complex tachycardia may result from a supraventricular rhythm with aberrant conduction, the European Resuscitation Council advise that in a peri-arrest situation it is assumed to be ventricular in origin

If the patient has adverse signs (systolic BP < 90 mmHg, chest pain, heart failure or rate > 150 beats/min) then immediate cardioversion is indicated. In the absence of such signs antiarrhythmics may be used. If these fail, then electrical cardioversion may be needed with synchronised DC shocks

Drug therapy
- amiodarone: ideally administered through a central line
- lidocaine: use with caution in severe left ventricular impairment
- procainamide

Verapamil should NOT be used in VT

If drug therapy fails
- electrophysiological study (EPS)
- implant able cardioverter-defibrillator (ICD) - this is particularly indicated in patients with significantly impaired LV function

Question 35 of 220

One of your patients who has a family history of Marfan's syndrome has recently been diagnosed with the condition. What is the most important investigation to monitor their condition?

- A. Urea and electrolytes
- B. Echocardiography
- C. Spirometry
- D. Electrocardiogram
- E. DEXA scan

Question 35 of 220

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Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 patients.

Features

- tall stature with arm span to height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Question 36 of 220

What is the most common cardiac defect seen in patients with Down's syndrome?

- A. Ventricular septal defect
- B. Endocardial cushion defect
- C. Secundum atrial septal defect
- D. Tetralogy of Fallot
- E. Patent ductus arteriosus

Question 36 of 220

What is the most common cardiac defect seen in patients with Down's syndrome?

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- ✓ B. Endocardial cushion defect
- C. Secundum atrial septal defect
- D. Tetralogy of Fallot
- E. Patent ductus arteriosus

Endocardial cushion defects account for about 40% of congenital heart disease seen in patients with Down's syndrome

Down syndrome: features

Clinical features
- face: upslanting palpebral fissures, epicanthic folds, Brushfield spots in iris, protruding tongue, small ears, round/flat face
- flat occiput
- single palmar crease, pronounced 'sandal gap' between big and first toe
- hypotonia
- congenital heart defects (40-50%, see below)
- duodenal atresia
- Hirschsprung's disease

Cardiac complications
- multiple cardiac problems may be present
- endocardial cushion defect (c. 40%, also known as atrioventricular septal canal defects)
- ventricular septal defect (c. 30%)
- secundum atrial septal defect (c. 10%)
- tetralogy of Fallot (c. 5%)
- isolated patent ductus arteriosus (c. 5%)

Later complications
- subfertility: males are almost always infertile due to impaired spermatogenesis. Females are usually subfertile, and have an increased incidence of problems with pregnancy and labour
- learning difficulties
- short stature
- repeated respiratory infections (+hearing impairment from glue ear)
- acute lymphoblastic leukaemia
- hypothyroidism
- Alzheimer's
- atlantoaxial instability

Question 37 of 220

Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

A. Fever > 38ºC

B. Positive molecular assays for specific gene targets

C. Indwelling central line

D. Elevated CRP

E. Janeway lesions

Question 37 of 220

Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

- A. Fever > 38ºC
- B. Positive molecular assays for specific gene targets
- ✓ C. Indwelling central line
- D. Elevated CRP
- E. Janeway lesions

The modified Duke criteria have now been adopted in the latest guidelines from the European Society of Cardiology. Details can be found in the link below

Infective endocarditis: Modified Duke criteria

Infective endocarditis diagnosed if
- pathological criteria positive, or
- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

Pathological criteria

Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments or intracardiac abscess content)

Major criteria

Positive blood cultures
- two positive blood cultures showing typical organisms consistent with infective endocarditis, such as *Streptococcus viridans* and the HACEK group, or
- persistent bacteraemia from two blood cultures taken > 12 hours apart or three or more positive blood cultures where the pathogen is less specific such as Staph aureus and Staph epidermidis, or
- positive serology for *Coxiella burnetii*, Bartonella species or *Chlamydia psittaci*, or
- positive molecular assays for specific gene targets

Evidence of endocardial involvement
- positive echocardiogram (oscillating structures, abscess formation, new valvular regurgitation or dehiscence of prosthetic valves), or
- new valvular regurgitation

Minor criteria
- predisposing heart condition or intravenous drug use
- microbiological evidence does not meet major criteria
- fever > 38ºC
- vascular phenomena: major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae or purpura
- immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots, Janeway lesions
- elevated ESR or CRP

Question 38 of 220

A 61-year-old woman is admitted to the Emergency Department with central chest pain. It feels like her previous angina but is not relieved by nitrates. She has a history of ischaemic heart disease and 4 weeks ago underwent a percutaneous coronary intervention during which a stent was placed. This is her first episode of angina since the procedure. What is the most likely diagnosis?

- A. Pericarditis
- B. Aortic dissection
- C. Coronary artery dissection
- D. Restenosis
- E. Stent thrombosis

Question 38 of 220

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- C. Coronary artery dissection
- D. Restenosis
- ✓ E. Stent thrombosis

Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

Question 39 of 220

A patient is reviewed in the cardiology clinic. During auscultation you hear paradoxical splitting of the second heart sound. Which one of the following conditions is most associated with this finding?

A. Atrial septal defect

B. Right bundle branch block

C. Deep inspiration

D. Left bundle branch block

E. Pulmonary stenosis

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- ✓ D. Left bundle branch block
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Second heart sound (S2)
- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

Paradoxical splitting is also known as reverse splitting.

Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2
- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2
- aortic stenosis

Causes of fixed split S2
- atrial septal defect

Causes of a widely split S2
- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)
- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

Question 40 of 220

Which one of the following would not be considered a normal variant on the ECG of an athletic 28-year-old man?

- A. Wenckebach phenomenon
- B. Sinus bradycardia
- C. Junctional rhythm
- D. First degree heart block
- E. LBBB

Question 40 of 220

Which one of the following would not be considered a normal variant on the ECG of an athletic 28-year-old man?

- A. Wenckebach phenomenon
- B. Sinus bradycardia
- C. Junctional rhythm
- D. First degree heart block
- ✓ E. LBBB

ECG: normal variants

The following ECG changes are considered normal variants in an athlete:

- sinus bradycardia
- junctional rhythm
- first degree heart block
- Wenckebach phenomenon

Question 41 of 220

A patient with severe aortic stenosis is noted to have a fourth heart sound. Which part of the ECG does this best correlate with?

- A. U wave
- B. QRS complex
- C. P wave
- D. ST segment
- E. T wave

Question 41 of 220

A patient with severe aortic stenosis is noted to have a fourth heart sound. Which part of the ECG does this best correlate with?

- A. U wave
- B. QRS complex
- ✓ C. P wave
- D. ST segment
- E. T wave

Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

S1
- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

S2
- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

S3
- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure, constrictive pericarditis

S4
- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Question 42 of 220

A 41-year-old man is admitted with left-sided pleuritic chest pain. He has a dry cough and reports that the pain is relieved by sitting forward. For the past three days he has been experiencing flu-like symptoms. Given the likely diagnosis, what is the most likely finding on ECG?

- A. Large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III
- B. Atrial fibrillation
- C. Widespread ST elevation
- D. ST segment depression in the anterior leads
- E. Hyperacute T waves

Question 42 of 220

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- ✓ C. Widespread ST elevation
- D. ST segment depression in the anterior leads
- E. Hyperacute T waves

Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

Features
- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

Causes
- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma
- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

ECG changes
- widespread 'saddle-shaped' ST elevation
- PR depression

Question 43 of 220

Which of the following is responsible for the plateau phase of the myocardial action potential?

- A. Slow calcium efflux
- B. Efflux of potassium
- C. Rapid sodium influx
- D. Slow influx of calcium
- E. Slow sodium efflux

Question 43 of 220

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Slow influx of calcium is responsible for the plateau phase of the action potential

Electrical activity of the heart

Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by Na^+/K^+ ATPase There is slow entry of Na^+ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles

Question 44 of 220

A 57-year-old man presents to the Emergency Department with palpitations for the past 36 hours. He has no past history of note. There is no associated chest pain or shortness of breath. Clinical examination is unremarkable other than an irregular tachycardia. An ECG shows atrial fibrillation at a rate of 126 bpm with no other changes. What is the most appropriate management?

- A. Beta-blocker + warfarin
- B. Immediate cardioversion in the Emergency Department
- C. Heparinise + transthoracic echo followed by electrical cardioversion during admission
- D. Beta-blocker + aspirin
- E. Warfarinise + transthoracic echo with elective electrical cardioversion in 4 weeks

Question 44 of 220

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- D. Beta-blocker + aspirin
- E. Warfarinise + transthoracic echo with elective electrical cardioversion in 4 weeks

This patient is a good example of someone who would benefit from electrical cardioversion.

Atrial fibrillation: cardioversion

Onset < 48 hours

If atrial fibrillation (AF) is of less than 48 hours onset patients should be heparinised and a transthoracic echocardiogram performed to exclude a thrombus. Following this patients may be cardioverted, either:

- electrical - 'DC cardioversion'
- pharmacology - amiodarone if structural heart disease, flecainide in those without structural heart disease

Following electrical cardioversion if AF is confirmed as being less than 48 hours duration then further anticoagulation is unnecessary

Onset > 48 hours

If AF is of greater than 48 hours then patients should have therapeutic anticoagulation for at least 3 weeks. If there is a high risk of cardioversion failure (e.g. Previous failure or AF recurrence) then it is recommend to have at least 4 weeks amiodarone or sotalol prior to electrical cardioversion

Following electrical cardioversion patients should be anticoagulated for at least 4 weeks. After this time decisions about anticoagulation should be taken on an individual basis depending on the risk of recurrence

Question 45 of 220

A 17-year-old male is taken to the Emergency Department due to alcohol intoxication. On examination he is noted to be tachycardic with a rate of 140bpm. An ECG shows atrial fibrillation. The following morning he is noted to be in sinus rhythm. What is the most appropriate management?

- A. Sotalol and aspirin
- B. Sotalol and warfarin
- C. Refer for accessory pathway ablation
- D. Amiodarone and aspirin
- E. Discharge

Question 45 of 220

A 17-year-old male is taken to the Emergency Department due to alcohol intoxication. On examination he is noted to be tachycardic with a rate of 140bpm. An ECG shows atrial fibrillation. The following morning he is noted to be in sinus rhythm. What is the most appropriate management?

- A. Sotalol and aspirin
- B. Sotalol and warfarin
- C. Refer for accessory pathway ablation
- D. Amiodarone and aspirin
- ✓ E. Discharge

Supraventricular arrhythmias secondary to acute alcohol intake are well characterised and have been termed 'holiday heart syndrome'. No specific treatment is required

Atrial fibrillation: classification

An attempt was made in the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines to simplify and clarify the classification of atrial fibrillation (AF).

It is recommended that AF be classified into 3 patterns:

- first detected episode (irrespective of whether it is symptomatic or self-terminating)
- recurrent episodes, when a patient has 2 or more episodes of AF. If episodes of AF terminate spontaneously then the term **paroxysmal AF** is used. Such episodes last less than 7 days (typically < 24 hours). If the arrhythmia is not self-terminating then the term **persistent AF** is used. Such episodes usually last greater than 7 days
- in **permanent AF** there is continuous atrial fibrillation which cannot be cardioverted or if attempts to do so are deemed inappropriate. Treatment goals are therefore rate control and anticoagulation if appropriate

Question 46 of 220

A 72-year-old man is admitted to the Emergency Department with chest pain. On initial assessment he is noted to be pale, have a heart rate of 40/min and a blood pressure of 90/60 mmHg. Which one of the coronary arteries is most likely to be affected?

- A. Posterior descending
- B. Left anterior descending
- C. Right coronary
- D. Anterior interventricular
- E. Left circumflex

Question 46 of 220

A 72-year-old man is admitted to the Emergency Department with chest pain. On initial assessment he is noted to be pale, have a heart rate of 40/min and a blood pressure of 90/60 mmHg. Which one of the coronary arteries is most likely to be affected?

- A. Posterior descending
- B. Left anterior descending
- ✓ C. Right coronary
- D. Anterior interventricular
- E. Left circumflex

This patient has developed complete heart block secondary to a right coronary artery (RCA) infarction. The atrioventricular node is supplied by the posterior interventricular artery, which in the majority of patients is a branch of the right coronary artery. In the remainder of patients the posterior interventricular artery is supplied by the left circumflex artery.

Complete heart block

Features
- syncope
- heart failure
- regular bradycardia (30-50 bpm)
- wide pulse pressure
- JVP: cannon waves in neck
- variable intensity ofS1

Question 47 of 220

Which one of the following conditions is most associated with a bisferiens pulse?

- A. Cardiac tamponade
- B. Severe left ventricular failure
- C. Aortic stenosis
- D. Patent ductus arteriosus
- E. Mixed aortic valve disease

Question 47 of 220

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Pulses

Pulsus parodoxus
- greater than the normal (10 mmHg) fall in systolic blood pressure during inspiration --> faint or absent pulse in inspiration
- severe asthma, cardiac tamponade

Slow-rising/plateau
- aortic stenosis

Collapsing
- aortic regurgitation
- patent ductus arteriosus
- hyperkinetic (anaemia, thyrotoxic, fever, exercise/pregnancy)

Pulsus alternans
- regular alternation of the force of the arterial pulse
- severe LVF

Bisferiens pulse
- 'double pulse' - two systolic peaks
- mixed aortic valve disease

'Jerky' pulse
- hypertrophic obstructive cardiomyopathy*

*HOCM may occasionally be associated with a bisferiens pulse

Question 48 of 220

A woman who is 34 weeks pregnant is admitted to the obstetric ward. She has been monitored for the past few weeks due to pregnancy-induced hypertension but has now developed proteinuria. Her blood pressure is 162/94 mmHg. Which one of the following antihypertensives is it most appropriate to commence?

- A. Moxonidine
- B. Atenolol
- C. Methyldopa
- D. Losartan
- E. Verapamil

Question 48 of 220

A woman who is 34 weeks pregnant is admitted to the obstetric ward. She has been monitored for the past few weeks due to pregnancy-induced hypertension but has now developed proteinuria. Her blood pressure is 162/94 mmHg. Which one of the following antihypertensives is it most appropriate to commence?

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Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m^2
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count < 100 * 10^6/l, abnormal liver enzymes or HELLP syndrome

Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral methyldopa is often used first-line with oral labetalol, nifedipine , hydralazine also being used
- for severe hypertension IV labetalol and IV hydralazine are used in addition to the above
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Question 49 of 220

A 35-year-old female presents with a deep vein thrombosis in the third trimester of pregnancy. Whilst in the Emergency Department she develops a left hemiparesis. What underlying cardiac abnormality is most likely to be responsible?

- A. Primum ASD
- B. Secundum ASD
- C. Patent foramen ovale
- D. VSD
- E. Patent ductus arteriosus

Question 49 of 220

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- D. VSD
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Whilst atrial septal defects may allow emboli to pass from the right side of the heart to the left side, the most common cause is a patent foramen ovale

Patent foramen ovale

Patent foramen ovale (PFO) is present in around 20% of the population. It may allow embolus (e.g. from DVT) to pass from right side of the heart to the left side leading to a stroke - 'a paradoxical embolus'

There also appears to be an association between migraine and PFO. Some studies have reported improvement in migraine symptoms following closure of the PFO

Question 50 of 220

Which one of the following statements regarding B-type natriuretic peptide is incorrect?

- A. Effective treatment for heart failure lowers a patients BNP level
- B. Acts as a diuretic
- C. A hormone produced mainly by the left ventricular myocardium in response to strain
- D. Is a good marker of prognosis in patients with chronic heart failure
- E. The positive predictive value of BNP is greater than the negative predictive value

Question 50 of 220

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- ✓ E. The positive predictive value of BNP is greater than the negative predictive value

BNP has a good negative predictive value rather than positive predictive value

B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

Clinical uses of BNP

Diagnosing patients with acute dyspnoea
- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

Prognosis in patients with chronic heart failure
- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure
- effective treatment lowers BNP levels

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 51 of 220

A 1-year-old girl is noted to have a continuous murmur, loudest at the left sternal edge. She is not cyanosed. A diagnosis of patent ductus arteriosus is suspected. What pulse abnormality is most associated with this condition?

- A. Collapsing pulse
- B. Bisferiens pulse
- C. Pulsus parodoxus
- D. 'Jerky' pulse
- E. Pulsus alternans

Question 51 of 220

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- ✓ A. Collapsing pulse
- B. Bisferiens pulse
- C. Pulsus parodoxus
- D. 'Jerky' pulse
- E. Pulsus alternans

Patent ductus arteriosus - collapsing pulse

Patent ductus arteriosus

Overview
- acyanotic congenital heart defect
- connection between the pulmonary trunk and descending aorta
- more common in premature babies, born at high altitude or maternal rubella infection in the first trimester

Features
- left subclavicular thrill
- continuous 'machinery' murmur
- large volume, collapsing pulse
- wide pulse pressure
- heaving apex beat

Management
- indomethacin closes the connection in the majority of cases
- if associated with another congenital heart defect amenable to surgery then prostaglandin E1 is useful to keep the duct open until after surgical repair

Question 52 of 220

A 79-year-old woman is reviewed. She has taken bendroflumethiazide 2.5mg od for the past 10 years for hypertension. Her current blood pressure is 150/94 mmHg. Clinical examination is otherwise unremarkable. An echocardiogram from two months ago is reported as follows:

Ejection fraction 48%, moderate left ventricular hypertrophy. Minimal MR noted

What is the most appropriate next step in management?

- A. Increase bendroflumethiazide to 5mg od
- B. Stop bendroflumethiazide + start frusemide 40mg od
- C. Add ramipril 1.25mg od
- D. Stop bendroflumethiazide + start ramipril 1.25mg od
- E. Add amlodipine 5mg od

Question 52 of 220

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- ✓ C. Add ramipril 1.25mg od
- D. Stop bendroflumethiazide + start ramipril 1.25mg od
- E. Add amlodipine 5mg od

The echocardiogram shows a degree of left ventricular impairment. It is important an ACE inhibitor is started in such patients. This will help to both control her blood pressure and also slow the deterioration in her cardiac function.

Hypertension: management

NICE published updated guidelines for the management of hypertension in June 2006

Initial drug choice
- patients < 55-years-old: ACE inhibitor
- patients > 55-years-old or of Afro-Caribbean origin: calcium channel blocker or thiazide diuretic

The target blood pressure is 140/90 mmHg. For diabetics the target is 140/80 mmHg (or 130/80 mmHg if end-organ damage is present)

If this fails to control the blood pressure then use a combination of an ACE inhibitor plus either a calcium channel blocker or thiazide diuretic

If this still fails then a combination of an ACE inhibitor + calcium channel blocker + thiazide diuretic should be used

Following this further diuretic therapy, alpha blockers or beta blockers should be considered

New drugs

Direct renin inhibitors
- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Question 53 of 220

A 50-year-old man is admitted to Resus with a suspected anterior myocardial infarction. An ECG on arrival confirms the diagnosis and thrombolysis is prepared. The patient is stable and his pain is well controlled with intravenous morphine. Clinical examination shows a blood pressure of 140/84 mmHg, pulse 90 bpm and oxygen saturations on room air of 97%. What is the most appropriate management with regards to oxygen therapy?

- A. 2-4 l/min via nasal cannulae
- B. No oxygen therapy
- C. 15 l/min via reservoir mask
- D. 28% via Venturi mask
- E. 35% via Venturi mask

Question 53 of 220

A 50-year-old man is admitted to Resus with a suspected anterior myocardial infarction. An ECG on arrival confirms the diagnosis and thrombolysis is prepared. The patient is stable and his pain is well controlled with intravenous morphine. Clinical examination shows a blood pressure of 140/84 mmHg, pulse 90 bpm and oxygen saturations on room air of 97%. What is the most appropriate management with regards to oxygen therapy?

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- ✓ B. No oxygen therapy
- C. 15 l/min via reservoir mask
- D. 28% via Venturi mask
- E. 35% via Venturi mask

Please see the note below and provided link - there are now specific guidelines relating to the use of oxygen in emergency situations.

Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive
- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

Antithrombin treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

Clopidogrel 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

Coronary angiography should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

Aspirin	Antiplatelet - inhibits the production of thromboxane A2
Clopidogrel	Antiplatelet - inhibits ADP binding to its platelet receptor
Enoxaparin	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Fondaparinux	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Bivalirudin	Reversible direct thrombin inhibitor

Question 54 of 220

An elderly man with aortic stenosis is assessed. Which one of the following would make the ejection systolic murmur quieter?

- A. Left ventricular systolic dysfunction
- B. Thyrotoxicosis
- C. Mixed aortic valve disease
- D. Expiration
- E. Anaemia

Question 54 of 220

An elderly man with aortic stenosis is assessed. Which one of the following would make the ejection systolic murmur quieter?

- ✓ A. Left ventricular systolic dysfunction
- B. Thyrotoxicosis
- C. Mixed aortic valve disease
- D. Expiration
- E. Anaemia

Left ventricular systolic dysfunction will result in a decreased flow-rate across the aortic valve and hence a quieter murmur.

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 55 of 220

A 25-year-old woman is brought to the Emergency Department by a friend. She developed palpitations around 30 minutes ago whilst drinking a cup of coffee. Her only past medical history of note is asthma and menorrhagia for which she uses a salbutamol inhaler and takes tranexamic acid respectively. The admission ECG shows a supraventricular tachycardia at a rate of 160 bpm. Vagal manoeuvres are unsuccessful. What is the most appropriate next step in her management?

- A. Intravenous verapamil
- B. Intravenous amiodarone
- C. Intravenous adenosine
- D. Electrical cardioversion
- E. Intravenous esmolol

Question 55 of 220

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- B. Intravenous amiodarone
- C. Intravenous adenosine
- D. Electrical cardioversion
- E. Intravenous esmolol

The administration of adenosine is contraindicated by her history of asthma. Verapamil should therefore be given.

Supraventricular tachycardia

Whilst strictly speaking the term supraventricular tachycardia (SVT) refers to any tachycardia that is not ventricular in origin the term is generally used in the context of paroxysmal SVT. Episodes are characterised by the sudden onset of a narrow complex tachycardia, typically an atrioventricular nodal re-entry tachycardia (AVNRT). Other causes include atrioventricular re-entry tachycardias (AVRT) and junctional tachycardias.

Acute management
- vagal manoeuvres: e.g. Valsalva manoeuvre
- intravenous adenosine: contraindicated in asthmatics - verapamil is a preferable option
- electrical cardioversion

Prevention of episodes
- beta-blockers
- radio-frequency ablation

Question 56 of 220

A 62-year-old man is referred from the Emergency Department with a pulse of 40 beats/min. Which one of the following factors carries the least risk of asystole when risk stratifying the patient?

A. Ventricular pause of 5 seconds

B. Recent asystole

C. Complete heart block with a narrow complex QRS

D. Mobitz type II AV block

E. Complete heart block with a broad complex QRS

Question 56 of 220

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- A. Ventricular pause of 5 seconds
- B. Recent asystole
- ✓ C. Complete heart block with a narrow complex QRS
- D. Mobitz type II AV block
- E. Complete heart block with a broad complex QRS

Complete heart block with a narrow complex QRS complex carries the least risk of asystole as the atrioventricular junctional pacemaker may provide an haemodynamically acceptable and stable heart rate. The other four factors are indications for transvenous pacing

Peri-arrest rhythms: bradycardia

The joint European Resuscitation Council and Resuscitation Council (UK) 2005 guidelines emphasise that the management of bradycardia depends on:

- 1. identifying the presence of signs indicating haemodynamic compromise - 'adverse signs'
- 2. identifying the potential risk of asystole

Adverse signs

The following factors indicate haemodynamic compromise and hence the need for treatment:

- heart rate < 40 bpm
- systolic blood pressure < 100 mmHg
- heart failure
- ventricular arrhythmias requiring suppression

Atropine is the first line treatment in this situation. If this fails to work, or there is the potential risk of asystole then transvenous pacing is indicated

Potential risk of asystole

The following indicate a potential risk of asystole and hence the need for treatment with transvenous pacing:

- complete heart block with broad complex QRS
- recent asystole
- Mobitz type II AV block
- ventricular pause > 3 seconds

If there is a delay in the provision of transvenous pacing the following interventions may be used:

- atropine, up to maximum of 3mg
- transcutaneous pacing
- adrenaline infusion titrated to response

Question 57 of 220

A 57-year-old man who had a prosthetic mitral valve replacement 7 years ago presents with fever. An urgent echocardiogram shows features consistent with endocarditis. What is the most suitable antibiotic therapy until blood culture results are known?

- A. IV ceftriaxone + benzylpenicillin
- B. IV vancomycin + rifampicin + gentamicin
- C. IV benzylpenicillin + gentamicin
- D. IV flucloxacillin + gentamicin
- E. IV vancomycin + benzylpenicillin

Question 57 of 220

A 57-year-old man who had a prosthetic mitral valve replacement 7 years ago presents with fever. An urgent echocardiogram shows features consistent with endocarditis. What is the most suitable antibiotic therapy until blood culture results are known?

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- ✓ B. IV vancomycin + rifampicin + gentamicin
- C. IV benzylpenicillin + gentamicin
- D. IV flucloxacillin + gentamicin
- E. IV vancomycin + benzylpenicillin

If the patient has a prosthetic valve and endocarditis is suspected the initial therapy should consist of intravenous vancomycin + rifampicin + gentamicin.

Infective endocarditis: prognosis and management

Poor prognostic factors
- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism
- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)
- initial blind therapy - flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
- initial blind therapy if prosthetic valve is present or patient is penicillin allergic - vancomycin + rifampicin + gentamicin
- endocarditis caused by staphylococci - flucloxacillin (vancomycin + rifampicin if penicillin allergic or MRSA)
- endocarditis caused by streptococci - benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

Indications for surgery
- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Question 58 of 220

A 54-year-old schizophrenic man is found to have torsade de pointes on his ECG recording. Blood pressure is 110/70 mmHg with a pulse of 170 bpm. What is the most appropriate management?

A. IV beta-blocker

B. IV verapamil

C. IV magnesium

D. IV amiodarone

E. Synchronised DC cardioversion

Question 58 of 220

A 54-year-old schizophrenic man is found to have torsade de pointes on his ECG recording. Blood pressure is 110/70 mmHg with a pulse of 170 bpm. What is the most appropriate management?

- A. IV beta-blocker
- B. IV verapamil
- ✓ C. IV magnesium
- D. IV amiodarone
- E. Synchronised DC cardioversion

The ALS guidelines make specific recommendations regarding the use of magnesium in torsade de pointes

Peri-arrest rhythms: tachycardia

The joint European Resuscitation Council and Resuscitation Council (UK) 2005 guidelines have simplified the advice given for the management of peri-arrest tachycardias. Separate algorithms for the management of broad-complex tachycardia, narrow complex tachycardia and atrial fibrillation have been replaced by one unified treatment algorithm

Following basic ABC assessment, patients are classified as being stable or unstable according to the presence of any adverse signs:

- systolic BP < 90 mmHg
- reduced conscious level
- chest pain
- heart failure

If any of the above adverse signs are present then synchronised DC shocks should be given

Treatment following this is given according to whether the QRS complex is narrow or broad and whether the rhythm is regular or irregular. The full treatment algorithm can be found at the Resuscitation Council website, below is a very limited summary:

Broad-complex tachycardia

Regular

- assume ventricular tachycardia (unless previously confirmed SVT with bundle branch block)
- loading dose of amiodarone followed by 24 hour infusion

Irregular

- 1. AF with bundle branch block - treat as for narrow complex tachycardia
- 2. Polymorphic VT (e.g. torsade de pointes) - IV magnesium

Narrow-complex tachycardia

Regular

- vagal manoeuvres followed by IV adenosine
- if above unsuccessful consider diagnosis of atrial flutter and control rate (e.g. beta-blockers)

Irregular

- probable atrial fibrillation
- if onset < 48 hr consider electrical or chemical cardioversion
- rate control (e.g. beta-blocker or digoxin) and anticoagulation

Question 59 of 220

Which of the following signs is not associated with the development of Eisenmenger's syndrome in a patient with a ventricular septal defect?

A. Worsening of systolic murmur

B. Raised JVP

C. Loud second heart sound

D. Cyanosis

E. Large 'a' waves in jugular venous waveform

Question 59 of 220

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- ✓ A. Worsening of systolic murmur
- B. Raised JVP
- C. Loud second heart sound
- D. Cyanosis
- E. Large 'a' waves in jugular venous waveform

Eisenmenger's syndrome is characterised by the reversal of the left-right shunt due to pulmonary hypertension. The original murmur may disappear once Eisenmenger's syndrome develops

Eisenmenger's syndrome

Describes the reversal of a left to right shunt in a congenital heart defect due to pulmonary hypertension

Associated with
- VSD
- ASD
- PDA

Features
- original murmur may disappear
- cyanosis
- clubbing
- right ventricular failure
- haemoptysis, embolism

Management
- heart-lung transplantation is required

Question 60 of 220

A 34-year-old man is seen in the cardiology clinic. He has been referred by his GP with a history of increasing dyspnoea and exercise-related syncope. His father died suddenly when at the age of 42-years-old. An ECG attached to the admission letter shows left ventricular hypertrophy with widespread T wave inversion. Given the likely diagnosis, what is the most appropriate next investigation?

- A. Cardiac angiogram
- B. Transthoracic echo
- C. Transoesophageal echo
- D. Exercise ECG
- E. 24-hour ECG

Question 60 of 220

A 34-year-old man is seen in the cardiology clinic. He has been referred by his GP with a history of increasing dyspnoea and exercise-related syncope. His father died suddenly when at the age of 42-years-old. An ECG attached to the admission letter shows left ventricular hypertrophy with widespread T wave inversion. Given the likely diagnosis, what is the most appropriate next investigation?

- A. Cardiac angiogram
- ✓ B. Transthoracic echo
- C. Transoesophageal echo
- D. Exercise ECG
- E. 24-hour ECG

The likely diagnosis is hypertrophic obstructive cardiomyopathy which should be investigated with a transthoracic echocardiogram

HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Features
- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

Associations
- Friedreich's ataxia
- Wolff-Parkinson White

Echo
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)
- mitral regurgitation

ECG
- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Question 61 of 220

An 82-year-old man is referred to cardiology by his GP with increasing dyspnoea or exertion and a systolic murmur. Examination demonstrates a blood pressure of 100/80 mmHg and a slow rising pulse. What is the most likely cause of his underlying condition?

- A. Bicuspid aortic valve
- B. Ventricular septal defect
- C. Post rheumatic fever
- D. Calcification of the aortic valve
- E. Hypertrophic obstructive cardiomyopathy

Question 61 of 220

An 82-year-old man is referred to cardiology by his GP with increasing dyspnoea or exertion and a systolic murmur. Examination demonstrates a blood pressure of 100/80 mmHg and a slow rising pulse. What is the most likely cause of his underlying condition?

- A. Bicuspid aortic valve
- B. Ventricular septal defect
- C. Post rheumatic fever
- ✓ D. Calcification of the aortic valve
- E. Hypertrophic obstructive cardiomyopathy

Aortic stenosis - most common cause:
- young patients: bicuspid aortic valve
- elderly patients: calcification

This patient has aortic stenosis.

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 62 of 220

Which part of the jugular venous waveform is associated with the closure of the tricuspid valve?

- A. a wave
- B. c wave
- C. x descent
- D. y descent
- E. v wave

Question 62 of 220

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- A. a wave
- ✓ B. c wave
- C. x descent
- D. y descent
- E. v wave

JVP: **C** wave - **c**losure of the tricuspid valve

The c wave of the jugular venous waveform is associated with the closure of the tricuspid valve

Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis

'a' wave = atrial contraction
- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves
- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave
- closure of tricuspid valve
- not normally visible

'v' wave
- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Question 63 of 220

Which one of the following complications is least associated with ventricular septal defects?

- A. Right heart failure
- B. Aortic regurgitation
- C. Eisenmenger's complex
- D. Infective endocarditis
- E. Atrial fibrillation

Question 63 of 220

Which one of the following complications is least associated with ventricular septal defects?

- A. Right heart failure
- B. Aortic regurgitation
- C. Eisenmenger's complex
- D. Infective endocarditis
- ✓ E. Atrial fibrillation

Atrial fibrillation is associated more with atrial septal defects

Ventricular septal defects

Ventricular septal defects are the most common cause of congenital heart disease. They close spontaneously in around 50% of cases. Non-congenital causes include post myocardial infarction

Features
- classically a pan-systolic murmur which is louder in smaller defects

Complications
- aortic regurgitation*
- infective endocarditis
- Eisenmenger's complex
- right heart failure

*aortic regurgitation is due to a poorly supported right coronary cusp resulting in cusp prolapse

Question 64 of 220

A 72-year-old man presents to the Emergency Department with a broad complex tachycardia. Which of the following features would make it more likely that this was due to a supraventricular tachycardia rather than a ventricular tachycardia?

- A. History of ischaemic heart disease
- B. Left axis deviation
- C. Capture beats
- D. Absence of QRS concordance in chest leads
- E. QRS complex greater than 160 ms

Question 64 of 220

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- A. History of ischaemic heart disease
- B. Left axis deviation
- C. Capture beats
- ✓ D. Absence of QRS concordance in chest leads
- E. QRS complex greater than 160 ms

Positive QRS concordance in the chest leads is associated with ventricular tachycardia

Broad complex tachycardia

Features suggesting VT rather than SVT with aberrant conduction

- AV dissociation
- fusion or capture beats
- positive QRS concordance in chest leads
- marked left axis deviation
- history of IHD
- lack of response to adenosine or carotid sinus massage
- QRS > 160 ms

Question 65 of 220

A 67-year-old man with a history of chronic obstructive pulmonary disease and ischaemic heart disease is taken to the Emergency Department with dyspnoea. On examination his respiratory rate is 24 / min, JVP is not elevated and crackles are heard in both lung bases. Which other finding would most strongly indicate that his dyspnoea is secondary to isolated left ventricular failure?

- A. Pulsus alternans
- B. Gallop rhythm
- C. Tachycardia
- D. Peripheral oedema
- E. Cardiomegaly on chest x-ray

Question 65 of 220

A 67-year-old man with a history of chronic obstructive pulmonary disease and ischaemic heart disease is taken to the Emergency Department with dyspnoea. On examination his respiratory rate is 24 / min, JVP is not elevated and crackles are heard in both lung bases. Which other finding would most strongly indicate that his dyspnoea is secondary to isolated left ventricular failure?

- A. Pulsus alternans
- ✓ B. Gallop rhythm
- C. Tachycardia
- D. Peripheral oedema
- E. Cardiomegaly on chest x-ray

Gallop rhythm (S3) is an early sign of LVF

Whilst all of the above features may be seen in patients with left ventricular failure a gallop rhythm is one of the most specific and early signs

Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

S1
- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

S2
- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

S3
- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure, constrictive pericarditis

S4
- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Question 66 of 220

Which one of the following is least associated with ST depression on ECG?

- A. Myocardial ischaemia
- B. Syndrome X
- C. Acute pericarditis
- D. Hypokalaemia
- E. Digoxin

Question 66 of 220

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- A. Myocardial ischaemia
- B. Syndrome X
- ✓ C. Acute pericarditis
- D. Hypokalaemia
- E. Digoxin

ECG: ST depression

Causes of ST depression

- normal if upward sloping
- ischaemia
- digoxin
- hypokalaemia
- syndrome X

Question 67 of 220

A 54-year-old man with angina has a percutaneous coronary intervention with insertion of a drug-eluting stent. What is the single most important risk factor for stent thrombosis?

A. Age of patient

B. Premature withdrawal of antiplatelet therapy

C. Failing to adhere to cardiac rehabilitation program

D. Duration of procedure

E. History of diabetes mellitus

Question 67 of 220

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- A. Age of patient
- ✓ B. Premature withdrawal of antiplatelet therapy
- C. Failing to adhere to cardiac rehabilitation program
- D. Duration of procedure
- E. History of diabetes mellitus

PCI: stent thrombosis - withdrawal of antiplatelets biggest risk factor

Diabetes mellitus is a risk factor for restenosis rather than stent thrombosis

Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

Question 68 of 220

Each one of the following is associated with atrial myxoma, except:

- A. Clubbing
- B. Mid-diastolic murmur
- C. Pyrexia
- D. 'J' wave on ECG
- E. Atrial fibrillation

Question 68 of 220

Each one of the following is associated with atrial myxoma, except:

- A. Clubbing
- B. Mid-diastolic murmur
- C. Pyrexia
- ✓ D. 'J' wave on ECG
- E. Atrial fibrillation

A 'J' wave is seen in hypothermia

Atrial myxoma

Overview
- 75% occur in left atrium
- more common in females

Features
- systemic: weight loss, fever, clubbing
- emboli
- atrial fibrillation
- mid-diastolic murmur, 'tumour plop'

Question 69 of 220

A patient with known heart failure has slight limitation of physical activity. She is comfortable at rest but housework results in fatigue, palpitations or dyspnoea. What New York Heart Association class best describes the severity of their disease?

- A. NYHA Class 0
- B. NYHA Class I
- C. NYHA Class II
- D. NYHA Class III
- E. NYHA Class IV

Question 69 of 220

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- A. NYHA Class 0
- B. NYHA Class I
- ✓ C. NYHA Class II
- D. NYHA Class III
- E. NYHA Class IV

Heart failure: NYHA classification

The New York Heart Association (NYHA) classification is widely used to classify the severity of heart failure:

NYHA Class I
- no symptoms
- no limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea or palpitations

NYHA Class II
- mild symptoms
- slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnoea

NYHA Class III
- moderate symptoms
- marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms

NYHA Class IV
- severe symptoms
- unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity

Question 70 of 220

A 62-year-old man is reviewed. His blood pressure is poorly controlled at 152/90 mmHg despite treatment with ramipril 10mg od, bendroflumethiazide 2.5mg od and amlodipine 10mg od. There is no other past medical history of note apart from benign prostatic hyperplasia. In addition to the antihypertensives he also takes aspirin and simvastatin. What is the most appropriate change to his medication?

- A. Add frusemide
- B. Increase ramipril to 20mg od
- C. Add doxazosin
- D. Add candesartan
- E. Add atenolol

Question 70 of 220

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- ✓ C. Add doxazosin
- D. Add candesartan
- E. Add atenolol

Looking at the NICE guidelines the main options here are further diuretic therapy, an alpha-blocker or a beta-blocker. Given his history of benign prostatic hyperplasia an alpha-blocker such as doxazosin seems a good choice.

Hypertension: management

NICE published updated guidelines for the management of hypertension in June 2006

Initial drug choice
- patients < 55-years-old: ACE inhibitor
- patients > 55-years-old or of Afro-Caribbean origin: calcium channel blocker or thiazide diuretic

The target blood pressure is 140/90 mmHg. For diabetics the target is 140/80 mmHg (or 130/80 mmHg if end-organ damage is present)

If this fails to control the blood pressure then use a combination of an ACE inhibitor plus either a calcium channel blocker or thiazide diuretic

If this still fails then a combination of an ACE inhibitor + calcium channel blocker + thiazide diuretic should be used

Following this further diuretic therapy, alpha blockers or beta blockers should be considered

New drugs

Direct renin inhibitors
- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Question 71 of 220

A 44-year-old female is investigated for suspected idiopathic pulmonary hypertension. Which one of the following is the best method for deciding upon management strategy?

- A. Genetic testing
- B. Acute vasodilator testing
- C. Trial of endothelin receptor antagonists
- D. Serial echocardiography
- E. Trial of calcium channel blockers

Question 71 of 220

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- E. Trial of calcium channel blockers

Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

Features
- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing
- oral calcium channel blockers

If there is a negative response to acute vasodilator testing
- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Question 72 of 220

Which one of the following is least associated with myocarditis?

- A. Chagas' disease
- B. Lyme disease
- C. Leishmaniasis
- D. Coxsackie virus
- E. Toxoplasmosis

Question 72 of 220

Which one of the following is least associated with myocarditis?

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- B. Lyme disease
- ✓ C. Leishmaniasis
- D. Coxsackie virus
- E. Toxoplasmosis

Myocarditis

Causes
- viral: coxsackie, HIV
- bacteria: diphtheria, clostridia
- spirochaetes: Lyme disease
- protozoa: Chagas' disease, toxoplasmosis
- autoimmune
- drugs

Presentation
- usually young patient with acute history
- chest pain, SOB,

Question 73 of 220

A 44-year-old man is seen in the cardiology clinic. For the past 6 months he has been experiencing episodes of palpitations associated with pre-syncopal symptoms. An ECG taken in clinic shows T wave inversion in leads V1-3 associated with a notch at the end of the QRS complex. He is known to have a family history of sudden cardiac death. What is the most likely diagnosis?

- A. Arrhythmogenic right ventricular cardiomyopathy
- B. Catecholaminergic polymorphic ventricular tachycardia
- C. Hypertrophic obstructive cardiomyopathy
- D. Long QT syndrome
- E. Brugada syndrome

Question 73 of 220

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- D. Long QT syndrome
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The notch at the end of the QRS complex is referred to as an epsilon wave.

Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a form of inherited cardiovascular disease which may present with syncope or sudden cardiac death. It is generally regarded as the second most common cause of sudden cardiac death in the young after hypertrophic cardiomyopathy.

Pathophysiology
- inherited in an autosomal dominant pattern with variable expression
- the right ventricular myocardium is replaced by fibrofatty tissue

Presentation
- palpitations
- syncope
- sudden cardiac death

Investigation
- ECG abnormalities in V1-3, typically T wave inversion. An epsilon wave is found in about 50% of those with ARV - this is best described as a terminal notch in the QRS complex
- echo changes are often subtle in the early stages but may show an enlarged, hypokinetic right ventricle with a thin free wall
- magnetic resonance imaging is useful to show fibrofatty tissue

Management
- drugs: sotalol is the most widely used antiarrhythmic
- catheter ablation to prevent ventricular tachycardia
- implantable cardioverter-defibrillator

Naxos disease
- an autosomal recessive variant of ARVC
- a triad of ARVC, palmoplantar keratosis, and woolly hair

Question 74 of 220

A 64-year-old man who is known to have ischaemic heart disease is due to start a chemotherapy regime which includes doxorubicin. His cardiologist wants to accurately assess his left ventricular function as he is concerned the doxorubicin may damage his myocardium. Which one of the following is the most accurate method to determine his left ventricular function?

- A. Cardiac computed tomography
- B. Echocardiography
- C. Exercise ECG
- D. MUGA scan
- E. Coronary angiography

Question 74 of 220

A 64-year-old man who is known to have ischaemic heart disease is due to start a chemotherapy regime which includes doxorubicin. His cardiologist wants to accurately assess his left ventricular function as he is concerned the doxorubicin may damage his myocardium. Which one of the following is the most accurate method to determine his left ventricular function?

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Cardiac imaging: non-invasive techniques excluding echocardiography

The ability to image the heart using non-invasive techniques such as MRI, CT and radionuclides has evolved rapidly over recent years.

Nuclear imaging

These techniques use radiotracers which are extracted by normal myocardium. Examples include:

- thallium
- technetium (99mTc) sestamibi: a coordination complex of the radioisotope technetium-99m with the ligand methoxyisobutyl isonitrile (MIBI), used in 'MIBI' or cardiac Single Photon Emission Computed Tomography (SPECT) scans
- fluorodeoxyglucose (FDG): used in Positron Emission Tomography (PET) scans

The primary role of SPECT is to assess myocardial perfusion and myocardial viability. Two sets of images are usually acquired. First the myocardium at rest followed by images of the myocardium during stress (either exercise or following adenosine / dipyridamole). By comparing the rest with stress images any areas of ischaemia can classified as reversible or fixed (e.g. Following a myocardial infarction). Cardiac PET is predominately a research tool at the current time

MUGA

- Multi Gated Acquisition Scan, also known as radionuclide angiography
- radionuclide (technetium-99m) is injected intravenously
- the patient is placed under a gamma camera
- may be performed as a stress test
- can accurately measure left ventricular ejection fraction. Typically used before and after cardiotoxic drugs are used

Cardiac Computed Tomography (CT)

Cardiac CT is useful for assessing suspected ischaemic heart disease, using two main methods:

- calcium score: there is known to be a correlation between the amount of atherosclerotic plaque calcium and the risk of future ischaemic events. Cardiac CT can quantify the amount of calcium producing a 'calcium score'
- contrast enhanced CT: allows visualisation of the coronary artery lumen

If these two techniques are combined cardiac CT has a very high negative predictive value for ischaemic heart disease.

Cardiac MRI

Cardiac MRI (commonly termed CMR) has become the gold standard for providing structural images of the heart. It is particularly useful when assessing congenital heart disease, determining right and left ventricular mass and differentiating forms of cardiomyopathy. Myocardial perfusion can also be assessed following the administration of gadolinium. Currently CMR provides limited data on the extent of coronary artery disease.

Question 75 of 220

A 51-year-old female presents to the Emergency Department following an episode of transient right sided weakness lasting 10-15 minutes. Examination reveals the patient to be in atrial fibrillation. If the patient remains in chronic atrial fibrillation what is the most suitable form of anticoagulation?

- A. Aspirin
- B. Warfarin, target INR 2-3
- C. No anticoagulation
- D. Warfarin, target INR 3-4
- E. Warfarin, target INR 2-3 for six months then aspirin

Question 75 of 220

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- E. Warfarin, target INR 2-3 for six months then aspirin

Atrial fibrillation: anticoagulation

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006

The guidelines suggest a stroke risk stratification approach when determining how to anticoagulate a patient, as detailed below:

Low risk - annual risk of stroke = 1% • age < 65 years with no moderate or high risk factors • use aspirin	**Moderate risk** - annual risk of stroke = 4% • age > 65 years with no high risk factors, or: • age < 75 years with diabetes, hypertension or cardiovascular disease • use aspirin or warfarin depending on individual circumstances	**High risk** - annual risk of stroke = 8-12% • age > 75 years with diabetes, hypertension or cardiovascular disease • previous TIA, ischaemic stroke or thromboembolic event • valve disease, heart failure or impaired left ventricular function • use warfarin

An alternative approach is the **CHADS2** score:

	Condition	**Points**
C	Congestive heart failure	1
H	Hypertension (or treated hypertension)	1
A	Age > 75 years	1
D	Diabetes	1
S2	Prior Stroke or TIA	2

The table below shows a suggested anticoagulation strategy based on the score:

Score	**Anticoagulation**
0	Aspirin
1	Aspirin or warfarin, depending on patient preference and individual factors
2-6	Warfarin if not contraindicated

Question 76 of 220

Which of the following is least associated with mitral valve prolapse?

- A. Osteogenesis imperfecta
- B. Pseudoxanthoma elasticum
- C. Turner's syndrome
- D. Marfan's syndrome
- E. Acromegaly

Question 76 of 220

Which of the following is least associated with mitral valve prolapse?

- A. Osteogenesis imperfecta
- B. Pseudoxanthoma elasticum
- C. Turner's syndrome
- D. Marfan's syndrome
- ✓ E. Acromegaly

Whilst some patients with acromegaly have mitral valve prolapse (MVP) it is not a common association. It should be remembered that the prevalence of MVP in a standard population is around 5-10%

Mitral valve prolapse

Mitral valve prolapse is common, occurring in around 5-10 % of the population. It is usually idiopathic but may be associated with a wide variety of cardiovascular disease and other conditions

Associations

- congenital heart disease: PDA, ASD
- cardiomyopathy
- Turner's syndrome
- Marfan's syndrome, Fragile X
- osteogenesis imperfecta
- pseudoxanthoma elasticum
- Wolff-Parkinson White syndrome
- long-QT syndrome
- Ehlers-Danlos Syndrome
- polycystic kidney disease

Features

- patients may complain of atypical chest pain or palpitations
- mid-systolic click (occurs later if patient squatting)
- late systolic murmur (longer if patient standing)
- complications: mitral regurgitation, arrhythmias (including long QT), emboli, sudden death

Question 77 of 220

Each one of the following physiological changes occur during exercise, except:

- A. Increased myocardial contractibility
- B. 50% increase in stroke volume
- C. Up to 3-fold increase in heart rate
- D. Rise in diastolic blood pressure
- E. Venous constriction

Question 77 of 220

Each one of the following physiological changes occur during exercise, except:

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Exercise: physiological changes

Blood pressure
- systolic increases, diastolic decreases
- leads to increased pulse pressure
- in healthy young people the increase in MABP is only slight

Cardiac output
- increase in cardiac output may be 3-5 fold
- results from venous constriction, vasodilation and increased myocardial contractibility, as well as from the maintenance of right atrial pressure by an increase in venous return
- heart rate up to 3-fold increase
- stroke volume up to 1.5-fold increase

Question 78 of 220

A 64-year-old man is admitted to the Emergency Department with chest pain radiating through to his back. On examination pulse 90 regular, BP 140/90. A CXR shows mediastinal widening. A CT shows dissection of the descending aorta. What is the most suitable initial management?

- A. Observe only
- B. IV labetalol
- C. IV sodium nitroprusside
- D. Immediate surgical referral
- E. Oral verapamil

Question 78 of 220

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- C. IV sodium nitroprusside
- D. Immediate surgical referral
- E. Oral verapamil

Aortic dissection
- type A - ascending aorta - control BP(IV labetalol) + surgery
- type B - descending aorta - control BP(IV labetalol)

Dissection of the descending aorta indicates a type B dissection, which should be managed medically with IV labetalol

Aortic dissection: management

Classification
- type A - ascending aorta (2/3 of cases)
- type B - descending aorta, distal to left subclavian origin (1/3 of cases)

Type A
- surgical management, but blood pressure should be controlled to a target systolic of 100-120 mmHg whilst awaiting intervention

Type B*
- conservative management
- bed rest
- reduce blood pressure IV labetalol to prevent progression

*endovascular repair of type B aortic dissection may have a role in the future

Question 79 of 220

Which one of the following is least likely to cause dilated cardiomyopathy?

- A. Wilson's disease
- B. Haemochromatosis
- C. Coxsackie A
- D. Hypertension
- E. Alcohol

Question 79 of 220

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Haemochromatosis is more commonly associated with restrictive cardiomyopathy but a dilated pattern may also be seen. There is a known association between Wilson's disease and cardiomyopathy but this is extremely rare and not often clinically significant

Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) basics
- dilated heart leading to systolic (+/- diastolic) dysfunction
- all 4 chambers affected but LV more so than RV
- features include arrhythmias, emboli, mitral regurgitation
- absence of congenital, valvular or ischaemic heart disease

Causes often considered separate entities
- alcohol: may improve with thiamine
- postpartum
- hypertension

Other causes
- inherited (see below)
- infections e.g. Coxsackie A and B, HIV, diphtheria, parasitic
- endocrine e.g. Hyperthyroidism
- infiltrative* e.g. Haemochromatosis, sarcoidosis
- neuromuscular e.g. Duchenne muscular dystrophy
- nutritional e.g. Kwashiorkor, pellagra, thiamine/selenium deficiency
- drugs e.g. Doxorubicin

Inherited dilated cardiomyopathy
- around a third of patients with DCM are thought to have a genetic predisposition
- a large number of heterogeneous defects have been identified
- the majority of defects are inherited in an autosomal dominant fashion although other patterns of inheritance are seen

*these causes may also lead to restrictive cardiomyopathy

Question 80 of 220

A 62-year-old female with a history of mitral regurgitation attends her dentist, who intends to perform dental polishing. She is known to be penicillin allergic. What prophylaxis against infective endocarditis should be given?

- A. Oral doxycycline
- B. Oral erythromycin
- C. No antibiotic prophylaxis needed
- D. Oral ofloxacin
- E. Oral clindamycin

Question 80 of 220

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The 2008 NICE guidelines have fundamentally changed the approach to infective endocarditis prophylaxis. What is not yet clear is if there are any circumstances in which NICE would recommend using antibiotic prophylaxis

Infective endocarditis: prophylaxis

The 2008 guidelines from NICE have radically changed the list of procedures for which antibiotic prophylaxis is recommended

NICE recommends the following procedures do not require prophylaxis:

- dental procedures
- upper and lower gastrointestinal tract procedures
- genitourinary tract; this includes urological, gynaecological and obstetric procedures and childbirth
- upper and lower respiratory tract; this includes ear, nose and throat procedures and bronchoscopy

The guidelines do however suggest:

- any episodes of infection in people at risk of infective endocarditis should be investigated and treated promptly to reduce the risk of endocarditis developing
- if a person at risk of infective endocarditis is receiving antimicrobial therapy because they are undergoing a gastrointestinal or genitourinary procedure at a site where there is a suspected infection they should be given an antibiotic that covers organisms that cause infective endocarditis

Question 81 of 220

A 23-year-old man with a family history of sudden cardiac death is diagnosed as having hypertrophic obstructive cardiomyopathy. Which one of the following is the strongest marker of poor prognosis?

- A. Mitral regurgitation
- B. Apical hypertrophy
- C. Systolic anterior motion of the anterior mitral valve leaflet
- D. Septal wall thickness of > 3cm
- E. Asymmetric hypertrophy

Question 81 of 220

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- C. Systolic anterior motion of the anterior mitral valve leaflet
- ✓ D. Septal wall thickness of > 3cm
- E. Asymmetric hypertrophy

HOCM - poor prognostic factor on echo = septal wall thickness of > 3cm

HOCM: prognostic factors

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

Question 82 of 220

Which one of the following conditions is most associated with aortic dissection?

- A. Acromegaly
- B. Actinomycosis
- C. Sarcoidosis
- D. Bicuspid aortic valve
- E. Adult polycystic kidney disease

Question 82 of 220

Which one of the following conditions is most associated with aortic dissection?

- A. Acromegaly
- B. Actinomycosis
- C. Sarcoidosis
- ✓ D. Bicuspid aortic valve
- E. Adult polycystic kidney disease

A bicuspid aortic valve increases the risk of aortic dissection six-fold

Aortic dissection

Aortic dissection may be classified as type A or B:
- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

Associations
- hypertension
- trauma
- bicuspid aortic valve
- collagens: Marfan's syndrome, Ehlers-Danlos syndrome
- Turner's and Noonan's syndrome
- pregnancy
- syphilis

Complications of backward tear
- aortic incompetence/regurgitation
- MI: inferior pattern often seen due to right coronary involvement

Complications of forward tear
- unequal arm pulses and BP
- stroke
- renal failure

Question 83 of 220

You are called to assess a man who has collapsed in the clinic waiting room. A staff nurse has already bleeped the cardiac arrest team. On arrival the man is laid on his back. You open the airway with a head-tilt chin lift - after assessing for 10 seconds there are no signs of breathing. What is the most appropriate next step?

- A. Start chest compressions at a ratio of 15:2
- B. Place in the recovery position
- C. Check for a carotid pulse for 10 seconds
- D. Give 2 rescue breaths
- E. Start chest compressions at a ratio of 30:2

Question 83 of 220

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- B. Place in the recovery position
- C. Check for a carotid pulse for 10 seconds
- D. Give 2 rescue breaths
- ✓ E. Start chest compressions at a ratio of 30:2

The 2005 guidelines removed the concept of 'checking for circulation'; absence of breathing, in a non-responsive individual, is now used as the main sign of cardiac arrest. In reality most medical professionals will check for a carotid pulse whilst assessing breathing, but in this scenario to wait a further 10 seconds before starting chest compressions is not justifiable. Please see the link to the BLS guidelines

Adult advanced life support

The joint European Resuscitation Council and Resuscitation Council (UK) 2005 guidelines propose radical changes in the provision of advanced life support (ALS)

Major changes include

- 2 initial 'rescue breaths' are no longer given
- ratio of chest compressions to ventilation changed from 15:2 to 30:2
- a single shock for VF/pulseless VT followed by 2 minutes of CPR, rather than a series of 3 shocks followed by 1 minute of CPR
- asystole/pulseless-electrical activity should be treated with 2 minutes of CPR, rather than 3, prior to reassessment of the rhythm

Question 84 of 220

A 62-year-old man is admitted to hospital following a myocardial infarction. Four days after admission he develops a further episode of central crushing chest pain. Which is the best cardiac marker to investigate his chest pain?

- A. LDH
- B. Troponin I
- C. Troponin T
- D. CK-MB
- E. AST

Question 84 of 220

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- B. Troponin I
- C. Troponin T
- ✓ D. CK-MB
- E. AST

By day four the CK-MB levels should have returned to normal from the initial myocardial infarction. If the CK-MB levels are elevated it would indicate a further coronary event

Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superceded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	**Peak value**	**Returns to normal**
Myoglobin	1-2 hours	6-8 hours	1-2 days
CK-MB	2-6 hours	16-20 hours	2-3 days
CK	4-8 hours	16-24 hours	3-4 days
Trop T	4-6 hours	12-24 hours	7-10 days
AST	12-24 hours	36-48 hours	3-4 days
LDH	24-48 hours	72 hours	8-10 days

Question 85 of 220

Which of the following congenital heart defects is associated with a bicuspid aortic valve

- A. Tetralogy of Fallot
- B. Ventricular septal defect
- C. Atrial septal defect
- D. Coarctation of the aorta
- E. Transposition of the great arteries

Question 85 of 220

Which of the following congenital heart defects is associated with a bicuspid aortic valve

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- B. Ventricular septal defect
- C. Atrial septal defect
- ✓ D. Coarctation of the aorta
- E. Transposition of the great arteries

Bicuspid aortic valve

Overview
- occurs in 1-2% of the population
- usually asymptomatic in childhood
- the majority eventually develop aortic stenosis or regurgitation
- associated with a left dominant coronary circulation (the posterior descending artery arises from the circumflex instead of the right coronary artery) and Turner's syndrome
- around 5% of patients also have coarctation of the aorta

Complications
- aortic stenosis/regurgitation as above
- higher risk for aortic dissection and aneurysm formation of the ascending aorta

Question 86 of 220

A 52-year-old man with no significant past medical history is admitted to the Emergency Department with chest pain. His admission ECG shows anterior T wave inversion. On examination his blood pressure is 120/82 mmHg, pulse 90 / min and oxygen saturations are 97% on room air. He is now pain free. You calculate his 6 month mortality using GRACE to be 1.0%. What initial therapy should be given?

- A. Oxygen + aspirin + enoxaparin
- B. Aspirin + enoxaparin
- C. Oxygen + aspirin + clopidogrel + enoxaparin
- D. Aspirin + fondaparinux
- E. Aspirin

Question 86 of 220

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- C. Oxygen + aspirin + clopidogrel + enoxaparin
- ✓ D. Aspirin + fondaparinux
- E. Aspirin

Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive
- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

Antithrombin treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

Clopidogrel 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

Coronary angiography should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

Aspirin	Antiplatelet - inhibits the production of thromboxane A2
Clopidogrel	Antiplatelet - inhibits ADP binding to its platelet receptor
Enoxaparin	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Fondaparinux	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Bivalirudin	Reversible direct thrombin inhibitor

Question 87 of 220

A 28-year-old man with hypertrophic obstructive cardiomyopathy is investigated for palpitations. A 24 hour ECG reveals runs of non-sustained ventricular tachycardia. What is the most appropriate management?

- A. AV node ablation
- B. Accessory pathway ablation
- C. Amiodarone
- D. Implantable cardioverter defibrillator
- E. Sotalol

Question 87 of 220

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- C. Amiodarone
- ✓ D. Implantable cardioverter defibrillator
- E. Sotalol

Most cardiologists would now proceed to inserting an implantable cardioverter defibrillator to lower the risk of sudden cardiac death

HOCM: management

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Management
- **A**miodarone
- **B**eta-blockers or verapamil for symptoms
- **C**ardioverter defibrillator
- **D**ual chamber pacemaker
- **E**ndocarditis prophylaxis*

Drugs to avoid
- nitrates
- ACE-inhibitors
- inotropes

*although see the 2008 NICE guidelines on infective endocarditis prophylaxis

Question 88 of 220

You are called to the coronary care unit. A patient who has been admitted following a myocardial infarction has developed a broad complex tachycardia. You suspect a diagnosis of ventricular tachycardia. Which one of the following factors may have precipitated this?

- A. Hypoglycaemia
- B. Bisoprolol
- C. Hypomagnesaemia
- D. Dehydration
- E. Hyperkalaemia

Question 88 of 220

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- B. Bisoprolol
- ✓ C. Hypomagnesaemia
- D. Dehydration
- E. Hyperkalaemia

Ventricular tachycardia

Ventricular tachycardia (VT)is broad-complex tachycardia originating from a ventricular ectopic focus. It has the potential to precipitate ventricular fibrillation and hence requires urgent treatment.

There are two main types of VT:

- monomorphic VT: most commonly caused by myocardial infarction
- polymorphic VT: A subtype of polymorphic VT is torsades de pointes which is precipitated by prolongation of the QT interval. The causes of a long QT interval are listed below

Causes of a prolonged QT interval

Congenital	**Drugs**	**Other**
• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel) • Romano-Ward syndrome (no deafness)	• amiodarone, sotalol, class 1a antiarrhythmic drugs • tricyclic antidepressants, fluoxetine • chloroquine • terfenadine* • erythromycin	• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia • acute myocardial infarction • myocarditis • hypothermia • subarachnoid haemorrhage

Question 89 of 220

A 61-year-old woman who is normally fit and well is admitted with chest pain. An ECG shows anterolateral T wave inversion. The troponin T value at 12 hours is 0.54. On discharge her medications include aspirin, atorvastatin, bisoprolol and ramipril. Which one of the following statements best describes the role of clopidogrel in this situation?

- A. Is only given if aspirin is contraindicated
- B. Should be prescribed for life for patients < 65 years old
- C. Should be prescribed for the next 12 months for patients who have a 6 month mortality risk of greater than 1.5%
- D. Should be prescribed for the next 12 months for patients < 65 years old
- E. Should be prescribed for the next 12 months for patients who have a 12 month mortality risk of greater than 5%

Question 89 of 220

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- D. Should be prescribed for the next 12 months for patients < 65 years old
- E. Should be prescribed for the next 12 months for patients who have a 12 month mortality risk of greater than 5%

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:
- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

Please see the 2010 NICE unstable angina and NSTEMI guidelines for more details. The 6 month mortality may be calculated using a risk model such as GRACE.

Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:
- ACE inhibitor
- beta-blocker
- aspirin
- statin

Clopidogrel
- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk is > 1.5%

Aldosterone antagonists
- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

Question 90 of 220

How long should a patient stop driving for following an elective cardiac angioplasty?

- A. No restriction
- B. 1 week
- C. 2 weeks
- D. 4 weeks
- E. 8 weeks

Question 90 of 220

How long should a patient stop driving for following an elective cardiac angioplasty?

- A. No restriction
- ✓ B. 1 week
- C. 2 weeks
- D. 4 weeks
- E. 8 weeks

DVLA advice following angioplasty - cannot drive for 1 week

The April 2009 AKT feedback report made specific mention of fitness to drive rules.

DVLA: cardiovascular disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- angioplasty (elective) - 1 week off driving
- CABG - 4 weeks off driving
- acute coronary syndrome- 4 weeks off driving, 1 week if successfully treated by angioplasty
- angina - driving must cease if symptoms occur at rest/at the wheel
- pacemaker insertion - 1 week off driving
- implantable cardioverter-defibrillator: if implanted for sustained ventricular arrhythmia: cease driving for 6 months. If implanted prophylatically then cease driving for 1 month
- successful catheter ablation - 2 days off driving
- aortic aneurysm of 6cm or more - notify DVLA. Licensing will be permitted subject to annual review. An aortic diameter of 6.5 cm or more disqualifies patients from driving
- heart transplant: DVLA do not need to be notified

Question 91 of 220

You are asked to urgently review a 61-year-old female on the cardiology ward due to difficulty in breathing. On examination she has a raised JVP with bilateral fine crackles to the mid zones. Blood pressure is 100/60 mmHg and the pulse is 140-150 and irregular. ECG confirms atrial fibrillation. What is the most appropriate management?

- A. IV amiodarone
- B. IV digoxin
- C. Urgent synchronised DC cardioversion
- D. Oral digoxin
- E. IV flecainide

Question 91 of 220

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- A. IV amiodarone
- B. IV digoxin
- ✓ C. Urgent synchronised DC cardioversion
- D. Oral digoxin
- E. IV flecainide

Heart failure is one of the adverse signs indicating the need for urgent synchronised DC cardioversion

Peri-arrest rhythms: tachycardia

The joint European Resuscitation Council and Resuscitation Council (UK) 2005 guidelines have simplified the advice given for the management of peri-arrest tachycardias. Separate algorithms for the management of broad-complex tachycardia, narrow complex tachycardia and atrial fibrillation have been replaced by one unified treatment algorithm

Following basic ABC assessment, patients are classified as being stable or unstable according to the presence of any adverse signs:

- systolic BP < 90 mmHg
- reduced conscious level
- chest pain
- heart failure

If any of the above adverse signs are present then synchronised DC shocks should be given

Treatment following this is given according to whether the QRS complex is narrow or broad and whether the rhythm is regular or irregular. The full treatment algorithm can be found at the Resuscitation Council website, below is a very limited summary:

Broad-complex tachycardia
Regular

- assume ventricular tachycardia (unless previously confirmed SVT with bundle branch block)
- loading dose of amiodarone followed by 24 hour infusion

Irregular

- 1. AF with bundle branch block - treat as for narrow complex tachycardia
- 2. Polymorphic VT (e.g. torsade de pointes) - IV magnesium

Narrow-complex tachycardia
Regular

- vagal manoeuvres followed by IV adenosine
- if above unsuccessful consider diagnosis of atrial flutter and control rate (e.g. beta-blockers)

Irregular

- probable atrial fibrillation
- if onset < 48 hr consider electrical or chemical cardioversion
- rate control (e.g. beta-blocker or digoxin) and anticoagulation

Question 92 of 220

A 71-year-old woman is admitted with acute dyspnoea to the Emergency Department. Oxygen saturations are 94% on 28% supplementary oxygen and her respiratory rate is 30/min. A rapid B-type natriuretic peptide (BNP) assay is reported as follows:

BNP 62 pg/ml

What is the best interpretation of this result?

- A. No conclusion can be drawn from this result
- B. Pulmonary embolism is the most likely cause of her symptoms
- C. If a further BNP level is above 50 pg/ml after one hour then this is diagnostic of heart failure
- D. Heart failure is unlikely to be the cause of her dyspnoea
- E. Heart failure is highly likely to be the cause of her dyspnoea

Question 92 of 220

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- E. Heart failure is highly likely to be the cause of her dyspnoea

B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

Clinical uses of BNP

Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

Screening for cardiac dysfunction

- not currently recommended for population screening

Question 93 of 220

Which part of the jugular venous waveform may be exaggerated in tricuspid regurgitation?

- A. x descent
- B. v wave
- C. y descent
- D. a wave
- E. c wave

Question 93 of 220

Which part of the jugular venous waveform may be exaggerated in tricuspid regurgitation?

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- ✓ B. v wave
- C. y descent
- D. a wave
- E. c wave

JVP: giant v waves in tricuspid regurgitation

Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis

'a' wave = atrial contraction
- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves
- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave
- closure of tricuspid valve
- not normally visible

'v' wave
- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Question 94 of 220

Which one of the following types of hyperlipidaemia are palmar crease xanthoma most commonly associated with?

- A. Familial combined hyperlipidaemia
- B. Lipoprotein lipase deficiency
- C. Familial hypertriglyceridaemia
- D. Remnant hyperlipidaemia
- E. Familial hypercholesterolaemia

Question 94 of 220

Which one of the following types of hyperlipidaemia are palmar crease xanthoma most commonly associated with?

- A. Familial combined hyperlipidaemia
- B. Lipoprotein lipase deficiency
- C. Familial hypertriglyceridaemia
- ✓ D. Remnant hyperlipidaemia
- E. Familial hypercholesterolaemia

Palmar crease xanthoma are most strongly associated with remnant hyperlipidaemia

Hyperlipidaemia: xanthomata

Characteristic xanthomata seen in hyperlipidaemia:

Palmar xanthoma
- remnant hyperlipidaemia
- may less commonly be seen in familial hypercholesterolaemia

Eruptive xanthoma are due to high triglyceride levels and present as multiple red/yellow vesicles on the extensor surfaces (e.g. elbows, knees)

Causes of eruptive xanthoma
- familial hypertriglyceridaemia
- lipoprotein lipase deficiency

Tendon xanthoma, tuberous xanthoma, xanthelasma
- familial hypercholesterolaemia
- remnant hyperlipidaemia

Xanthelasma are also seen without lipid abnormalities

Management of xanthelasma, options include:
- surgical excision
- topical trichloroacetic acid
- laser therapy
- electrodesiccation

Question 95 of 220

A 23-year-old woman is investigated after collapsing whilst jogging. She felt briefly unwell and dizzy prior to collapsing but quickly recovered. There has been no previous similar episodes. Routine blood tests are normal but the ECG shows a corrected QT interval of 480ms. What is the most appropriate management?

- A. Implantable cardioverter defibrillator
- B. Propranolol
- C. Amiodarone
- D. Reassurance
- E. Accessory pathway ablation

Question 95 of 220

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A. Implantable cardioverter defibrillator

B. Propranolol

C. Amiodarone

D. Reassurance

E. Accessory pathway ablation

An implantable cardioverter defibrillator is only required in high risk cases, for example if the patient has a QTc > 500ms or previous episodes of cardiac arrest.

Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than marked left axis deviation in males and 450 ms in females.

Causes of a prolonged QT interval

Congenital	**Drugs**	**Other**
• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel) • Romano-Ward syndrome (no deafness)	• amiodarone, sotalol, class 1a antiarrhythmic drugs • tricyclic antidepressants, fluoxetine • chloroquine • terfenadine* • erythromycin	• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia • acute myocardial infarction • myocarditis • hypothermia • subarachnoid hemorrhage

Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 96 of 220

Which one of the following conditions is most associated with pulsus alternans?

- A. Cardiac tamponade
- B. Hypertrophic obstructive cardiomyopathy
- C. Aortic stenosis
- D. Severe left ventricular failure
- E. Mixed aortic valve disease

Question 96 of 220

Which one of the following conditions is most associated with pulsus alternans?

- A. Cardiac tamponade
- B. Hypertrophic obstructive cardiomyopathy
- C. Aortic stenosis
- ✓ D. Severe left ventricular failure
- E. Mixed aortic valve disease

Pulses

Pulsus parodoxus
- greater than the normal (10 mmHg) fall in systolic blood pressure during inspiration --> faint or absent pulse in inspiration
- severe asthma, cardiac tamponade

Slow-rising/plateau
- aortic stenosis

Collapsing
- aortic regurgitation
- patent ductus arteriosus
- hyperkinetic (anaemia, thyrotoxic, fever, exercise/pregnancy)

Pulsus alternans
- regular alternation of the force of the arterial pulse
- severe LVF

Bisferiens pulse
- 'double pulse' - two systolic peaks
- mixed aortic valve disease

'Jerky' pulse
- hypertrophic obstructive cardiomyopathy*

*HOCM may occasionally be associated with a bisferiens pulse

Question 97 of 220

Which one of the following features would indicate cardiac tamponade rather than constrictive pericarditis?

- A. Pulsus parodoxus
- B. Tachycardia
- C. Raised JVP
- D. Hypotension
- E. Muffled heart sounds

Question 97 of 220

Which one of the following features would indicate cardiac tamponade rather than constrictive pericarditis?

- ✓ A. Pulsus parodoxus
- B. Tachycardia
- C. Raised JVP
- D. Hypotension
- E. Muffled heart sounds

Cardiac tamponade

Features
- raised JVP, with an absent Y descent - this is due to the limited right ventricular filling
- tachycardia
- hypotension
- muffled heart sounds
- pulsus paradoxus
- Kussmaul's sign (much debate about this)
- ECG: electrical alternans

The key differences between constrictive pericarditis and cardiac tamponade are summarised in the table below:

	Cardiac tamponade	**Constrictive pericarditis**
JVP	Absent Y descent	X + Y present
Pulsus paradoxus	Present	Absent
Kussmaul's sign	Rare	Present
Characteristic features		Pericardial calcification on CXR

A commonly used mnemonic to remember the absent Y descent in cardiac tamponade is TAMponade = TAMpaX

Question 98 of 220

A 62-year-old man is admitted with pyrexia and found to have infective endocarditis. Which one of the following is most associated with a good prognosis?

A. *Staphylococcus aureus* infection

B. Culture negative endocarditis

C. *Streptococcus viridans* infection

D. Low complement levels

E. Prosthetic valve endocarditis

Question 98 of 220

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- B. Culture negative endocarditis
- ✓ C. *Streptococcus viridans* infection
- D. Low complement levels
- E. Prosthetic valve endocarditis

Infective endocarditis - streptococcal infection carries a good prognosis

Infective endocarditis: prognosis and management

Poor prognostic factors
- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism
- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)
- initial blind therapy - flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
- initial blind therapy if prosthetic valve is present or patient is penicillin allergic - vancomycin + rifampicin + gentamicin
- endocarditis caused by staphylococci - flucloxacillin (vancomycin + rifampicin if penicillin allergic or MRSA)
- endocarditis caused by streptococci - benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

Indications for surgery
- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Question 99 of 220

A 76-year-old female is admitted after being found on the floor at her home. On examination she has a core temperature of 30ºC. Her serum electrolytes are within normal range. Which one of the ECG findings is most likely to be seen?

- A. Long QT interval
- B. 'U' waves
- C. Short PR interval
- D. Second degree heart block
- E. Flattened T waves

Question 99 of 220

A 76-year-old female is admitted after being found on the floor at her home. On examination she has a core temperature of 30ºC. Her serum electrolytes are within normal range. Which one of the ECG findings is most likely to be seen?

- ✓ A. Long QT interval
- B. 'U' waves
- C. Short PR interval
- D. Second degree heart block
- E. Flattened T waves

ECG: hypothermia

The following ECG changes may be seen in hypothermia

- bradycardia
- 'J' wave - small hump at the end of the QRS complex
- first degree heart block
- long QT interval
- atrial and ventricular arrhythmias

Question 100 of 220

Pulmonary arterial hypertension may be seen in each one of the following conditions, except:

- A. Hepatitis B
- B. Eisenmenger's syndrome
- C. Sickle cell anaemia
- D. HIV
- E. Sarcoidosis

Question 100 of 220

Pulmonary arterial hypertension may be seen in each one of the following conditions, except:

- ✓ A. Hepatitis B
- B. Eisenmenger's syndrome
- C. Sickle cell anaemia
- D. HIV
- E. Sarcoidosis

Hepatitis B is not a recognised cause of pulmonary arterial hypertension

Pulmonary arterial hypertension: causes and classification

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise. PAH has recently been reclassified by the WHO:

Group 1: Pulmonary arterial hypertension (PAH)
– idiopathic*
– familial
– associated conditions: collagen vascular disease, congenital heart disease with systemic to pulmonary shunts, HIV**, drugs and toxins, sickle cell disease
– persistent pulmonary hypertension of the newborn

Group 2: Pulmonary hypertension with left heart disease
– left-sided atrial, ventricular or valvular disease such as left ventricular systolic and diastolic dysfunction, mitral stenosis and mitral regurgitation

Group 3: Pulmonary hypertension secondary to lung disease/hypoxia
– COPD
– interstitial lung disease
– sleep apnoea
– high altitude

Group 4: Pulmonary hypertension due to thromboembolic disease

Group 5: Miscellaneous conditions
– lymphangiomatosis e.g. secondary to carcinomatosis or sarcoidosis

*previously termed primary pulmonary hypertension
**the mechanism by which HIV infection produces pulmonary hypertension remains unknown

Question 101 of 220

In patients with atrial fibrillation (AF), which one of the following factors would make a rate control strategy, rather than rhythm control, more suitable?

- A. Congestive heart failure
- B. AF secondary to a corrected precipitant
- C. Symptomatic
- D. Age > 65 years
- E. First presentation

Question 101 of 220

In patients with atrial fibrillation (AF), which one of the following factors would make a rate control strategy, rather than rhythm control, more suitable?

- A. Congestive heart failure
- B. AF secondary to a corrected precipitant
- C. Symptomatic
- ✓ D. Age > 65 years
- E. First presentation

Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
• Older than 65 years • History of ischaemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 102 of 220

A 71-year-old man who had a bioprosthetic aortic valve replacement three years ago is reviewed. What antithrombotic therapy is he likely to be taking?

- A. Nothing
- B. Aspirin
- C. Warfarin: INR 2.0-3.0
- D. Aspirin + clopidogrel
- E. Warfarin: INR 3.0-4.0

Question 102 of 220

A 71-year-old man who had a bioprosthetic aortic valve replacement three years ago is reviewed. What antithrombotic therapy is he likely to be taking?

- A. Nothing
- ✓ B. Aspirin
- C. Warfarin: INR 2.0-3.0
- D. Aspirin + clopidogrel
- E. Warfarin: INR 3.0-4.0

Prosthetic heart valves - antithrombotic therapy:
- bioprosthetic: aspirin
- mechanical: warfarin + aspirin

Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	**Mechanical valves**
Usually bovine or porcine in origin Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays Mechanical valves have a low failure rate Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication. Target INR • aortic: 2.0-3.0 • mitral: 2.5-3.5

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Question 103 of 220

A 34-year-old man is noted to have a pan-systolic murmur associated with large V waves in the JVP and pulsatile hepatomegaly. Which one of the following types of congenital heart disease is most associated with tricuspid regurgitation?

- A. Atrial septal defect
- B. Ebstein's anomaly
- C. Coarctation of the aorta
- D. Patent ductus arteriosus
- E. Ventricular septal defect

Question 103 of 220

A 34-year-old man is noted to have a pan-systolic murmur associated with large V waves in the JVP and pulsatile hepatomegaly. Which one of the following types of congenital heart disease is most associated with tricuspid regurgitation?

- A. Atrial septal defect
- ✓ B. Ebstein's anomaly
- C. Coarctation of the aorta
- D. Patent ductus arteriosus
- E. Ventricular septal defect

Tricuspid regurgitation

Signs
- pan-systolic murmur
- giant V waves in JVP
- pulsatile hepatomegaly
- left parasternal heave

Causes
- right ventricular dilation
- pulmonary hypertension e.g. COPD
- rheumatic heart disease
- infective endocarditis (especially intravenous drug users)
- Ebstein's anomaly
- carcinoid syndrome

Question 104 of 220

What is the most common cardiac defect seen in Marfan's syndrome

- A. Mitral valve prolapse
- B. Coarctation of the aorta
- C. Bicuspid aortic valve
- D. Dilation of the aortic sinuses
- E. Ventricular septal defect

Question 104 of 220

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- B. Coarctation of the aorta
- C. Bicuspid aortic valve
- ✓ D. Dilation of the aortic sinuses
- E. Ventricular septal defect

Whilst mitral valve prolapse is seen in Marfan's syndrome, dilation of the aortic sinuses is more common

Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 patients.

Features

- tall stature with arm span to height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Question 105 of 220

Which one of the following ECG findings is least associated with digoxin use?

- A. Bradycardia
- B. Down-sloping ST depression
- C. Flattened T waves
- D. Prolonged QT interval
- E. AV block

Question 105 of 220

Which one of the following ECG findings is least associated with digoxin use?

- A. Bradycardia
- B. Down-sloping ST depression
- C. Flattened T waves
- ✓ D. Prolonged QT interval
- E. AV block

ECG: digoxin

ECG features
- down-sloping ST depression ('reverse tick')
- flattened/inverted T waves
- short QT interval
- arrhythmias e.g. AV block, bradycardia

Question 106 of 220

A 47-year-old man is admitted to hospital following an acute coronary syndrome. He has a history peptic ulcer disease and his cardiologist decides to use clopidogrel. What is the mechanism of action of clopidogrel?

- A. Non-selective phosphodiesterase inhibitor
- B. Phosphodiesterase V inhibitor
- C. Inhibits ATP binding to its platelet receptor
- D. Inhibits ADP binding to its platelet receptor
- E. Glycoprotein IIb/IIIa inhibitor

Question 106 of 220

A 47-year-old man is admitted to hospital following an acute coronary syndrome. He has a history peptic ulcer disease and his cardiologist decides to use clopidogrel. What is the mechanism of action of clopidogrel?

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- B. Phosphodiesterase V inhibitor
- C. Inhibits ATP binding to its platelet receptor
- ✓ D. Inhibits ADP binding to its platelet receptor
- E. Glycoprotein IIb/IIIa inhibitor

Clopidogrel inhibits ADP binding to platelet receptors

Clopidogrel

Clopidogrel is an antiplatelet agent used in the management of cardiovascular disease. It is often used when aspirin is not tolerated or contraindicated but there are now a number of conditions for which clopidogrel is used in addition to aspirin, for example in patients with an acute coronary syndrome.

Mechanism
- inhibits ADP binding to its platelet receptor

Interactions
- concurrent use of proton pump inhibitors (PPIs) may make clopidogrel less effective (MHRA July 2009)
- this advice was updated by the MHRA in April 2010, evidence seems inconsistent but omeprazole and esomeprazole still cause for concern. Other PPIs such as lansoprazole should be OK - please see the link for more details

Question 107 of 220

Which one of the following features would best indicate severe aortic stenosis?

- A. Valvular gradient of 35 mmHg
- B. Quiet first heart sound
- C. Loudness of ejection systolic murmur
- D. Fourth heart sound
- E. Development of an opening snap

Question 107 of 220

Which one of the following features would best indicate severe aortic stenosis?

- A. Valvular gradient of 35 mmHg
- B. Quiet first heart sound
- C. Loudness of ejection systolic murmur
- ✓ D. Fourth heart sound
- E. Development of an opening snap

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 108 of 220

A 76-year-old woman is admitted with palpitations. During the cardiovascular examination you notice irregular cannon 'a' waves. Which one of the following would account for this finding?

- A. Atrio-ventricular nodal re-entry tachycardia
- B. Atrial fibrillation with tricuspid stenosis
- C. Ventricular tachycardia with 1:1 ventricular-atrial conduction
- D. Complete heart block
- E. Tricuspid regurgitation

Question 108 of 220

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- B. Atrial fibrillation with tricuspid stenosis
- C. Ventricular tachycardia with 1:1 ventricular-atrial conduction
- ✓ D. Complete heart block
- E. Tricuspid regurgitation

JVP: cannon waves

Caused by the right atrium contracting against a closed tricuspid valve. May be subdivided into regular or intermittent

Regular cannon waves
- ventricular tachycardia (with 1:1 ventricular-atrial conduction)
- atrio-ventricular nodal re-entry tachycardia (AVNRT)

Irregular cannon waves
- complete heart block

Question 109 of 220

A 72-year-old man with a history of chronic heart failure secondary to ischaemic cardiomyopathy is reviewed. He was discharged two weeks ago from hospital following a myocardial infarction. An echocardiogram done during his admission showed a left ventricular ejection fraction of 40% but did not demonstrate any valvular problems.

Despite his current treatment with furosemide, ramipril, carvedilol, aspirin and simvastatin he remains short of breath on minimal exertion such as walking 30 metres. On examination his chest is clear and there is minimal peripheral oedema. What is the most appropriate next step in management?

- A. Stop aspirin
- B. Refer for cardiac resynchronisation therapy
- C. Switch carvedilol to bisoprolol
- D. Add angiotensin-2 receptor blocker
- E. Add an aldosterone antagonist

Question 109 of 220

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A. Stop aspirin

B. Refer for cardiac resynchronisation therapy

C. Switch carvedilol to bisoprolol

D. Add angiotensin-2 receptor blocker

✓ E. Add an aldosterone antagonist

The updated 2010 NICE guidelines now suggest that in addition to aldosterone antagonists both angiotensin-2 receptor blockers and hydralazine in combination with a nitrate are suitable second-line treatments for heart failure. However, given that he has had a recent myocardial infarction the best choice is an aldosterone antagonist - please see the NICE guidelines for more details.

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:
- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:
- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off** pneumococcal vaccine

*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

**adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Question 110 of 220

A 43-year-old man who is known to have Wolff-Parkinson White syndrome presents to the Emergency Department with palpitations. He has no other significant history of note. The palpitations started around 4 hours ago and are not associated with chest pain or shortness of breath. On examination blood pressure is 124/80 mmHg and the chest is clear on auscultation. An ECG show atrial fibrillation at a rate of 154 bpm. Of the following options, what is the most appropriate management?

- A. Adenosine
- B. Flecainide
- C. Verapamil
- D. Digoxin
- E. Sotalol

Question 110 of 220

A 43-year-old man who is known to have Wolff-Parkinson White syndrome presents to the Emergency Department with palpitations. He has no other significant history of note. The palpitations started around 4 hours ago and are not associated with chest pain or shortness of breath. On examination blood pressure is 124/80 mmHg and the chest is clear on auscultation. An ECG show atrial fibrillation at a rate of 154 bpm. Of the following options, what is the most appropriate management?

- A. Adenosine
- ✓ B. Flecainide
- C. Verapamil
- D. Digoxin
- E. Sotalol

Adenosine should be avoided as blocking the AV node can paradoxically increase ventricular rate resulting in fall in cardiac output. Verapamil and digoxin should also be avoided in patients with Wolff-Parkinson White as they may precipitate VT or VF.

Another option to consider in this situation would be DC cardioversion

Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:
- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway*
- right axis deviation if left-sided accessory pathway*

Differentiating between type A and type B
- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW
- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management
- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol**, amiodarone, flecainide

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

**sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Question 111 of 220

A 57-year-old man presents to the Emergency Department with a 15 minute history of severe central chest pain radiating to his left arm. ECG shows T-wave inversion in leads I, V5 and V6. Which coronary artery is most likely to be affected?

- A. Left circumflex
- B. Posterior interventricular
- C. Left main stem
- D. Right coronary
- E. Left anterior descending

Question 112 of 220

Which one of the following is a cause of a soft second heart sound?

- A. Aortic stenosis
- B. Aortic regurgitation
- C. Mitral stenosis
- D. Mitral regurgitation
- E. Pulmonary hypertension

Question 112 of 220

Which one of the following is a cause of a soft second heart sound?

- ✓ A. Aortic stenosis
- B. Aortic regurgitation
- C. Mitral stenosis
- D. Mitral regurgitation
- E. Pulmonary hypertension

Second heart sound (S2)
- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

S2 is soft in severe aortic stenosis

Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2
- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2
- aortic stenosis

Causes of fixed split S2
- atrial septal defect

Causes of a widely split S2
- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)
- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

Question 113 of 220

Which one of the following is the strongest risk factor for developing infective endocarditis?

- A. Previous episode of infective endocarditis
- B. Intravenous drug use
- C. Previous rheumatic fever
- D. Permanent central venous access line
- E. Recent dental surgery

Question 113 of 220

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- C. Previous rheumatic fever
- D. Permanent central venous access line
- E. Recent dental surgery

Infective endocarditis - strongest risk factor is previous episode of infective endocarditis

Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. Other factors include:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- Bartonella
- Brucella
- HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in Staph aureus infections

Question 114 of 220

A 72-year-old male is admitted to the Emergency Room following a collapse at church. ECG reveals dissociation between the P and QRS complexes with a rate of 40 / minute. Which one of the following clinical findings may also be found?

- A. Loud S1
- B. Narrow pulse pressure
- C. Giant v waveforms in the JVP
- D. Variable intensity of S1
- E. Soft S2

Question 114 of 220

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- A. Loud S1
- B. Narrow pulse pressure
- C. Giant v waveforms in the JVP
- ✓ D. Variable intensity of S1
- E. Soft S2

Complete heart block

Features

- syncope
- heart failure
- regular bradycardia (30-50 bpm)
- wide pulse pressure
- JVP: cannon waves in neck
- variable intensity ofS1

Question 115 of 220

Which of the following conditions is not associated with the development of aortic regurgitation?

- A. Rheumatic fever
- B. Ankylosing spondylitis
- C. Marfan's syndrome
- D. Syphilis
- E. Dilated cardiomyopathy

Question 115 of 220

Which of the following conditions is not associated with the development of aortic regurgitation?

- A. Rheumatic fever
- B. Ankylosing spondylitis
- C. Marfan's syndrome
- D. Syphilis
- ✓ E. Dilated cardiomyopathy

Dilated cardiomyopathy is associated with the development of mitral regurgitation, not aortic regurgitation

Aortic regurgitation

Features
- early diastolic murmur
- collapsing pulse
- wide pulse pressure
- mid-diastolic Austin-Flint murmur in severe AR - due to partial closure of the anterior mitral valve cusps caused by the regurgitation streams

Causes (due to valve disease)
- rheumatic fever
- infective endocarditis
- connective tissue diseases e.g. RA/SLE
- bicuspid aortic valve

Causes (due to aortic root disease)
- aortic dissection
- spondylarthropathies (e.g. ankylosing spondylitis)
- hypertension
- syphilis
- Marfan's, Ehler-Danlos syndrome

Question 116 of 220

Which one of the following types of hyperlipidaemia are eruptive xanthoma most commonly associated with?

A. Familial hypertriglyceridaemia

B. Familial hypercholesterolaemia

C. Familial combined hyperlipidaemia

D. Remnant hyperlipidaemia

E. Hyperlipidaemia secondary to nephrotic syndrome

Question 116 of 220

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- B. Familial hypercholesterolaemia
- C. Familial combined hyperlipidaemia
- D. Remnant hyperlipidaemia
- E. Hyperlipidaemia secondary to nephrotic syndrome

Hyperlipidaemia: xanthomata

Characteristic xanthomata seen in hyperlipidaemia:

Palmar xanthoma
- remnant hyperlipidaemia
- may less commonly be seen in familial hypercholesterolaemia

Eruptive xanthoma are due to high triglyceride levels and present as multiple red/yellow vesicles on the extensor surfaces (e.g. elbows, knees)

Causes of eruptive xanthoma
- familial hypertriglyceridaemia
- lipoprotein lipase deficiency

Tendon xanthoma, tuberous xanthoma, xanthelasma
- familial hypercholesterolaemia
- remnant hyperlipidaemia

Xanthelasma are also seen without lipid abnormalities

Management of xanthelasma, options include:
- surgical excision
- topical trichloroacetic acid
- laser therapy
- electrodesiccation

Question 117 of 220

A 74-year-old man is admitted with chest pain associated with ECG changes. A troponin T taken 12 hours after admission indicates an acute myocardial infarction. Which one of the following is most likely to predict a poor prognosis?

- A. History of diabetes mellitus
- B. Loss of heart rate variability
- C. Left ventricular ejection fraction of 40%
- D. Diastolic blood pressure of 110 mmHg
- E. Male sex

Question 117 of 220

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- D. Diastolic blood pressure of 110 mmHg
- E. Male sex

Acute coronary syndrome: prognostic factors

The 2006 Global Registry of Acute Coronary Events (GRACE) study has been used to derive regression models to predict death in hospital and death after discharge in patients with acute coronary syndrome

Poor prognostic factors

- age
- development (or history) of heart failure
- peripheral vascular disease
- reduced systolic blood pressure
- Killip class*
- initial serum creatinine concentration
- elevated initial cardiac markers
- cardiac arrest on admission
- ST segment deviation

***Killip class** - system used to stratify risk post myocardial infarction

Killip class	Features	30 day mortality
I	No clinical signs heart failure	6%
II	Lung crackles, S3	17%
III	Frank pulmonary oedema	38%
IV	Cardiogenic shock	81%

Question 118 of 220

Which one of the following is not a recognised treatment in primary pulmonary hypertension?

- A. Endothelin-1 receptor agonists
- B. Heart-lung transplant
- C. IV prostaglandins
- D. Diuretics
- E. Calcium channel blockers

Question 118 of 220

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- D. Diuretics
- E. Calcium channel blockers

Endothelin-1 receptor antagonists such as bosentan, not agonists may be used

Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)
- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

Features
- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

Management
- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

Question 119 of 220

Each one of the following is an indication for an implantable cardiac defibrillator, except:

- A. Previous myocardial infarction with non-sustained VT on 24 hr monitoring
- B. Wolff-Parkinson White syndrome
- C. Hypertrophic obstructive cardiomyopathy
- D. Previous cardiac arrest due to VF
- E. Long QT syndrome

Question 119 of 220

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- C. Hypertrophic obstructive cardiomyopathy
- D. Previous cardiac arrest due to VF
- E. Long QT syndrome

Implantable cardiac defibrillators

Indications

- long QT syndrome
- hypertrophic obstructive cardiomyopathy
- previous cardiac arrest due to VT/VF
- previous myocardial infarction with non-sustained VT on 24 hr monitoring, inducible VT on electrophysiology testing and ejection fraction < 35%
- Brugada syndrome

Question 120 of 220

A 64-year-old female presents with central chest pain radiating down her left arm of 20 minutes duration. On examination the pulse is 90 bpm and regular and the BP is 205/110 mmHg. ECG shows 2 mm ST elevation in leads V2-6. Morphine and aspirin have already been given. What is the most appropriate next step?

- A. Observe
- B. IV streptokinase
- C. IV alteplase
- D. IV GTN
- E. Temporary pacing

Question 120 of 220

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- B. IV streptokinase
- C. IV alteplase
- ✓ D. IV GTN
- E. Temporary pacing

The elevated blood pressure would be a contraindication to giving thrombolysis is this patient

Thrombolysis

Thrombolytic drugs activate plasminogen to form plasmin. This in turn degrades fibrin and help breaks up thrombi. They in primarily used in patients who present with a ST elevation myocardial infarction. Other indications include acute ischaemic stroke and pulmonary embolism, although strict inclusion criteria apply.

Examples
- alteplase
- tenecteplase
- streptokinase

Contraindications to thrombolysis
- active internal bleeding
- recent haemorrhage, trauma or surgery (including dental extraction)
- coagulation and bleeding disorders
- intracranial neoplasm
- stroke < 2 months
- aortic dissection
- recent head injury
- pregnancy
- severe hypertension

Side-effects
- haemorrhage
- hypotension - more common with streptokinase
- allergic reactions may occur with streptokinase

Question 121 of 220

A 62-year-old patient presents to the Emergency Department with a 25 minute history of crushing central chest pain. ECG shows ST elevation in leads I and aVL. Which coronary territory is likely to be affected?

- A. Lateral
- B. Posterior
- C. Anteroseptal
- D. Anterolateral
- E. Inferior

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- B. Posterior
- C. Anteroseptal
- D. Anterolateral
- E. Inferior

These ECG changes are most consistent with a lateral myocardial infarction. An anterolateral infarction is more likely to have changes in the chest leads.

ECG: coronary territories

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	**Coronary artery**
Anteroseptal	V1-V4	Left anterior descending
Inferior	II, III, aVF	Right coronary
Anterolateral	V4-6, I, aVL	Left anterior descending or left circumflex
Lateral	I, aVL +/- V5-6	Left circumflex
Posterior	Tall R waves V1-2	Usually left circumflex, also right coronary

Question 122 of 220

You review a 75-year-old man who complains of palpitations. He was diagnosed with atrial fibrillation around four months ago and started on digoxin 125 mcg od and warfarin. Despite this treatment he still feels his 'heart race' regularly. On examination his pulse is 96 / min irregularly irregular and respiratory examination is unremarkable. What is the most appropriate next step in management?

- A. Switch digoxin for verapamil
- B. Refer for electrical cardioversion
- C. Add amiodarone
- D. Add bisoprolol
- E. Make no change to his regular medication but prescribe flecainide as a 'pill in the pocket'

Question 122 of 220

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- E. Make no change to his regular medication but prescribe flecainide as a 'pill in the pocket'

Adding a beta-blocker would be the best option here. It will help control the heart rate and may have cardioprotective properties in certain patients (e.g. Those with heart failure, ischaemic heart disease or hypertension).

Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents used to control rate in patients with atrial fibrillation
- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation
- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
• Older than 65 years • History of ischaemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 123 of 220

Which one of the following statements regarding prosthetic heart valves is correct?

- A. Antibiotic prophylaxis is still recommended for patients with mechanical valves who have dental procedures
- B. The majority of mechanical valves are of the ball-and-cage type
- C. Bioprosthetic valves are now usually obtained from human cadavers
- D. The target INR for patients with mechanical aortic valves is 3.0-4.0
- E. Mechanical valves have a lower failure rate than bioprosthetic valves

Question 123 of 220

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- ✓ E. Mechanical valves have a lower failure rate than bioprosthetic valves

Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	**Mechanical valves**
Usually bovine or porcine in origin Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays Mechanical valves have a low failure rate Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication. Target INR • aortic: 2.0-3.0 • mitral: 2.5-3.5

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Question 124 of 220

A 37-year-old woman presents for review. She is 26 weeks pregnant and has had no problems with her pregnancy to date. Blood pressure is 144/92 mmHg, a rise from her booking reading of 110/80 mmHg. Urine dipstick reveals the following:

Protein	negative
Leucocytes	negative
Blood	negative

What is the most appropriate description of her condition?

- A. Moderate pre-eclampsia
- B. Mild pre-eclampsia
- C. Gestational hypertension
- D. Normal physiological change in blood pressure
- E. Pre-existing hypertension

Question 124 of 220

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Leucocytes negative

Blood negative

What is the most appropriate description of her condition?

- A. Moderate pre-eclampsia
- B. Mild pre-eclampsia
- ✓ C. Gestational hypertension
- D. Normal physiological change in blood pressure
- E. Pre-existing hypertension

Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy in usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	Pregnancy-induced hypertension (PIH, also known as gestational hypertension)	Pre-eclampsia
A history of hypertension before pregnancy or an elevated blood pressure > 140/90 mmHg before 20 weeks gestation No proteinuria, no oedema Occurs in 3-5% of pregnancies and is more common in older women	Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks) No proteinuria, no oedema Occurs in around 5-7% of pregnancies Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life	Pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours) Oedema may occur but is now less commonly used as a criteria Occurs in around 5% of pregnancies

Question 125 of 220

A 60-year-old man who is investigated for exertional chest pain is diagnosed as having angina pectoris. Which one of the following drugs is most likely to improve his long-term prognosis?

- A. Atenolol
- B. Aspirin
- C. Isosorbide mononitrate
- D. Ramipril
- E. Nicorandil

Question 125 of 220

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- ✓ B. Aspirin
- C. Isosorbide mononitrate
- D. Ramipril
- E. Nicorandil

Strong evidence exists supporting the use of aspirin in stable angina. The benefit of ACE inhibitors and beta-blockers are significant in patients who've had a myocardial infarction but modest in those with stable angina. Please see the CKS link for a review of the most recent trials.

Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery.

Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- beta-blocker is the preferred initial treatment. For patients unable to take a beta-blocker there is no clear guidelines on the best alternative. Options include a rate-limiting calcium-channel blocker (verapamil or diltiazem); a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine); a nitrate; or a potassium-channel activator
- if there is a poor response to initial treatment then the beta-blocker should be increased to the maximum tolerated dose (e.g. atenolol 100mg od)
- again, there is no clear guidelines on the next step treatment. CKS advise adding a long-acting dihydropyridine (e.g. nifedipine) although other options include isosorbide mononitrate and nicorandil

Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Question 126 of 220

Which one of the following is least associated with prolongation of the PR interval?

- A. Digoxin toxicity
- B. Hypocalcaemia
- C. Lyme disease
- D. Rheumatic fever
- E. Ischaemic heart disease

Question 126 of 220

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- C. Lyme disease
- D. Rheumatic fever
- E. Ischaemic heart disease

Hypocalcaemia is associated with a prolonged QT interval. Hypokalaemia is associated with a prolonged PR interval

ECG: PR interval

Causes of a prolonged PR interval

- idiopathic
- ischaemic heart disease
- digoxin toxicity
- hypokalaemia*
- rheumatic fever
- aortic root pathology e.g. abscess secondary to endocarditis
- Lyme disease
- sarcoidosis
- myotonic dystrophy

A prolonged PR interval may also be seen in athletes

*hyperkalaemia can rarely cause a prolonged PR interval, but this is a much less common association than hypokalaemia

Question 127 of 220

A 54-year-old man with exercise-related chest pain is referred to cardiology. An exercise ECG shows non-specific ST and T wave changes. Following this an coronary angiogram is performed which demonstrates no evidence of atherosclerosis. A diagnosis of Prinzmetal's angina is suspected. What is the most appropriate first-line treatment?

- A. Nicorandil
- B. Atenolol
- C. Felodipine
- D. Fluoxetine
- E. Isosorbide mononitrate

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Prinzmetal angina - treatment = dihydropyridine calcium channel blocker

See the SIGN guidelines for more details.

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- if there is a poor response to initial treatment then the beta-blocker should be increased to the maximum tolerated dose (e.g. atenolol 100mg od)
- again, there is no clear guidelines on the next step treatment. CKS advise adding a long-acting dihydropyridine (e.g. nifedipine) although other options include isosorbide mononitrate and nicorandil

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- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
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Question 128 of 220

Which one of the following statements regarding percutaneous coronary intervention (PCI) is incorrect?

- A. Stent thrombosis usually occurs in the first month
- B. Restenosis is more common than stent thrombosis
- C. Around 95% of patients have a stent fitted during a PCI
- D. Renal impairment is a risk factor for restenosis
- E. Patients with drug-eluting stents require a shorter duration of clopidogrel therapy

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PCI - patients with drug-eluting stents require a longer duration of clopidogrel therapy

Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

Question 129 of 220

Which one of the following is least associated with Tetralogy of Fallot?

- A. Right ventricular outflow tract obstruction
- B. Overriding aorta
- C. Ejection systolic murmur
- D. Left-to-right shunt
- E. Right ventricular hypertrophy

Question 129 of 220

Which one of the following is least associated with Tetralogy of Fallot?

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- ✓ D. Left-to-right shunt
- E. Right ventricular hypertrophy

Right-to-left shunting is characteristic of Fallot's. It is however known that a small number of asymptomatic infants may initially have a degree of left-to-right shunting through the ventricular septal defect

Tetralogy of Fallot

Tetralogy of Fallot (TOF) is the most common cause of cyanotic congenital heart disease*. It typically presents at around 1-2 months, although may not be picked up until the baby is 6 months old

The four characteristic features are:
- ventricular septal defect (VSD)
- right ventricular hypertrophy
- right ventricular outflow tract obstruction, pulmonary stenosis
- overriding aorta

The severity of the right ventricular outflow tract obstruction determines the degree of cyanosis and clinical severity

Other features
- cyanosis
- causes a right-to-left shunt
- ejection systolic murmur due to pulmonary stenosis (the VSD doesn't usually cause a murmur)
- a right-sided aortic arch is seen in 25% of patients
- chest x-ray shows a 'boot-shaped' heart, ECG shows right ventricular hypertrophy

Management
- surgical repair is often undertaken in two parts
- cyanotic episodes may be helped by beta-blockers to reduce infundibular spasm

*however, at birth transposition of the great arteries is the more common lesion as patients with TOF generally present at around 1-2 months

Question 130 of 220

Each one of the following may cause secondary hypertension, except:

- A. Patent ductus arteriosus
- B. Cushing's syndrome
- C. Liddle's syndrome
- D. 11-beta hydroxylase deficiency
- E. Combined oral contraceptive pill

Question 130 of 220

Each one of the following may cause secondary hypertension, except:

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- B. Cushing's syndrome
- C. Liddle's syndrome
- D. 11-beta hydroxylase deficiency
- E. Combined oral contraceptive pill

Hypertension: secondary causes

Renal - accounts for 80% of secondary hypertension
- glomerulonephritis
- pyelonephritis
- adult polycystic kidney disease
- renal artery stenosis

Endocrine disorders
- Cushing's syndrome
- primary hyperaldosteronism including Conn's syndrome
- Liddle's syndrome
- congenital adrenal hyperplasia (11-beta hydroxylase deficiency)
- phaeochromocytoma
- acromegaly

Others
- pregnancy
- coarctation of the aorta
- the combined oral contraceptive pill
- steroids
- MAOI

Question 131 of 220

A 52-year-old female is referred from the Emergency Department with a pulse of 36 beats/min. The ECG shows complete heart block with a narrow QRS complex. Blood pressure is 110/70 and there is no evidence of heart failure. What is the most appropriate management?

- A. Transvenous pacing
- B. Transcutaneous pacing
- C. Isoprenaline infusion, titrated to heart rate
- D. No intervention but cardiac monitoring
- E. Intravenous atropine

Question 131 of 220

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- D. No intervention but cardiac monitoring
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Peri-arrest rhythms: bradycardia

The joint European Resuscitation Council and Resuscitation Council (UK) 2005 guidelines emphasise that the management of bradycardia depends on:

- 1. identifying the presence of signs indicating haemodynamic compromise - 'adverse signs'
- 2. identifying the potential risk of asystole

Adverse signs

The following factors indicate haemodynamic compromise and hence the need for treatment:

- heart rate < 40 bpm
- systolic blood pressure < 100 mmHg
- heart failure
- ventricular arrhythmias requiring suppression

Atropine is the first line treatment in this situation. If this fails to work, or there is the potential risk of asystole then transvenous pacing is indicated

Potential risk of asystole

The following indicate a potential risk of asystole and hence the need for treatment with transvenous pacing:

- complete heart block with broad complex QRS
- recent asystole
- Mobitz type II AV block
- ventricular pause > 3 seconds

If there is a delay in the provision of transvenous pacing the following interventions may be used:

- atropine, up to maximum of 3mg
- transcutaneous pacing
- adrenaline infusion titrated to response

Question 132 of 220

Which one of the following is an example of a centrally acting antihypertensive?

- A. Minoxidil
- B. Hydralazine
- C. Sodium nitroprusside
- D. Moxonidine
- E. Diazoxide

Question 132 of 220

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- C. Sodium nitroprusside
- ✓ D. Moxonidine
- E. Diazoxide

Centrally acting antihypertensives

Examples of centrally acting antihypertensives include:

- methyldopa: used in the management of hypertension during pregnancy
- moxonidine: used in the management of essential hypertension when conventional antihypertensives have failed to control blood pressure
- clonidine: the antihypertensive effect is mediated through stimulating alpha-2 adrenoceptors in the vasomotor centre

Question 133 of 220

Which part of the jugular venous waveform is associated with the fall in atrial pressure during ventricular systole?

- A. y descent
- B. v wave
- C. x descent
- D. c wave
- E. a wave

Question 133 of 220

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- E. a wave

JVP: x descent = fall in atrial pressure during ventricular systole

Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis

'a' wave = atrial contraction
- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves
- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave
- closure of tricuspid valve
- not normally visible

'v' wave
- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Question 134 of 220

A 57-year-old man with NYHA class III heart failure is currently treated with furosemide and ramipril. What is the most suitable beta-blocker to add to improve his long-term prognosis?

- A. Acebutolol
- B. Labetalol
- C. Bisoprolol
- D. Sotalol
- E. Esmolol

Question 134 of 220

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Both carvedilol and bisoprolol have been shown to reduce mortality in stable heart failure. The other beta-blockers have no evidence base to support their use

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off** pneumococcal vaccine

*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

**adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Question 135 of 220

A 68-year-old man with a past history of aortic stenosis is reviewed in clinic. Which one of the following features would most guide the timing of surgery?

- A. Symptomatology of patient
- B. Aortic valve gradient of 50 mmHg
- C. Pulse pressure
- D. Loudness of murmur
- E. Left ventricular ejection fraction

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Aortic stenosis management: AVR if symptomatic, otherwise cut-off is gradient of 50 mmHg

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 136 of 220

Which of the following congenital heart defects may progress to Eisenmenger's syndrome?

- A. Tetralogy of Fallot
- B. Coarctation of the aorta
- C. Patent ductus arteriosus
- D. Tricuspid atresia
- E. Transposition of the great arteries

Question 136 of 220

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- ✓ C. Patent ductus arteriosus
- D. Tricuspid atresia
- E. Transposition of the great arteries

Although patients with tetralogy of Fallot have, by definition, a ventricular septal defect they do not go on to develop Eisenmenger's syndrome

Eisenmenger's syndrome

Describes the reversal of a left to right shunt in a congenital heart defect due to pulmonary hypertension

Associated with
- VSD
- ASD
- PDA

Features
- original murmur may disappear
- cyanosis
- clubbing
- right ventricular failure
- haemoptysis, embolism

Management
- heart-lung transplantation is required

Question 137 of 220

The use of beta-blockers in treating hypertension has declined sharply in the past five years. Which one of the following best describes the reasons why this has occurred?

- A. Less likely to prevent stroke + potential impairment of glucose tolerance
- B. Less likely to prevent myocardial infarctions + potential impairment of glucose tolerance
- C. High rate of interactions with other commonly prescribed medications (e.g. Calcium channel blockers)
- D. Increased incidence of reported adverse effects
- E. Increased incidence of chronic obstructive pulmonary disease

Question 137 of 220

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- D. Increased incidence of reported adverse effects
- E. Increased incidence of chronic obstructive pulmonary disease

This was demonstrated in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA).

Hypertension: management

NICE published updated guidelines for the management of hypertension in June 2006

Initial drug choice
- patients < 55-years-old: ACE inhibitor
- patients > 55-years-old or of Afro-Caribbean origin: calcium channel blocker or thiazide diuretic

The target blood pressure is 140/90 mmHg. For diabetics the target is 140/80 mmHg (or 130/80 mmHg if end-organ damage is present)

If this fails to control the blood pressure then use a combination of an ACE inhibitor plus either a calcium channel blocker or thiazide diuretic

If this still fails then a combination of an ACE inhibitor + calcium channel blocker + thiazide diuretic should be used

Following this further diuretic therapy, alpha blockers or beta blockers should be considered

New drugs

Direct renin inhibitors
- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Question 138 of 220

A 70-year-old man is admitted to the Acute Medicine Unit as he is pyrexial and feeling generally unwell. He has a history of ischaemic heart disease and had a bioprosthetic mitral valve replacement 5 years ago. An echocardiogram is arranged which shows a vegetation around the mitral valve. Blood cultures are taken which are reported as follows:

Streptococcus viridans

What is the most appropriate antibiotic therapy?

- A. IV benzylpenicillin + gentamicin
- B. IV ceftriaxone + benzylpenicillin
- C. IV flucloxacillin + gentamicin
- D. IV vancomycin + rifampicin + gentamicin
- E. IV vancomycin + benzylpenicillin

Question 138 of 220

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- D. IV vancomycin + rifampicin + gentamicin
- E. IV vancomycin + benzylpenicillin

Infective endocarditis: prognosis and management

Poor prognostic factors
- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism
- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)
- initial blind therapy - flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
- initial blind therapy if prosthetic valve is present or patient is penicillin allergic - vancomycin + rifampicin + gentamicin
- endocarditis caused by staphylococci - flucloxacillin (vancomycin + rifampicin if penicillin allergic or MRSA)
- endocarditis caused by streptococci - benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

Indications for surgery
- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Question 139 of 220

A 78-year-old woman with no past medical history of note is admitted with palpitations and shortness of breath, having been unwell for the past three days. Examination reveals an irregularly irregular pulse of 130 bpm, blood pressure of 108/70 mmHg, oxygen saturations of 96% on air and bibasal lung crepitations. What is the most appropriate therapy to control her heart rate?

- A. Amiodarone
- B. Flecainide
- C. Verapamil
- D. Digoxin
- E. Bisoprolol

Question 139 of 220

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- C. Verapamil
- ✓ D. Digoxin
- E. Bisoprolol

Digoxin is strongly indicated for coexistent atrial fibrillation and heart failure. Beta-blockers should not be introduced until any heart failure has been stabilised. Giving amiodarone or flecainide may result in cardioversion before the patient has been adequately anticoagulated

If there was a more acute history and the patient was in significant heart failure then DC cardioversion would be appropriate, as per Advanced Life Support guidelines

Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
• Older than 65 years • History of ischaemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 140 of 220

Which of the following statements concerning the third heart sound is correct?

- A. Caused by systolic filling of the ventricle
- B. May be heard in constrictive pericarditis
- C. Associated with atrial septal defects
- D. Is characteristically soft in aortic stenosis
- E. Caused by atrial contraction against a stiff ventricle

Question 140 of 220

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- ✓ B. May be heard in constrictive pericarditis
- C. Associated with atrial septal defects
- D. Is characteristically soft in aortic stenosis
- E. Caused by atrial contraction against a stiff ventricle

A third heart sound is often heard in left ventricular failure and constrictive pericarditis

Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

S1
- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

S2
- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

S3
- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure, constrictive pericarditis

S4
- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Question 141 of 220

A 14-year-old boy is admitted with palpitations and is noted to have a long QT interval. His only past medical history is deafness. What is the likely diagnosis?

- A. Leriche's syndrome
- B. Wolff-Parkinson White syndrome
- C. Jervell-Lange-Nielsen syndrome
- D. Romano-Ward syndrome
- E. Osler-Weber-Rendu syndrome

Question 141 of 220

A 14-year-old boy is admitted with palpitations and is noted to have a long QT interval. His only past medical history is deafness. What is the likely diagnosis?

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- B. Wolff-Parkinson White syndrome
- ✓ C. Jervell-Lange-Nielsen syndrome
- D. Romano-Ward syndrome
- E. Osler-Weber-Rendu syndrome

Jervell-Lange-Nielsen syndrome is associated with profound deafness and a prolonged QT interval

Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than marked left axis deviation in males and 450 ms in females.

Causes of a prolonged QT interval

Congenital	**Drugs**	**Other**
• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel) • Romano-Ward syndrome (no deafness)	• amiodarone, sotalol, class 1a antiarrhythmic drugs • tricyclic antidepressants, fluoxetine • chloroquine • terfenadine* • erythromycin	• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia • acute myocardial infarction • myocarditis • hypothermia • subarachnoid hemorrhage

Features
- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

Management
- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 142 of 220

Which of the following features is not associated with patent ductus arteriosus?

- A. Continuous 'machinery' murmur
- B. Bisferiens pulse
- C. Heaving apex beat
- D. Wide pulse pressure
- E. Left subclavicular thrill

Question 142 of 220

Which of the following features is not associated with patent ductus arteriosus?

- A. Continuous 'machinery' murmur
- ✓ B. Bisferiens pulse
- C. Heaving apex beat
- D. Wide pulse pressure
- E. Left subclavicular thrill

PDA is associated with a collapsing pulse

Patent ductus arteriosus

Overview
- acyanotic congenital heart defect
- connection between the pulmonary trunk and descending aorta
- more common in premature babies, born at high altitude or maternal rubella infection in the first trimester

Features
- left subclavicular thrill
- continuous 'machinery' murmur
- large volume, collapsing pulse
- wide pulse pressure
- heaving apex beat

Management
- indomethacin closes the connection in the majority of cases
- if associated with another congenital heart defect amenable to surgery then prostaglandin E1 is useful to keep the duct open until after surgical repair

Question 143 of 220

You are called to review a 78-year-old man on the surgical wards. He is three days post-op following a colectomy. He was recently diagnosed with colon cancer (Duke's C) and has a history of polymyalgia rheumatica. Current medications include co-codamol 30/500, prednisolone and prophylactic dose low-molecular weight heparin. Five minutes ago he started to complain of severe central chest pain. An ECG performed by the nurses shows ST elevation in the anterior leads. Aspirin and oxygen have been given by the Foundation 1 doctor. What is the most appropriate treatment?

- A. IV diamorphine + increase low-molecular weight heparin to treatment dose + double his prednisolone dose
- B. IV diamorphine + arrange echocardiogram urgently to exclude pericardial tamponade
- C. IV diamorphine + call the family in to discuss withdrawal of treatment
- D. IV diamorphine + arrange percutaneous coronary intervention
- E. IV diamorphine + thrombolysis

Question 143 of 220

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- ✓ D. IV diamorphine + arrange percutaneous coronary intervention
- E. IV diamorphine + thrombolysis

Primary percutaneous coronary intervention is the most appropriate treatment given his recent operation and associated risk of bleeding.

Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Question 144 of 220

Which of the following conditions is least associated with coarctation of the aorta?

- A. Neurofibromatosis
- B. Bicuspid aortic valve
- C. Prader-Willi syndrome
- D. Turner's syndrome
- E. Berry aneurysms

Question 144 of 220

Which of the following conditions is least associated with coarctation of the aorta?

- A. Neurofibromatosis
- B. Bicuspid aortic valve
- ✓ C. Prader-Willi syndrome
- D. Turner's syndrome
- E. Berry aneurysms

Coarctation of the aorta

Coarctation of the aorta describes a congenital narrowing of the descending aorta

Overview
- more common in males (despite association with Turner's syndrome)

Features
- infancy: heart failure
- adult: hypertension
- radio-femoral delay
- mid systolic murmur, maximal over back
- apical click from the aortic valve
- notching of the inferior border of the ribs (due to collateral vessels) is not seen in young children

Associations
- Turner's syndrome
- bicuspid aortic valve
- berry aneurysms
- neurofibromatosis

Question 145 of 220

Which of the following is responsible for the rapid depolarisation phase of the myocardial action potential?

- A. Rapid sodium influx
- B. Slow sodium efflux
- C. Slow efflux of calcium
- D. Efflux of potassium
- E. Rapid calcium influx

Question 145 of 220

Which of the following is responsible for the rapid depolarisation phase of the myocardial action potential?

- ✓ A. Rapid sodium influx
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- C. Slow efflux of calcium
- D. Efflux of potassium
- E. Rapid calcium influx

Electrical activity of the heart

Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by Na^+/K^+ ATPase There is slow entry of Na^+ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles

Question 146 of 220

Which one of the following is least associated with Wolff-Parkinson White syndrome?

- A. Mitral valve prolapse
- B. Ebstein's anomaly
- C. Thyrotoxicosis
- D. Coarctation of the aorta
- E. Hypertrophic cardiomyopathy

Question 146 of 220

Which one of the following is least associated with Wolff-Parkinson White syndrome?

- A. Mitral valve prolapse
- B. Ebstein's anomaly
- C. Thyrotoxicosis
- ✓ D. Coarctation of the aorta
- E. Hypertrophic cardiomyopathy

Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:
- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway*
- right axis deviation if left-sided accessory pathway*

Differentiating between type A and type B
- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW
- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management
- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol**, amiodarone, flecainide

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

**sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Question 147 of 220

A 29-year-old woman who is 28 weeks pregnant is reviewed. She has developed pre-eclampsia with her current blood pressure being 156/104 mmHg and the urine dipstick reported as follows:

Protein	+
Leucocytes	negative
Blood	negative

There is no oedema and the patient is otherwise asymptomatic. Of the following drugs, which one is least suitable to use?

- A. Labetalol
- B. Nifedipine
- C. Losartan
- D. Methyldopa
- E. Hydralazine

Question 147 of 220

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- D. Methyldopa
- E. Hydralazine

ACE inhibitors and angiotensin-2 receptor blockers should be avoided as they are teratogenic. Most clinicians would either use methyldopa or labetalol first-line in this situation

Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m^2
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count < 100 * 10^6/l, abnormal liver enzymes or HELLP syndrome

Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral methyldopa is often used first-line with oral labetalol, nifedipine and hydralazine also being used
- for severe hypertension IV labetalol and IV hydralazine are used in addition to the above
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Question 148 of 220

A 28-year-old female with a history of primary amenorrhoea and short stature is reviewed in clinic. On examination blood pressure in her right arm is 175/84 mmHg and 170/82 mmHg in her left. What is the most likely cause for her elevated blood pressure?

- A. Coarctation of the aorta
- B. Conn's syndrome
- C. Essential hypertension
- D. Renal aplasia
- E. Renal artery stenosis

Question 148 of 220

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- ✓ A. Coarctation of the aorta
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- C. Essential hypertension
- D. Renal aplasia
- E. Renal artery stenosis

This patient has Turner's syndrome which is associated with coarctation of the aorta. The site of the coarctation, for example if it involves the origin of the left subclavian artery, determines whether there is a difference between the right and left arm blood pressure readings. There is no significant difference in this case.

Another cause worth considering in a young hypertensive patient with primary amenorrhoea would be congenital adrenal hyperplasia

Essential hypertension would be unusual in a 28-year-old

Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 149 of 220

A 76-year-old man is reviewed. He was recently admitted after being found to be in atrial fibrillation. This was his second episode of atrial fibrillation. He also takes ramipril for hypertension but has no other history of note. During admission he was warfarinised and discharged with planned follow-up in the cardiology clinic. However, on review today he is found to be in sinus rhythm. What should happen regarding anticoagulation?

- A. Stop warfarin
- B. Continue warfarin for 1 month
- C. Stop warfarin + start aspirin
- D. Continue lifelong warfarin
- E. Continue warfarin for 6 months

Question 149 of 220

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- E. Continue warfarin for 6 months

Warfarin should be continued indefinitely as this is his second episode of atrial fibrillation and he has risk factors for stroke (age, hypertension)

Atrial fibrillation: anticoagulation

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006

The guidelines suggest a stroke risk stratification approach when determining how to anticoagulate a patient, as detailed below:

Low risk - annual risk of stroke = 1% • age < 65 years with no moderate or high risk factors • use aspirin	**Moderate risk** - annual risk of stroke = 4% • age > 65 years with no high risk factors, or: • age < 75 years with diabetes, hypertension or cardiovascular disease • use aspirin or warfarin depending on individual circumstances	**High risk** - annual risk of stroke = 8-12% • age > 75 years with diabetes, hypertension or cardiovascular disease • previous TIA, ischaemic stroke or thromboembolic event • valve disease, heart failure or impaired left ventricular function • use warfarin

An alternative approach is the **CHADS2** score:

	Condition	Points
C	Congestive heart failure	1
H	Hypertension (or treated hypertension)	1
A	Age > 75 years	1
D	Diabetes	1
S2	Prior Stroke or TIA	2

The table below shows a suggested anticoagulation strategy based on the score:

Score	Anticoagulation
0	Aspirin
1	Aspirin or warfarin, depending on patient preference and individual factors
2-6	Warfarin if not contraindicated

Question 150 of 220

A 62-year-old man is reviewed two hours after a successful elective DC cardioversion for atrial fibrillation. Six weeks ago he presented in fast atrial fibrillation. A decision was made at the time to warfarinise him for six weeks after which he was to be cardioverted. During this time he had a normal transthoracic echocardiogram. He has no past medical history of note other than treatment for a basal cell carcinoma. What is the most appropriate plan regarding anticoagulation?

- A. Can stop immediately
- B. Continue warfarinisation for 1 week then review following
- C. Lifelong warfarin
- D. Lifelong aspirin
- E. Continue warfarinisation for 4 weeks then review

Question 150 of 220

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- B. Continue warfarinisation for 1 week then review following
- C. Lifelong warfarin
- D. Lifelong aspirin
- ✓ E. Continue warfarinisation for 4 weeks then review

Atrial fibrillation: cardioversion

Onset < 48 hours

If atrial fibrillation (AF) is of less than 48 hours onset patients should be heparinised and a transthoracic echocardiogram performed to exclude a thrombus. Following this patients may be cardioverted, either:

- electrical - 'DC cardioversion'
- pharmacology - amiodarone if structural heart disease, flecainide in those without structural heart disease

Following electrical cardioversion if AF is confirmed as being less than 48 hours duration then further anticoagulation is unnecessary

Onset > 48 hours

If AF is of greater than 48 hours then patients should have therapeutic anticoagulation for at least 3 weeks. If there is a high risk of cardioversion failure (e.g. Previous failure or AF recurrence) then it is recommend to have at least 4 weeks amiodarone or sotalol prior to electrical cardioversion

Following electrical cardioversion patients should be anticoagulated for at least 4 weeks. After this time decisions about anticoagulation should be taken on an individual basis depending on the risk of recurrence

Question 151 of 220

Which one of the following statements regarding catecholaminergic polymorphic ventricular tachycardia (CPVT) is correct?

A. Resting ECG typically shows T wave inversion in leads V1-V3

B. Beta-blockers are contraindicated in patients with CPVT

C. Is associated with cleft palate

D. In the majority of cases is due to a defect in the potassium channel

E. Symptoms generally develop before the age of 20 years

Question 151 of 220

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- C. Is associated with cleft palate
- D. In the majority of cases is due to a defect in the potassium channel
- ✓ E. Symptoms generally develop before the age of 20 years

Catecholaminergic polymorphic ventricular tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a form of inherited cardiac disease associated with sudden cardiac death. It is inherited in an autosomal dominant fashion and has a prevalence of around 1:10,000.

Pathophysiology
- the most common cause is a defect in the ryanodine receptor (RYR2) which is found in the myocardial sarcoplasmic reticulum

Features
- exercise or emotion induced polymorphic ventricular tachycardia resulting in syncope
- sudden cardiac death
- symptoms generally develop before the age of 20 years

Management
- beta-blockers
- implantable cardioverter-defibrillator

Question 152 of 220

Which one of the following is least associated with aortic regurgitation?

- A. Rheumatic fever
- B. William's syndrome
- C. Syphilis
- D. Bicuspid aortic valve
- E. Post-rheumatic disease

Question 152 of 220

Which one of the following is least associated with aortic regurgitation?

- A. Rheumatic fever
- ✓ B. William's syndrome
- C. Syphilis
- D. Bicuspid aortic valve
- E. Post-rheumatic disease

William's syndrome is associated with supravalvular aortic stenosis.

Aortic regurgitation

Features
- early diastolic murmur
- collapsing pulse
- wide pulse pressure
- mid-diastolic Austin-Flint murmur in severe AR - due to partial closure of the anterior mitral valve cusps caused by the regurgitation streams

Causes (due to valve disease)
- rheumatic fever
- infective endocarditis
- connective tissue diseases e.g. RA/SLE
- bicuspid aortic valve

Causes (due to aortic root disease)
- aortic dissection
- spondylarthropathies (e.g. ankylosing spondylitis)
- hypertension
- syphilis
- Marfan's, Ehler-Danlos syndrome

Question 153 of 220

Which one of the following cardiac conditions is most associated with a louder murmur following the Valsalva manoeuvre?

A. Mitral stenosis

B. Aortic stenosis

C. Ventricular septal defect

D. Hypertrophic obstructive cardiomyopathy

E. Aortic regurgitation

Question 153 of 220

Which one of the following cardiac conditions is most associated with a louder murmur following the Valsalva manoeuvre?

- A. Mitral stenosis
- B. Aortic stenosis
- C. Ventricular septal defect
- ✓ D. Hypertrophic obstructive cardiomyopathy
- E. Aortic regurgitation

HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Features
- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

Associations
- Friedreich's ataxia
- Wolff-Parkinson White

Echo
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)
- mitral regurgitation

ECG
- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Question 154 of 220

Your next patient is a 74-year-old woman who is known to have type 2 diabetes mellitus. Her blood pressure has been borderline for a number of weeks now but you have decided she would benefit from treatment. Her latest blood pressure is 146/88 mmHg, HbA1c is 7.5% and her BMI is 25 kg/m^2. What is the most appropriate drug to prescribe?

- A. Bisoprolol
- B. Bendroflumethiazide
- C. Amlodipine
- D. Ramipril
- E. Orlistat

Question 154 of 220

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- C. Amlodipine
- ✓ D. Ramipril
- E. Orlistat

Hypertension in diabetics - ACE-inhibitors are first-line regardless of age

Diabetes mellitus: hypertension management

Hypertension is an added cardiovascular risk factor for diabetics and should therefore by actively looked for and treated. It is also a risk factor for the development of diabetic nephropathy.

Selected points

- the blood pressure target for diabetics is 140/80 mmHg. If there is end-organ damage the target is 130/80 mmHg
- ACE inhibitors are first-line*. Otherwise managed according to standard NICE hypertension guidelines
- the BNF advises to avoid the routine use of beta-blockers in uncomplicated hypertension, particularly when given in combination with thiazides, as they may cause insulin resistance, impair insulin secretion and alter the autonomic response to hypoglycaemia

*increase insulin sensitivity and can therefore theoretically cause hypoglycaemia - rarely clinically relevant

Question 155 of 220

Eight months after having a prosthetic heart valve a patient develops infective endocarditis. What is the most likely causative organism?

- A. *Streptococcus viridans*
- B. *Staphylococcus aureus*
- C. *Staphylococcus epidermidis*
- D. *Coxiella burnetii*
- E. One of the HACEK group

Question 155 of 220

Eight months after having a prosthetic heart valve a patient develops infective endocarditis. What is the most likely causative organism?

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- B. *Staphylococcus aureus*
- C. *Staphylococcus epidermidis*
- D. *Coxiella burnetii*
- E. One of the HACEK group

Most common cause of endocarditis:
- *Streptococcus viridans*
- *Staphylococcus epidermidis* if < 2 months post valve surgery

Staphylococcus epidermidis is the most common causative organism in the first two months following surgery. After this time the spectrum of organisms causing endocarditis returns to normal, with *Streptococcus viridans* being the most common organism

Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. Other factors include:
- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

Causes
- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

Culture negative causes
- prior antibiotic therapy
- *Coxiella burnetii*
- Bartonella
- Brucella
- HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in Staph aureus infections

Question 156 of 220

NICE have produced guidelines on the management of non-ST elevation myocardial infarction (NSTEMI) in which they recommend an approach to treatment based on risk assessment. What cut-off do they recommend for the use of coronary angiography within 96 hours in patients with a NSTEMI?

- A. All patients with a 12 month mortality risk of greater than 5%
- B. All patients with a 6 month mortality risk of greater than 5%
- C. All patients with a 12 month mortality risk of greater than 10%
- D. All patients with a 6 month mortality risk of greater than 1.5%
- E. All patients with a 6 month mortality risk of greater than 3%

Question 156 of 220

NICE have produced guidelines on the management of non-ST elevation myocardial infarction (NSTEMI) in which they recommend an approach to treatment based on risk assessment. What cut-off do they recommend for the use of coronary angiography within 96 hours in patients with a NSTEMI?

- A. All patients with a 12 month mortality risk of greater than 5%
- B. All patients with a 6 month mortality risk of greater than 5%
- C. All patients with a 12 month mortality risk of greater than 10%
- D. All patients with a 6 month mortality risk of greater than 1.5%
- ✓ E. All patients with a 6 month mortality risk of greater than 3%

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:
- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive
- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

Antithrombin treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

Clopidogrel 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

Coronary angiography should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

Aspirin	Antiplatelet - inhibits the production of thromboxane A2
Clopidogrel	Antiplatelet - inhibits ADP binding to its platelet receptor
Enoxaparin	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Fondaparinux	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Bivalirudin	Reversible direct thrombin inhibitor

Question 157 of 220

A 60-year-old man is admitted with severe central chest pain to the resus department. The admission ECG shows ST elevation in leads V1-V4 with reciprocal changes in the inferior leads. Which one of the following is most likely to account for these findings?

- A. 75% occlusion of the left anterior descending artery
- B. 75% occlusion of the left circumflex artery
- C. 75% occlusion of the right coronary artery
- D. 100% occlusion of the left circumflex artery
- E. 100% occlusion of the left anterior descending artery

Question 157 of 220

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- C. 75% occlusion of the right coronary artery
- D. 100% occlusion of the left circumflex artery
- ✓ E. 100% occlusion of the left anterior descending artery

Widespread ST elevation in this territory implies a complete occlusion of the left anterior descending artery.

ECG: ST elevation

Causes of ST elevation
- myocardial infarction
- pericarditis
- normal variant - 'high take-off'
- left ventricular aneurysm
- Prinzmetal's angina (coronary artery spasm)
- rare: subarachnoid haemorrhage, part of spectrum of changes in hyperkalaemia

Question 158 of 220

What is the normal cross sectional area of the mitral valve?

- A. 1-2 sq cm
- B. 3-4 sq cm
- C. 4-6 sq cm
- D. 6-8 sq cm
- E. 8-10 sq cm

Question 158 of 220

What is the normal cross sectional area of the mitral valve?

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- D. 6-8 sq cm
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Mitral stenosis

It is said that the causes of mitral stenosis are rheumatic fever, rheumatic fever and rheumatic fever. Rarer causes that may be seen in the MRCP include mucopolysaccharidoses, carcinoid and endocardial fibroelastosis

Features
- mid-diastolic murmur (best heard in expiration)
- loud S1, opening snap
- low volume pulse
- malar flush
- atrial fibrillation

Features of severe MS
- length of murmur increases
- opening snap becomes closer to S2

Echocardiography
- the normal cross sectional area of the mitral valve is 4-6 sq cm. A 'tight' mitral stenosis implies a cross sectional area of < 1 sq cm

Question 159 of 220

A 64-year-old man with a history of ischaemic heart disease and poor left ventricular function presents with a broad complex tachycardia of 140 bpm. On examination blood pressure is 110/74 mmHg. Fusion and capture beats are seen on the 12 lead ECG. What is the first line drug management?

- A. Sotalol
- B. Amiodarone
- C. Adenosine
- D. Flecainide
- E. Lidocaine

Question 159 of 220

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- C. Adenosine
- D. Flecainide
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The history of ischaemic heart disease combined with the presence of fusion and capture beats strongly suggests a diagnosis of ventricular tachycardia (VT). Whilst lidocaine can also be used in VT, amiodarone would be preferred given his history of poor left ventricular function. In the 2005 joint European Resuscitation Council and Resuscitation Council (UK) guidelines amiodarone is also considered first-line in a peri-arrest situation

Ventricular tachycardia: management

Whilst a broad complex tachycardia may result from a supraventricular rhythm with aberrant conduction, the European Resuscitation Council advise that in a peri-arrest situation it is assumed to be ventricular in origin

If the patient has adverse signs (systolic BP < 90 mmHg, chest pain, heart failure or rate > 150 beats/min) then immediate cardioversion is indicated. In the absence of such signs antiarrhythmics may be used. If these fail, then electrical cardioversion may be needed with synchronised DC shocks

Drug therapy

- amiodarone: ideally administered through a central line
- lidocaine: use with caution in severe left ventricular impairment
- procainamide

Verapamil should NOT be used in VT

If drug therapy fails

- electrophysiological study (EPS)
- implant able cardioverter-defibrillator (ICD) - this is particularly indicated in patients with significantly impaired LV function

Question 160 of 220

Each one of the following is associated with left axis deviation on ECG, except:

- A. Left anterior hemiblock
- B. Ostium primum ASD
- C. Left posterior hemiblock
- D. Obesity
- E. Left bundle branch block

Question 160 of 220

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- B. Ostium primum ASD
- ✓ C. Left posterior hemiblock
- D. Obesity
- E. Left bundle branch block

ECG: axis deviation

Causes of left axis deviation (LAD)
- left anterior hemiblock
- left bundle branch block
- Wolff-Parkinson-White syndrome* - right-sided accessory pathway
- hyperkalaemia
- congenital: ostium primum ASD, tricuspid atresia
- minor LAD in obese people

Causes of right axis deviation (RAD)
- right ventricular hypertrophy
- left posterior hemiblock
- chronic lung disease
- pulmonary embolism
- ostium secundum ASD
- Wolff-Parkinson-White syndrome* - left-sided accessory pathway
- normal in infant < 1 years old
- minor RAD in tall people

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

Question 161 of 220

Each one of the following may cause left bundle branch block, except:

- A. Cardiomyopathy
- B. Atrial septal defect
- C. Hypertension
- D. Idiopathic fibrosis
- E. Ischaemic heart disease

Question 161 of 220

Each one of the following may cause left bundle branch block, except:

- A. Cardiomyopathy
- ✓ B. Atrial septal defect
- C. Hypertension
- D. Idiopathic fibrosis
- E. Ischaemic heart disease

Atrial septal defects, both primum and secundum, are associated with right rather than left bundle branch block

ECG: LBBB

Causes of LBBB

- ischaemic heart disease
- hypertension
- cardiomyopathy
- idiopathic fibrosis

Question 162 of 220

A 34-year-old man is investigated following an unexplained collapse whilst at work. A resting ECG shows convex ST elevation in V1-V3 with a partial right bundle branch block pattern. What is the most likely diagnosis?

- A. Catecholaminergic polymorphic ventricular tachycardia
- B. Hypertrophic obstructive cardiomyopathy
- C. Arrhythmogenic right ventricular cardiomyopathy
- D. Brugada syndrome
- E. Normal variant

Question 162 of 220

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- B. Hypertrophic obstructive cardiomyopathy
- C. Arrhythmogenic right ventricular cardiomyopathy
- ✓ D. Brugada syndrome
- E. Normal variant

Brugada syndrome

Brugada syndrome is a form of inherited cardiovascular disease with may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

Pathophysiology
- a large number of variants exist
- around 20-40% of cases are caused by a mutation in the SCN5A gene which encodes the myocardial sodium ion channel protein

ECG changes
- convex ST elevation V1-V3
- partial right bundle branch block
- changes may be more apparent following flecainide

Management
- implantable cardioverter-defibrillator

Question 163 of 220

You have ordered a B-type natriuretic peptide (BNP) test on a patient with suspected heart failure. It has come back as being slightly elevated. Which one of the following factors may account for a falsely elevated BNP?

- A. ACE inhibitor therapy
- B. Beta-blocker therapy
- C. Furosemide therapy
- D. Obesity
- E. COPD

Question 163 of 220

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- B. Beta-blocker therapy
- C. Furosemide therapy
- D. Obesity
- ✓ E. COPD

Heart failure: diagnosis

NICE issued updated guidelines on diagnosis and management in 2010. The choice of investigation is determined by whether the patient has previously had a myocardial infarction or not.

Previous myocardial infarction
- arrange echocardiogram within 2 weeks

No previous myocardial infarction
- measure serum natriuretic peptides (BNP)
- if levels are 'high' arrange echocardiogram within 2 weeks
- if levels are 'raised' arrange echocardiogram within 6 weeks

Serum natriuretic peptides

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain. Very high levels are associated with a poor prognosis.

	BNP	**NTproBNP**
High levels	> 400 pg/ml (116 pmol/litre)	> 2000 pg/ml (236 pmol/litre)
Raised levels	100–400 pg/ml (29–116 pmol/litre)	400–2000 pg/ml (47–236 pmol/litre)
Normal levels	< 100 pg/ml (29 pmol/litre)	< 400 pg/ml (47 pmol/litre)

Factors which alter the BNP level:

Increase BNP levels	**Decrease BNP levels**
Left ventricular hypertrophy Ischaemia Tachycardia Right ventricular overload Hypoxaemia (including pulmonary embolism) GFR < 60 ml/min Sepsis COPD Diabetes Age > 70 Liver cirrhosis	Obesity Diuretics ACE inhibitors Beta-blockers Angiotensin 2 receptor blockers Aldosterone antagonists

Question 164 of 220

A 65-year-old man is discharged from hospital following a thrombolysed ST-elevation myocardial infarction. Other than a history of depression he has no past medical history of note. His stay on the coronary care unit was complicated by the development of dyspnoea and an echo show a reduced left ventricular ejection fraction. The patient was not given clopidogrel during his hospital admission. Other than standard treatment with an ACE inhibitor, beta-blocker, aspirin and statin, what other type of drug should he be taking?

- A. Angiotensin 2 receptor antagonist
- B. Potassium channel activator
- C. Aldosterone antagonist
- D. Thiazide diuretic
- E. Clopidogrel

Question 164 of 220

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- A. Angiotensin 2 receptor antagonist
- B. Potassium channel activator
- ✓ C. Aldosterone antagonist
- D. Thiazide diuretic
- E. Clopidogrel

An aldosterone antagonist is recommended by current NICE guidelines as the patient has a reduced left ventricular ejection fraction. If clopidogrel was given during the first 24 hours then it should be continued for the next 4 weeks

Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

Clopidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk is > 1.5%

Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

Question 165 of 220

The most common cause of restrictive cardiomyopathy in the UK is:

- A. Diabetes mellitus
- B. Systemic lupus erythematous
- C. Haemochromatosis
- D. Tuberculosis
- E. Amyloidosis

Question 165 of 220

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- A. Diabetes mellitus
- B. Systemic lupus erythematous
- C. Haemochromatosis
- D. Tuberculosis
- ✓ E. Amyloidosis

Restrictive cardiomyopathy: amyloid (most common), haemochromatosis, Loffler's syndrome, sarcoidosis, scleroderma

Restrictive cardiomyopathy

Features
- similar to constrictive pericarditis

Features suggesting restrictive cardiomyopathy rather than constrictive pericarditis
- prominent apical pulse
- absence of pericardial calcification on CXR
- heart may be enlarged
- ECG abnormalities e.g. bundle branch block, Q waves

Causes
- amyloidosis (e.g. secondary to myeloma) - most common cause in UK
- haemochromatosis
- Loffler's syndrome
- sarcoidosis
- scleroderma

Question 166 of 220

Which part of the ECG complex corresponds with the closure of the mitral valve?

- A. P wave
- B. PR interval
- C. QRS complex
- D. ST segment
- E. T wave

Question 166 of 220

Which part of the ECG complex corresponds with the closure of the mitral valve?

- A. P wave
- B. PR interval
- ✓ C. QRS complex
- D. ST segment
- E. T wave

A diagram of the cardiac cycle can be found on the external link

Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

S1
- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

S2
- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

S3
- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure, constrictive pericarditis

S4
- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Question 167 of 220

A 56-year-old man with a past history of ischaemic heart disease is admitted with central chest pain radiating to his left arm associated with nausea. On arrival in the Coronary Care Unit he is noted to be in complete heart block. Which coronary artery is likely to be affected?

- A. Circumflex
- B. Right coronary
- C. Obtuse marginal
- D. Left anterior descending
- E. Posterior descending

Question 167 of 220

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- A. Circumflex
- ✓ B. Right coronary
- C. Obtuse marginal
- D. Left anterior descending
- E. Posterior descending

The right coronary artery supplies the atrioventricular node in 90% of patients

Coronary circulation

Arterial supply of the heart
- posterior aortic sinus --> left coronary artery (LCA)
- anterior aortic sinus --> right coronary artery (RCA)
- LCA --> LAD + circumflex
- RCA --> posterior descending
- RCA supplies SA node in 60%, AV node in 90%

Venous drainage of the heart
- coronary sinus drains into the right atrium

Question 168 of 220

A 42-year-old man of Afro-Caribbean origin is diagnosed as having hypertension. Secondary causes of hypertension have been excluded. What is the most appropriate initial drug therapy?

- A. Losartan
- B. Bisoprolol
- C. Doxazosin
- D. Perindopril
- E. Amlodipine

Question 168 of 220

A 42-year-old man of Afro-Caribbean origin is diagnosed as having hypertension. Secondary causes of hypertension have been excluded. What is the most appropriate initial drug therapy?

- A. Losartan
- B. Bisoprolol
- C. Doxazosin
- D. Perindopril
- ✓ E. Amlodipine

ACE inhibitors have reduced efficacy in black patients and are therefore not used first-line

Hypertension: management

NICE published updated guidelines for the management of hypertension in June 2006

Initial drug choice
- patients < 55-years-old: ACE inhibitor
- patients > 55-years-old or of Afro-Caribbean origin: calcium channel blocker or thiazide diuretic

The target blood pressure is 140/90 mmHg. For diabetics the target is 140/80 mmHg (or 130/80 mmHg if end-organ damage is present)

If this fails to control the blood pressure then use a combination of an ACE inhibitor plus either a calcium channel blocker or thiazide diuretic

If this still fails then a combination of an ACE inhibitor + calcium channel blocker + thiazide diuretic should be used

Following this further diuretic therapy, alpha blockers or beta blockers should be considered

New drugs

Direct renin inhibitors
- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Question 169 of 220

A 62-year-old female with a known history of a sigmoid adenocarcinoma is admitted to hospital with shortness of breath and pyrexia. On examination a murmur is heard and an echo reveals a vegetation on the aortic valve. Which one of the following organisms is most characteristically associated with causing infective endocarditis in patients with colorectal cancer?

- A. *Escherichia coli*
- B. *Enterococcus faecalis*
- C. *Salmonella*
- D. *Campylobacter*
- E. *Streptococcus bovis*

Question 169 of 220

A 62-year-old female with a known history of a sigmoid adenocarcinoma is admitted to hospital with shortness of breath and pyrexia. On examination a murmur is heard and an echo reveals a vegetation on the aortic valve. Which one of the following organisms is most characteristically associated with causing infective endocarditis in patients with colorectal cancer?

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- B. *Enterococcus faecalis*
- C. *Salmonella*
- D. *Campylobacter*
- ✓ E. *Streptococcus bovis*

Streptococcus bovis endocarditis is associated with colorectal cancer

Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. Other factors include:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- Bartonella
- Brucella
- HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in Staph aureus infections

Question 170 of 220

A 17-year-old girl with Turner's syndrome is reviewed in the cardiology clinic. Other than coarctation of the aorta, what is the most common cardiac abnormality found in patients with Turner's syndrome?

- A. Ventricular septal defect
- B. Bicuspid aortic valve
- C. Aortic stenosis
- D. Pulmonary stenosis
- E. Partial anomalous venous drainage

Question 170 of 220

A 17-year-old girl with Turner's syndrome is reviewed in the cardiology clinic. Other than coarctation of the aorta, what is the most common cardiac abnormality found in patients with Turner's syndrome?

- A. Ventricular septal defect
- ✓ B. Bicuspid aortic valve
- C. Aortic stenosis
- D. Pulmonary stenosis
- E. Partial anomalous venous drainage

Up to 15% of adults with Turner's syndrome have bicuspid aortic valves

Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features
- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 171 of 220

A 61-year-old man is admitted with central crushing chest pain to the Emergency Department. An ECG taken immediately on arrival shows ST-elevation in leads II, III and aVF. His only past medical history of note is hypertension for which he takes ramipril, aspirin and simvastatin. What is the optimum management of this patient?

- A. Aspirin + clopidogrel + LMWH + repeat ECG in 20 minutes
- B. Clopidogrel + LMWH + alteplase
- C. Aspirin + clopidogrel + LMWH + tenecteplase
- D. Aspirin + clopidogrel + LMWH + alteplase
- E. Aspirin + clopidogrel + IV heparin + immediate percutaneous coronary intervention

Question 171 of 220

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- D. Aspirin + clopidogrel + LMWH + alteplase
- ✓ E. Aspirin + clopidogrel + IV heparin + immediate percutaneous coronary intervention

Primary percutaneous coronary intervention is the gold-standard treatment for ST-elevation myocardial infarction

Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given
- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:
- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:
- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation
- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Question 172 of 220

Which one of the following drugs is best avoided in patients with hypertrophic obstructive cardiomyopathy?

A. Amiodarone

B. Verapamil

C. Ramipril

D. Amoxicillin

E. Atenolol

Question 172 of 220

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- B. Verapamil
- ✓ C. Ramipril
- D. Amoxicillin
- E. Atenolol

HOCM - drugs to avoid: nitrates, ACE-inhibitors, inotropes

Verapamil should however be avoided in patients with coexistent Wolff-Parkinson White as it may precipitate VT or VF

HOCM: management

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

Management
- **A**miodarone
- **B**eta-blockers or verapamil for symptoms
- **C**ardioverter defibrillator
- **D**ual chamber pacemaker
- **E**ndocarditis prophylaxis*

Drugs to avoid
- nitrates
- ACE-inhibitors
- inotropes

Question 173 of 220

A 24-year-old female develops transient slurred speech following a flight from Australia to the United Kingdom. Both a CT head and ECG are normal. Which one of the following tests is most likely to reveal the underlying cause?

- A. Transoesophageal echo
- B. MRI brain
- C. Carotid USS Doppler
- D. Cerebral angiogram
- E. Transthoracic echo

Question 173 of 220

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- C. Carotid USS Doppler
- D. Cerebral angiogram
- E. Transthoracic echo

Paradoxical embolus - PFO most common cause - do TOE

Transesophageal echocardiography provides superior views of the atrial septum and therefore is preferred to transthoracic echocardiography for detecting patent foramen ovale

Paradoxical embolisation

For a right-sided thrombus (e.g. DVT) to cause a left-sided embolism (e.g. stroke) it must obviously pass from the right-to-left side of the heart

The following cardiac lesions may cause such events

- patent foramen ovale - present in around 20% of the population
- atrial septal defect - a much less common cause

Question 174 of 220

A 75-year-old woman is reviewed following a 'collapse' yesterday. Her husband found her unconscious on the bathroom floor and describes her 'quickly coming round'. In patients of this age group, what is the most common cause of syncope?

- A. Orthostatic syncope
- B. Cardiac syncope
- C. Reflex syncope
- D. Drug-induced syncope
- E. Unexplained

Question 174 of 220

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- B. Cardiac syncope
- ✓ C. Reflex syncope
- D. Drug-induced syncope
- E. Unexplained

Syncope

Syncope may be defined as a transient loss of consciousness due to global cerebral hypoperfusion with rapid onset, short duration and spontaneous complete recovery. Note how this definition excludes other causes of collapse such as epilepsy.

The European Society of Cardiology published guidelines in 2009 on the investigation and management of syncope. They suggested the following classification:

Reflex syncope (neurally mediated)
- vasovagal: triggered by emotion, pain or stress. Often referred to as 'fainting'
- situational: cough, micturition, gastrointestinal
- carotid sinus syncope

Orthostatic syncope
- primary autonomic failure: Parkinson's disease, Lewy body dementia
- secondary autonomic failure: e.g. Diabetic neuropathy, amyloidosis, uraemia
- drug-induced: diuretics, alcohol, vasodilators
- volume depletion: haemorrhage, diarrhoea

Cardiac syncope
- arrhythmias: bradycardias (sinus node dysfunction, AV conduction disorders) or tachycardias (supraventricular, ventricular)
- structural: valvular, myocardial infarction, hypertrophic obstructive cardiomyopathy
- others: pulmonary embolism

Reflex syncope is the most common cause in all age groups although orthostatic and cardiac causes become more common in older patients.

Evaluation
- cardiovascular examination
- postural blood pressure readings: a symptomatic fall in systolic BP > 20 mmHg or diastolic BP > 10 mmHg or decrease in systolic BP < 90 mmHg is considered diagnostic
- ECG
- carotid sinus massage
- tilt table test
- 24 hour ECG

Question 175 of 220

Which part of the jugular venous waveform is associated with the opening of the tricuspid valve?

- A. x descent
- B. v wave
- C. a wave
- D. c wave
- E. y descent

Question 175 of 220

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- C. a wave
- D. c wave
- ✓ E. y descent

JVP: y descent = opening of tricuspid valve

Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis

'a' wave = atrial contraction
- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves
- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave
- closure of tricuspid valve
- not normally visible

'v' wave
- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Question 176 of 220

Where is the most common site for primary cardiac tumours to occur in adults?

- A. Left atrium
- B. Right ventricle
- C. Right atrium
- D. Left atrial appendage
- E. Left ventricle

Question 176 of 220

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- ✓ A. Left atrium
- B. Right ventricle
- C. Right atrium
- D. Left atrial appendage
- E. Left ventricle

Atrial myxoma - commonest site = left atrium

The most common site of atrial myxomas is at the fossa ovalis border in the left atrium

Atrial myxoma

Overview
- 75% occur in left atrium
- more common in females

Features
- systemic: weight loss, fever, clubbing
- emboli
- atrial fibrillation
- mid-diastolic murmur, 'tumour plop'

Question 177 of 220

A 58-year-old man presents to the Emergency Department following an episode of transient right-sided weakness which lasted approximately 20 minutes. He has had two previous episodes of a similar nature. On examination he is found to be in atrial fibrillation at a rate of 80 bpm

CT head normal

What is the most suitable immediate management?

- A. Digoxin
- B. Aspirin 300mg od + dipyridamole 200mg bd
- C. Aspirin 300mg od
- D. Sotalol
- E. Warfarin

Question 177 of 220

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Whilst this patient is suitable for warfarin treatment in the long-term the question asks about initial management. As he has had a transient ischaemic attack an antiplatelet agent should be given whilst a decision is being made regarding anticoagulation.

The optimal timing of commencing warfarin in this situation is not clear, but the current NICE guidelines recommend waiting 2 weeks following a disabling ischaemic stroke in patients with associated atrial fibrillation

Atrial fibrillation: anticoagulation

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006

The guidelines suggest a stroke risk stratification approach when determining how to anticoagulate a patient, as detailed below:

Low risk - annual risk of stroke = 1%	**Moderate risk** - annual risk of stroke = 4%	**High risk** - annual risk of stroke = 8-12%
• age < 65 years with no moderate or high risk factors • use aspirin	• age > 65 years with no high risk factors, or: • age < 75 years with diabetes, hypertension or cardiovascular disease • use aspirin or warfarin depending on individual circumstances	• age > 75 years with diabetes, hypertension or cardiovascular disease • previous TIA, ischaemic stroke or thromboembolic event • valve disease, heart failure or impaired left ventricular function • use warfarin

An alternative approach is the **CHADS2** score:

	Condition	**Points**
C	Congestive heart failure	1
H	Hypertension (or treated hypertension)	1
A	Age > 75 years	1
D	Diabetes	1
S2	Prior Stroke or TIA	2

The table below shows a suggested anticoagulation strategy based on the score:

Score	**Anticoagulation**
0	Aspirin
1	Aspirin or warfarin, depending on patient preference and individual factors
2-6	Warfarin if not contraindicated

Question 178 of 220

A 49-year-old man with idiopathic pulmonary arterial hypertension has a negative acute vasodilator test. Which one of the following medications is least likely to be beneficial in his long-term management?

- A. Nifedipine
- B. Treprostinil
- C. Bosentan
- D. Sildenafil
- E. Warfarin

Question 178 of 220

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- ✓ A. Nifedipine
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- C. Bosentan
- D. Sildenafil
- E. Warfarin

Oral calcium channel blockers are unlikely to be beneficial following a negative acute vasodilator test

Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

Features
- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing
- oral calcium channel blockers

If there is a negative response to acute vasodilator testing
- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Question 179 of 220

A 51-year-old man presents four weeks after being discharged from hospital. He had been admitted with chest pain and thrombolysed for a myocardial infarction. This morning he developed marked tongue and facial swelling. Which one of the following drugs is most likely to be responsible?

- A. Atorvastatin
- B. Isosorbide mononitrate
- C. Atenolol
- D. Aspirin
- E. Ramipril

Question 179 of 220

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- C. Atenolol
- D. Aspirin
- ✓ E. Ramipril

ACE inhibitors are the most common cause of drug-induced angioedema.

Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are now the established first-line treatment in younger patients with hypertension and are also extensively used to treat heart failure. They are known to be less effective in treating hypertensive Afro-Caribbean patients. ACE inhibitors are also used to treat diabetic nephropathy and have a role in secondary prevention of ischaemic heart disease.

Mechanism of action:
- inhibit the conversion angiotensin I to angiotensin II

Side-effects:
- cough: occurs in around 15% of patients and may occur up to a year after starting treatment. Thought to be due to increased bradykinin levels
- angioedema: may occur up to a year after starting treatment
- hyperkalaemia
- first-dose hypotension: more common in patients taking diuretics

Cautions and contraindications
- pregnancy and breastfeeding - avoid
- renovascular disease - significant renal impairment may occur in patients who have undiagnosed bilateral renal artery stenosis
- aortic stenosis - may result in hypotension
- patients receiving high-dose diuretic therapy (more than 80 mg of furosemide a day) - significantly increases the risk of hypotension
- hereditary of idiopathic angioedema

Monitoring
- urea and electrolytes should be checked before treatment is initiated and after increasing the dose
- a rise in the creatinine and potassium may be expected after starting ACE inhibitors. Acceptable changes are an increase in serum creatinine, up to 30%* from baseline and an increase in potassium up to 5.5 mmol/l*.

*Renal Association UK, Clinical Knowledge Summaries quote 50% which seems rather high. SIGN advise that the fall in eGFR should be less than 20%. The NICE CKD guidelines suggest that a decrease in eGFR of up to 25% or a rise in creatinine of up to 30% is acceptable

Question 180 of 220

An 82-year-old man is reviewed. He is known to have ischaemic heart disease and is still getting regular attacks of angina despite taking atenolol 100mg od. Examination of his cardiovascular system is unremarkable with a pulse of 72 bpm and a blood pressure of 148/92 mmHg. What is the most appropriate next step in management?

- A. Add verapamil 80mg tds
- B. Add nicorandil 10mg bd
- C. Add diltiazem 60mg tds
- D. Add nifedipine MR 30mg od
- E. Add isosorbide mononitrate 30mg bd

Question 180 of 220

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- B. Add nicorandil 10mg bd
- C. Add diltiazem 60mg tds
- ✓ D. Add nifedipine MR 30mg od
- E. Add isosorbide mononitrate 30mg bd

There are no clear guidelines to indicate which is the best second-line treatment for stable angina. However, a logical choice would be to add nifedipine as this would also help lower his blood pressure. Verapamil is contraindicated whilst taking a beta-blocker and diltiazem should be used with caution due to the risk of bradycardia. Please see the SIGN guidelines for further details.

The starting dose of isosorbide mononitrate is 10mg bd.

Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery.

Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- beta-blocker is the preferred initial treatment. For patients unable to take a beta-blocker there is no clear guidelines on the best alternative. Options include a rate-limiting calcium-channel blocker (verapamil or diltiazem); a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine); a nitrate; or a potassium-channel activator
- if there is a poor response to initial treatment then the beta-blocker should be increased to the maximum tolerated dose (e.g. atenolol 100mg od)
- again, there is no clear guidelines on the next step treatment. CKS advise adding a long-acting dihydropyridine (e.g. nifedipine) although other options include isosorbide mononitrate and nicorandil

Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Question 181 of 220

A 30-year-old woman is admitted to the Emergency Department following the acute onset of palpitations. Blood pressure is 124/84 mmHg and her pulse is 150/min. An ECG shows a narrow complex tachycardia. Intravenous access is gained and 6mg of adenosine is given with no effect. What is the most appropriate next step?

- A. Intravenous adenosine 12 mg
- B. Intravenous adenosine 6mg
- C. Intravenous verapamil 2.5-5 mg
- D. Radio-frequency ablation
- E. Electrical cardioversion

Question 181 of 220

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- B. Intravenous adenosine 6mg
- C. Intravenous verapamil 2.5-5 mg
- D. Radio-frequency ablation
- E. Electrical cardioversion

A further dose of adenosine should be given if there is no response to the initial injection. Please see the Resuscitation Council (UK) link for further details.

Supraventricular tachycardia

Whilst strictly speaking the term supraventricular tachycardia (SVT) refers to any tachycardia that is not ventricular in origin the term is generally used in the context of paroxysmal SVT. Episodes are characterised by the sudden onset of a narrow complex tachycardia, typically an atrioventricular nodal re-entry tachycardia (AVNRT). Other causes include atrioventricular re-entry tachycardias (AVRT) and junctional tachycardias.

Acute management
- vagal manoeuvres: e.g. Valsalva manoeuvre
- intravenous adenosine: contraindicated in asthmatics - verapamil is a preferable option
- electrical cardioversion

Prevention of episodes
- beta-blockers
- radio-frequency ablation

Question 182 of 220

Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

A. Prolonged PR interval

B. Positive serology for *Coxiella burnetii*

C. Fever > 38ºC

D. Roth spots

E. Positive microbiology from embolic fragments

Question 182 of 220

Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

- ✓ A. Prolonged PR interval
- B. Positive serology for *Coxiella burnetii*
- C. Fever > 38ºC
- D. Roth spots
- E. Positive microbiology from embolic fragments

A prolonged PR interval is part of the diagnostic criteria of rheumatic fever. The modified Duke criteria have now been adopted in the latest guidelines from the European Society of Cardiology. Details can be found in the link below

Infective endocarditis: Modified Duke criteria

Infective endocarditis diagnosed if
- pathological criteria positive, or
- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

Pathological criteria

Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments or intracardiac abscess content)

Major criteria

Positive blood cultures
- two positive blood cultures showing typical organisms consistent with infective endocarditis, such as *Streptococcus viridans* and the HACEK group, or
- persistent bacteraemia from two blood cultures taken > 12 hours apart or three or more positive blood cultures where the pathogen is less specific such as Staph aureus and Staph epidermidis, or
- positive serology for *Coxiella burnetii*, Bartonella species or *Chlamydia psittaci*, or
- positive molecular assays for specific gene targets

Evidence of endocardial involvement
- positive echocardiogram (oscillating structures, abscess formation, new valvular regurgitation or dehiscence of prosthetic valves), or
- new valvular regurgitation

Minor criteria
- predisposing heart condition or intravenous drug use
- microbiological evidence does not meet major criteria
- fever > 38ºC
- vascular phenomena: major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae or purpura
- immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots, Janeway lesions
- elevated ESR or CRP

Question 183 of 220

A 55-year old man with a history of ischaemic heart disease presents to the Emergency Department with palpitations for the past 10 days. Examination of his pulse reveals a rate of 130 bpm which is irregularly irregular. He has had one previous episode of atrial fibrillation 3 months ago which was terminated by elective cardioversion following warfarinisation. What term best describes his arrhythmia?

- A. Paroxysmal atrial fibrillation
- B. Atrial flutter
- C. Permanent atrial fibrillation
- D. Persistent atrial fibrillation
- E. Secondary atrial fibrillation

Question 183 of 220

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- C. Permanent atrial fibrillation
- ✓ D. Persistent atrial fibrillation
- E. Secondary atrial fibrillation

Atrial fibrillation: classification

An attempt was made in the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines to simplify and clarify the classification of atrial fibrillation (AF).

It is recommended that AF be classified into 3 patterns:

- first detected episode (irrespective of whether it is symptomatic or self-terminating)
- recurrent episodes, when a patient has 2 or more episodes of AF. If episodes of AF terminate spontaneously then the term **paroxysmal AF** is used. Such episodes last less than 7 days (typically < 24 hours). If the arrhythmia is not self-terminating then the term **persistent AF** is used. Such episodes usually last greater than 7 days
- in **permanent AF** there is continuous atrial fibrillation which cannot be cardioverted or if attempts to do so are deemed inappropriate. Treatment goals are therefore rate control and anticoagulation if appropriate

Question 184 of 220

A 67-year-old man is admitted with palpitations. During examination of his JVP he is noted to have regular cannon waves. Which one of the following arrhythmias is most likely to be responsible for this finding?

- A. Atrio-ventricular nodal re-entry tachycardia
- B. Atrial fibrillation
- C. Atrial flutter
- D. Complete heart block
- E. Ventricular fibrillation

Question 184 of 220

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- B. Atrial fibrillation
- C. Atrial flutter
- D. Complete heart block
- E. Ventricular fibrillation

Atrio-ventricular nodal re-entry tachycardia and ventricular tachycardia with 1:1 ventricular-atrial conduction may produce regular cannon waves. Complete heart block causes irregular cannon waves

JVP: cannon waves

Caused by the right atrium contracting against a closed tricuspid valve. May be subdivided into regular or intermittent

Regular cannon waves
- ventricular tachycardia (with 1:1 ventricular-atrial conduction)
- atrio-ventricular nodal re-entry tachycardia (AVNRT)

Irregular cannon waves
- complete heart block

Question 185 of 220

A 29-year-old man with myotonic dystrophy has an electrocardiogram. Which one of the following findings is most likely to be present?

- A. Wide QRS complex
- B. Atrial fibrillation
- C. Voltage criteria for left ventricular hypertrophy
- D. Right axis deviation
- E. Prolonged PR interval

Question 185 of 220

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- B. Atrial fibrillation
- C. Voltage criteria for left ventricular hypertrophy
- D. Right axis deviation
- ✓ E. Prolonged PR interval

A prolonged PR interval is seen in around 20-40% of patients

Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics
- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	**DM2**
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features
- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features
- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Question 186 of 220

Which of the following is a cause of a loud second heart sound?

- A. Aortic regurgitation
- B. Ventricular septal defect
- C. Systemic hypertension
- D. Aortic stenosis
- E. Mitral stenosis

Question 186 of 220

Which of the following is a cause of a loud second heart sound?

- A. Aortic regurgitation
- B. Ventricular septal defect
- ✓ C. Systemic hypertension
- D. Aortic stenosis
- E. Mitral stenosis

Second heart sound (S2)
- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2
- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2
- aortic stenosis

Causes of fixed split S2
- atrial septal defect

Causes of a widely split S2
- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)
- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

Question 187 of 220

Which of the following is least associated with a poor prognosis in hypertrophic cardiomyopathy?

- A. Non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- B. Reduced left ventricular outflow gradient
- C. Family history of sudden death
- D. Syncope
- E. Early age at presentation

Question 187 of 220

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- ✓ B. Reduced left ventricular outflow gradient
- C. Family history of sudden death
- D. Syncope
- E. Early age at presentation

There is no recognised prognostic association with left ventricular outflow gradient

HOCM: prognostic factors

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

Question 188 of 220

A 76-year-old woman is admitted to the resus department after collapsing whilst shopping. The paramedics report she is hypotensive and tachycardia. Initial observations include a heart rate of 160 bpm and a blood pressure of 98 / 60 mmHg. A 12 lead ECG shows a broad complex tachycardia. Which one of the following features on the ECG would suggest a ventricular tachycardia rather than a supraventricular tachycardia with aberrant conduction?

- A. QRS < 160 ms
- B. A corrected QT interval of 420ms
- C. Atrioventricular dissociation
- D. Marked right axis deviation
- E. Heart rate of 160 bpm

Question 188 of 220

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- A. QRS < 160 ms
- B. A corrected QT interval of 420ms
- ✓ C. Atrioventricular dissociation
- D. Marked right axis deviation
- E. Heart rate of 160 bpm

Broad complex tachycardia

Features suggesting VT rather than SVT with aberrant conduction

- AV dissociation
- fusion or capture beats
- positive QRS concordance in chest leads
- marked left axis deviation
- history of IHD
- lack of response to adenosine or carotid sinus massage
- QRS > 160 ms

Question 189 of 220

A 53-year-old man is reviewed in the cardiology clinic with a history of chest pain and syncope. On examination he has an ejection systolic murmur radiating to the carotid area. What is the most likely cause of his symptoms?

- A. Bicuspid aortic valve
- B. Aortic root abscess
- C. Post rheumatic fever
- D. Posterior myocardial infarction
- E. Calcification of the aortic valve

Question 189 of 220

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- C. Post rheumatic fever
- D. Posterior myocardial infarction
- E. Calcification of the aortic valve

Aortic stenosis - most common cause:
- young patients: bicuspid aortic valve
- elderly patients: calcification

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 190 of 220

A 60-year-old man is investigated for progressive shortness of breath. On examination a loud P2 is noted associated with a left parasternal heave. An ECG shows evidence of right ventricular strain and a diagnosis of pulmonary hypertension is suspected. Which one of the following is the single most important test to confirm the diagnosis?

- A. Echocardiography
- B. High resolution CT thorax
- C. Cardiac catheterisation
- D. Pulmonary angiography
- E. Ventilation perfusion scanning

Question 190 of 220

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- A. Echocardiography
- B. High resolution CT thorax
- ✓ C. Cardiac catheterisation
- D. Pulmonary angiography
- E. Ventilation perfusion scanning

Whilst echocardiography may strongly point towards a diagnosis of pulmonary hypertension all patients need to have right heart pressures measured. Cardiac catheterisation is therefore the single most important investigation. Please see the British Thoracic Society guidelines for more details.

Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

Features
- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing
- oral calcium channel blockers

If there is a negative response to acute vasodilator testing
- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Question 191 of 220

Which one of the following clinical signs would best indicate severe calcified aortic stenosis?

- A. Loudness of murmur
- B. Loud second heart sound
- C. Radiation to the carotids
- D. Hypertension
- E. Displaced apex beat

Question 191 of 220

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- B. Loud second heart sound
- C. Radiation to the carotids
- D. Hypertension
- ✓ E. Displaced apex beat

The apex beat is not normally displaced in aortic stenosis. Displacement would indicate left ventricular dilatation and hence severe disease

Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 192 of 220

A 75-year-old woman is brought to the Emergency Department by her family. She has been getting more short-of-breath over the last 6 weeks and says her energy levels are low. An ECG on shows atrial fibrillation at a rate of 114 / min. Blood pressure is 128/80 mmHg and a chest x-ray is unremarkable. What is the appropriate drug to control the heart rate?

- A. Felodipine
- B. Amiodarone
- C. Digoxin
- D. Flecainide
- E. Bisoprolol

Question 192 of 220

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- C. Digoxin
- D. Flecainide
- ✓ E. Bisoprolol

Atrial fibrillation: rate control - beta blockers preferable to digoxin

This question reiterates an important point which frequently comes up in exams - digoxin is no longer first-line for rate control in atrial fibrillation. Her shortness-of-breath is likely to be rate related and does not necessarily mean that she is in heart failure. This is supported by a normal chest x-ray.

Please see the NICE guidelines for further information.

Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2002 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
• Older than 65 years • History of ischaemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 193 of 220

Each one of the following is associated with aortic dissection, except:

- A. Ventricular septal defect
- B. Turner's syndrome
- C. Noonan's syndrome
- D. Pregnancy
- E. Marfan's syndrome

Question 193 of 220

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- B. Turner's syndrome
- C. Noonan's syndrome
- D. Pregnancy
- E. Marfan's syndrome

Aortic dissection

Aortic dissection may be classified as type A or B:
- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

Associations
- hypertension
- trauma
- bicuspid aortic valve
- collagens: Marfan's syndrome, Ehlers-Danlos syndrome
- Turner's and Noonan's syndrome
- pregnancy
- syphilis

Complications of backward tear
- aortic incompetence/regurgitation
- MI: inferior pattern often seen due to right coronary involvement

Complications of forward tear
- unequal arm pulses and BP
- stroke
- renal failure

Question 194 of 220

A 62-year-old man who had a mechanical mitral valve replacement four years ago is reviewed. What long term antithrombotic therapy is he likely to be taking?

- A. Nothing
- B. Warfarin
- C. Aspirin
- D. Aspirin + clopidogrel for the first 12 months
- E. Warfarin + aspirin

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- D. Aspirin + clopidogrel for the first 12 months
- ✓ E. Warfarin + aspirin

Prosthetic heart valves - antithrombotic therapy:
- bioprosthetic: aspirin
- mechanical: warfarin + aspirin

Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	**Mechanical valves**
Usually bovine or porcine in origin Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays Mechanical valves have a low failure rate Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication. Target INR • aortic: 2.0-3.0 • mitral: 2.5-3.5

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Question 195 of 220

You are considering prescribing an antibiotic to a 28-year-old man who tells you he has Long QT syndrome. Which antibiotic is it most important to avoid?

- A. Doxycycline
- B. Trimethoprim
- C. Erythromycin
- D. Rifampicin
- E. Co-amoxiclav

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Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than marked left axis deviation in males and 450 ms in females.

Causes of a prolonged QT interval

Congenital	**Drugs**	**Other**
• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel) • Romano-Ward syndrome (no deafness)	• amiodarone, sotalol, class 1a antiarrhythmic drugs • tricyclic antidepressants, fluoxetine • chloroquine • terfenadine* • erythromycin	• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia • acute myocardial infarction • myocarditis • hypothermia • subarachnoid haemorrhage

Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 196 of 220

A 52-year-old man is admitted to the Emergency Department. He was found collapsed by neighbours. An ECG on arrival shows torsades de pointes. Which one of his medications is most likely to have contributed to this presentation?

- A. Bisoprolol
- B. Cimetidine
- C. Risperidone
- D. Phenytoin
- E. Doxycycline

Question 196 of 220

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- A. Bisoprolol
- B. Cimetidine
- ✓ C. Risperidone
- D. Phenytoin
- E. Doxycycline

Torsades de pointes

Torsades de pointes ('twisting of the points') is a rare arrhythmia associated with a long QT interval. It may deteriorate into ventricular fibrillation and hence lead to sudden death

Causes of long QT interval

- congenital: Jervell-Lange-Nielsen syndrome, Romano-Ward syndrome
- antiarrhythmics: amiodarone, sotalol, class 1a antiarrhythmic drugs
- tricyclic antidepressants
- antipsychotics
- chloroquine
- terfenadine
- erythromycin
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- myocarditis
- hypothermia
- subarachnoid haemorrhage

Management

- IV magnesium sulphate

Question 197 of 220

A 58-year-old man who is taking lithium for bipolar disorder presents for review. During routine examination he found to be hypertensive with a blood pressure of 166/82 mmHg. This is confirmed with two separate readings. Urine dipstick is negative and renal function is normal. What is the most appropriate medication to start?

- A. Amlodipine
- B. Ramipril
- C. Losartan
- D. Bendroflumethiazide
- E. Doxazosin

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- D. Bendroflumethiazide
- E. Doxazosin

Diuretics, ACE-inhibitors and angiotensin II receptor antagonists may cause lithium toxicity. The BNF advises that neurotoxicity may be increased when lithium is given with diltiazem or verapamil but there is no significant interaction with amlodipine. Alpha-blockers are not listed as interacting with lithium but they would not be first-line treatment for hypertension.

The NICE hypertension guidelines suggest amlodipine wouldn't be a bad first choice, even if we ignore his lithium treatment.

Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 198 of 220

Which of the following is least associated with primary pulmonary hypertension?

- A. HIV
- B. Fenfluramine
- C. Recurrent pulmonary embolism
- D. Loud P2
- E. Right ventricular heave

Question 198 of 220

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Recurrent pulmonary embolism is a cause of secondary pulmonary hypertension

Some *Candida*tes have questioned whether HIV, cocaine and fenfluramine should be regarded as secondary causes of pulmonary hypertension. This is a fair point and the situation should be improved with the new classification of pulmonary hypertension. However, faced with this question in the exam the correct answer would be recurrent pulmonary embolism - a classical cause of secondary pulmonary hypertension

Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)
- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

Features
- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

Management
- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

Question 199 of 220

A 71-year-old man who had rheumatic fever as a child is admitted to the cardiology ward with suspected infective endocarditis. This is confirmed by blood cultures and echocardiography. Which one of the following is most likely to be represent a need for surgical intervention?

- A. A septic embolism in the right kidney
- B. Persistent pyrexia after 48 hours of antibiotics
- C. Lengthening of the PR interval on ECG
- D. Pre-existing left ventricular impairment
- E. *Streptococcus viridans* isolated on blood cultures

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- D. Pre-existing left ventricular impairment
- E. *Streptococcus viridans* isolated on blood cultures

Lengthening of the PR interval is likely to represent an aortic root abscess which will require surgical intervention.

Infective endocarditis: prognosis and management

Poor prognostic factors
- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism
- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)
- initial blind therapy - flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
- initial blind therapy if prosthetic valve is present or patient is penicillin allergic - vancomycin + rifampicin + gentamicin
- endocarditis caused by staphylococci - flucloxacillin (vancomycin + rifampicin if penicillin allergic or MRSA)
- endocarditis caused by streptococci - benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

Indications for surgery
- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Question 200 of 220

Which one of the following treatments is not appropriate in the management of Wolff-Parkinson White?

- A. Verapamil
- B. Sotalol
- C. Amiodarone
- D. Flecainide
- E. Radiofrequency ablation of the accessory pathway

Question 200 of 220

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- E. Radiofrequency ablation of the accessory pathway

Verapamil and digoxin should be avoided in patients with Wolff-Parkinson White as they may precipitate VT or VF

Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:
- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway*
- right axis deviation if left-sided accessory pathway*

Differentiating between type A and type B
- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW
- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management
- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol**, amiodarone, flecainide

*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

**sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Question 201 of 220

Which one of the following statements regarding arrhythmogenic right ventricular cardiomyopathy is correct?

- A. Inherited in an autosomal recessive pattern
- B. It is now the most common cause of sudden cardiac death in the UK
- C. All patients should have an implantable cardioverter defibrillator fitted
- D. It is characterised by fibrofatty infiltration of the right ventricular myocardium
- E. Naxos disease is the association of arrhythmogenic right ventricular cardiomyopathy with deafness

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- E. Naxos disease is the association of arrhythmogenic right ventricular cardiomyopathy with deafness

Drug therapy is used in patients with well tolerated or non life-threatening ventricular arrhythmias.

Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a form of inherited cardiovascular disease which may present with syncope or sudden cardiac death. It is generally regarded as the second most common cause of sudden cardiac death in the young after hypertrophic cardiomyopathy.

Pathophysiology
- inherited in an autosomal dominant pattern with variable expression
- the right ventricular myocardium is replaced by fibrofatty tissue

Presentation
- palpitations
- syncope
- sudden cardiac death

Investigation
- ECG abnormalities in V1-3, typically T wave inversion. An epsilon wave is found in about 50% of those with ARV - this is best described as a terminal notch in the QRS complex
- echo changes are often subtle in the early stages but may show an enlarged, hypokinetic right ventricle with a thin free wall
- magnetic resonance imaging is useful to show fibrofatty tissue

Management
- drugs: sotalol is the most widely used antiarrhythmic
- catheter ablation to prevent ventricular tachycardia
- implantable cardioverter-defibrillator

Naxos disease
- an autosomal recessive variant of ARVC
- a triad of ARVC, palmoplantar keratosis, and woolly hair

Question 202 of 220

Which one of the following non-invasive methods provides the most accurate assessment of whether a patient has coronary artery disease?

A. Contrast enhanced cardiac CT

B. Cardiac MRI with gadolinium

C. Exercise ECG

D. Cardiac SPECT with reversibility studies

E. Transoesophageal echocardiography

Question 202 of 220

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- C. Exercise ECG
- D. Cardiac SPECT with reversibility studies
- E. Transoesophageal echocardiography

Cardiac imaging: non-invasive techniques excluding echocardiography

The ability to image the heart using non-invasive techniques such as MRI, CT and radionuclides has evolved rapidly over recent years.

Nuclear imaging
These techniques use radiotracers which are extracted by normal myocardium. Examples include:

- thallium
- technetium (99mTc) sestamibi: a coordination complex of the radioisotope technetium-99m with the ligand methoxyisobutyl isonitrile (MIBI), used in 'MIBI' or cardiac Single Photon Emission Computed Tomography (SPECT) scans
- fluorodeoxyglucose (FDG): used in Positron Emission Tomography (PET) scans

The primary role of SPECT is to assess myocardial perfusion and myocardial viability. Two sets of images are usually acquired. First the myocardium at rest followed by images of the myocardium during stress (either exercise or following adenosine / dipyridamole). By comparing the rest with stress images any areas of ischaemia can classified as reversible or fixed (e.g. Following a myocardial infarction). Cardiac PET is predominately a research tool at the current time

MUGA

- Multi Gated Acquisition Scan, also known as radionuclide angiography
- radionuclide (technetium-99m) is injected intravenously
- the patient is placed under a gamma camera
- may be performed as a stress test
- can accurately measure left ventricular ejection fraction. Typically used before and after cardiotoxic drugs are used

Cardiac Computed Tomography (CT)
Cardiac CT is useful for assessing suspected ischaemic heart disease, using two main methods:

- calcium score: there is known to be a correlation between the amount of atherosclerotic plaque calcium and the risk of future ischaemic events. Cardiac CT can quantify the amount of calcium producing a 'calcium score'
- contrast enhanced CT: allows visualisation of the coronary artery lumen

If these two techniques are combined cardiac CT has a very high negative predictive value for ischaemic heart disease.

Cardiac MRI
Cardiac MRI (commonly termed CMR) has become the gold standard for providing structural images of the heart. It is particularly useful when assessing congenital heart disease, determining right and left ventricular mass and differentiating forms of cardiomyopathy. Myocardial perfusion can also be assessed following the administration of gadolinium. Currently CMR provides limited data on the extent of coronary artery disease.

Question 203 of 220

A 65-year-old female is admitted with a suspected infective exacerbation of chronic obstructive pulmonary disease. On examination she is dyspnoeic with a blood pressure of 112/68 mmHg. Electrocardiogram shows an irregular, narrow-complex tachycardia with a rate of 130 bpm. At least three different P wave morphologies are seen. A diagnosis of multifocal tachycardia is suspected. What is the most appropriate management?

- A. Adenosine
- B. Digoxin
- C. Verapamil
- D. Atenolol
- E. DC cardioversion

Question 203 of 220

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- ✓ C. Verapamil
- D. Atenolol
- E. DC cardioversion

Multifocal atrial tachycardia

Multifocal atrial tachycardia (MAT) may be defined as a irregular cardiac rhythm caused by at least three different sites in the atria, which may be demonstrated by morphologically distinctive P waves. It is more common in elderly patients with chronic lung disease, for example COPD

Management

- correction of hypoxia and electrolyte disturbances
- rate-limiting calcium channel blockers are often used first-line
- cardioversion and digoxin are not useful in the management of MAT

Question 204 of 220

A 72-year-old man is started on amlodipine 5mg od for hypertension. He has no other past medical history of note and routine bloods (including fasting glucose) and ECG were normal. What should his target blood pressure be once on treatment?

- A. 130/80 mmHg
- B. 140/80 mmHg
- C. 140/85 mmHg
- D. 140/90 mmHg
- E. 150/90 mmHg

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- C. 140/85 mmHg
- ✓ D. 140/90 mmHg
- E. 150/90 mmHg

Blood pressure target on treatment = 140/90 mmHg

Hypertension: management

NICE published updated guidelines for the management of hypertension in June 2006

Initial drug choice
- patients < 55-years-old: ACE inhibitor
- patients > 55-years-old or of Afro-Caribbean origin: calcium channel blocker or thiazide diuretic

The target blood pressure is 140/90 mmHg. For diabetics the target is 140/80 mmHg (or 130/80 mmHg if end-organ damage is present)

If this fails to control the blood pressure then use a combination of an ACE inhibitor plus either a calcium channel blocker or thiazide diuretic

If this still fails then a combination of an ACE inhibitor + calcium channel blocker + thiazide diuretic should be used

Following this further diuretic therapy, alpha blockers or beta blockers should be considered

New drugs

Direct renin inhibitors
- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Question 205 of 220

Which one of the following agents is most useful in the maintenance of sinus rhythm in patients with atrial fibrillation?

- A. Verapamil
- B. Diltiazem
- C. Ibutilide
- D. Amiodarone
- E. Digoxin

Question 205 of 220

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- C. Ibutilide
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Atrial fibrillation: rate control and maintenance of sinus rhythm

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Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favoring rate control	Factors favoring rhythm control
• Older than 65 years • History of ischemic heart disease	• Younger than 65 years • Symptomatic • First presentation • Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) • Congestive heart failure

Question 206 of 220

You review a 69-year-old man who is known to have angina and heart failure. His current medications include aspirin, simvastatin, bisoprolol, glyceryl trinitrate, ramipril and frusemide. Despite his current medications he is still having frequent angina attacks when he exerts himself. You decide to add a calcium channel blocker. Which one of the following is it most appropriate to add?

- A. Felodipine
- B. Diltiazem
- C. Nimodipine
- D. Lacidipine
- E. Verapamil

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- C. Nimodipine
- D. Lacidipine
- E. Verapamil

Verapamil and diltiazem should be avoided given his history of heart failure. Nimodipine and lacidipine are neither licensed nor used in patients with angina.

Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery.

Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- beta-blocker is the preferred initial treatment. For patients unable to take a beta-blocker there is no clear guidelines on the best alternative. Options include a rate-limiting calcium-channel blocker (verapamil or diltiazem); a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine); a nitrate; or a potassium-channel activator
- if there is a poor response to initial treatment then the beta-blocker should be increased to the maximum tolerated dose (e.g. atenolol 100mg od)
- again, there is no clear guidelines on the next step treatment. CKS advise adding a long-acting dihydropyridine (e.g. nifedipine) although other options include isosorbide mononitrate and nicorandil

Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Question 207 of 220

A 62-year-old female with no past medical history is admitted to hospital with a left-sided hemiparesis. Examination reveals that she is in atrial fibrillation. CT scan of her brain shows a cerebral infarction. What is the most appropriate anticoagulation strategy for this patient?

- A. Life-long warfarin, started immediately
- B. Aspirin started immediately switching to life-long warfarin after 2 weeks
- C. Life-long aspirin, started immediately
- D. Life-long aspirin started after 2 weeks
- E. 6 months of warfarin, started immediately

Question 207 of 220

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- D. Life-long aspirin started after 2 weeks
- E. 6 months of warfarin, started immediately

Atrial fibrillation: post-stroke

NICE issued guidelines on atrial fibrillation (AF) in 2006. They included advice on the management of patients with AF who develop a stroke or transient-ischaemic attack (TIA).

Recommendations include:

- following a stroke or TIA warfarin should be given as the anticoagulant of choice. Aspirin/dipyridamole should only be given if needed for the treatment of other comorbidities
- in acute stroke patients, in the absence of haemorrhage, anticoagulation therapy should be commenced after 2 weeks. If imaging shows a very large cerebral infarction then the initiation of anticoagulation should be delayed

Question 208 of 220

Which of the following is responsible for the early repolarisation phase of the myocardial action potential?

- A. Rapid sodium influx
- B. Rapid calcium influx
- C. Slow sodium efflux
- D. Slow efflux of calcium
- E. Efflux of potassium

Question 208 of 220

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Electrical activity of the heart

Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by Na^+/K^+ ATPase There is slow entry of Na^+ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles

Question 209 of 220

A 78-year-old man with a four month history of exertional chest pain is reviewed. The pain typically comes on when he is walking up a hill, is centrally located and radiates to the left arm. Clinical examination and a resting 12 lead ECG are normal. Following NICE guidelines, what is the most appropriate diagnostic strategy?

- A. CT calcium scoring
- B. Manage as angina, no further diagnostic tests required
- C. Exercise tolerance test
- D. MPS with SPECT
- E. Coronary angiography

Question 209 of 220

A 78-year-old man with a four month history of exertional chest pain is reviewed. The pain typically comes on when he is walking up a hill, is centrally located and radiates to the left arm. Clinical examination and a resting 12 lead ECG are normal. Following NICE guidelines, what is the most appropriate diagnostic strategy?

- A. CT calcium scoring
- ✓ B. Manage as angina, no further diagnostic tests required
- C. Exercise tolerance test
- D. MPS with SPECT
- E. Coronary angiography

NICE do not recommend any further investigation for patients with an estimated coronary artery disease risk of greater than 90%. This includes all men over the age of 70 years who have typical symptoms.

Chest pain: assessment of patients with suspected cardiac chest pain

NICE issued guidelines in 2010 on the 'Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin'.

Below is a brief summary of the key points. Please see the link for more details.

Patients presenting with acute chest pain

Immediate management of suspected acute coronary syndrome (ACS)

- glyceryl trinitrate
- aspirin 300mg. NICE do not recommend giving other antiplatelet agents (i.e. Clopidogrel) outside of hospital
- do not routinely give oxygen, only give if sats < 94%*
- perform an ECG as soon as possible but do not delay transfer to hospital. A normal ECG does not exclude ACS

Referral

- current chest pain or chest pain in the last 12 hours with an abnormal ECG: emergency admission
- chest pain 12-72 hours ago: refer to hospital the same-day for assessment
- chest pain > 72 hours ago: perform full assessment with ECG and troponin measurement before deciding upon further action

*NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88-92% until blood gas analysis is available.

Patients presenting with stable chest pain

With all due respect to NICE the guidelines for assessment of patients with stable chest pain are rather complicated. They suggest an approach where the risk of a patient having coronary artery disease (CAD) is calculated based on their symptoms (whether they have typical angina, atypical angina or non-anginal chest pain), age, gender and risk factors.

NICE define anginal pain as the following:

- 1. constricting discomfort in the front of the chest, neck, shoulders, jaw or arms
- 2. precipitated by physical exertion
- 3. relieved by rest or GTN in about 5 minutes
- patients with all 3 features have typical angina
- patients with 2 of the above features have atypical angina
- patients with 1 or none of the above features have non-anginal chest pain

The risk tables are not reproduced here but can be found by clicking on the link.

If patients have typical anginal symptoms and a risk of CAD is greater than 90% then no further diagnostic testing is required. It should be noted that all men over the age of 70 years who have typical anginal symptoms fall into this category.

For patients with an estimated risk of 10-90% the following investigations are recommended. Note the absence of the exercise tolerance test:

Estimated likelihood of CAD	**Diagnostic testing**
61-90%	Coronary angiography
30-60%	Functional imaging, for example: • myocardial perfusion scan with SPECT • stress echocardiography • first-pass contrast-enhanced magnetic resonance (MR) perfusion • MR imaging for stress-induced wall motion abnormalities.
10-29%	CT calcium scoring

Question 210 of 220

Dilated cardiomyopathy may be caused by deficiency of which one of the following:

- A. Chromium
- B. Magnesium
- C. Pyridoxine
- D. Molybdenum
- E. Selenium

Question 210 of 220

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Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) basics
- dilated heart leading to systolic (+/- diastolic) dysfunction
- all 4 chambers affected but LV more so than RV
- features include arrhythmias, emboli, mitral regurgitation
- absence of congenital, valvular or ischaemic heart disease

Causes often considered separate entities
- alcohol: may improve with thiamine
- postpartum
- hypertension

Other causes
- inherited (see below)
- infections e.g. Coxsackie A and B, HIV, diphtheria, parasitic
- endocrine e.g. Hyperthyroidism
- infiltrative* e.g. Haemochromatosis, sarcoidosis
- neuromuscular e.g. Duchenne muscular dystrophy
- nutritional e.g. Kwashiorkor, pellagra, thiamine/selenium deficiency
- drugs e.g. Doxorubicin

Inherited dilated cardiomyopathy
- around a third of patients with DCM are thought to have a genetic predisposition
- a large number of heterogeneous defects have been identified
- the majority of defects are inherited in an autosomal dominant fashion although other patterns of inheritance are seen

*these causes may also lead to restrictive cardiomyopathy

Question 211 of 220

You review a 60-year-old man who had a drug-eluding stent inserted 6 months ago for ischaemic heart disease. His current medication includes aspirin, clopidogrel, atorvastatin, ramipril and bisoprolol. He has developed an inguinal hernia and is keen for surgical repair. The cardiologists plan was to continue clopidogrel for 12 months following stent insertion. What is the most appropriate course of action?

- A. Stop clopidogrel the day before the operation
- B. Stop clopidogrel 7 days before the operation
- C. Continue clopidogrel as normal
- D. Delay operation for 6 months
- E. Stop clopidogrel the day before the operation and start low-molecular weight heparin (prophylaxis dose)

Question 211 of 220

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The AHA/ACC/SCAI/ACS/ADA published recommendations in 2007 stressed the importance of 12 months of dual antiplatelet therapy after placement of a drug-eluting stent (DES).

Clopidogrel

Clopidogrel is an antiplatelet agent used in the management of cardiovascular disease. It is often used when aspirin is not tolerated or contraindicated but there are now a number of conditions for which clopidogrel is used in addition to aspirin, for example in patients with an acute coronary syndrome.

Mechanism
- inhibits ADP binding to its platelet receptor

Interactions
- concurrent use of proton pump inhibitors (PPIs) may make clopidogrel less effective (MHRA July 2009)
- this advice was updated by the MHRA in April 2010, evidence seems inconsistent but omeprazole and esomeprazole still cause for concern. Other PPIs such as lansoprazole should be OK - please see the link for more details

Question 212 of 220

A 45-year-old man presents with fever. On examination he is noted to have a pan-systolic murmur and splinter haemorrhages. He is generally unwell with a blood pressure of 100/60 mmHg and a temperature of 38.8ºC. What is the most suitable antibiotic therapy until blood culture results are known?

- A. IV flucloxacillin + gentamicin
- B. IV benzylpenicillin + gentamicin
- C. IV vancomycin + gentamicin
- D. IV vancomycin + benzylpenicillin
- E. IV ceftriaxone + benzylpenicillin

Question 212 of 220

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- D. IV vancomycin + benzylpenicillin
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Infective endocarditis: prognosis and management

Poor prognostic factors
- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism
- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)
- initial blind therapy - flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
- initial blind therapy if prosthetic valve is present or patient is penicillin allergic - vancomycin + rifampicin + gentamicin
- endocarditis caused by staphylococci - flucloxacillin (vancomycin + rifampicin if penicillin allergic or MRSA)
- endocarditis caused by streptococci - benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

Indications for surgery
- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Question 213 of 220

What is the target INR for a patient with a mechanical mitral valve?

- A. 4.0-4.5
- B. 4.0
- C. 3.0-4.0
- D. 2.5-3.5
- E. 2.0-3.0

Question 213 of 220

What is the target INR for a patient with a mechanical mitral valve?

- A. 4.0-4.5
- B. 4.0
- C. 3.0-4.0
- ✓ D. 2.5-3.5
- E. 2.0-3.0

Mechanical valves - target INR:
- aortic: 2.0-3.0
- mitral: 2.5-3.5

Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	**Mechanical valves**
Usually bovine or porcine in origin Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays Mechanical valves have a low failure rate Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication. Target INR • aortic: 2.0-3.0 • mitral: 2.5-3.5

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Question 214 of 220

Which one of the following statements regarding Brugada syndrome is correct?

- A. Usually inherited as an autosomal recessive disease
- B. Is associated with left bundle branch block
- C. Most common presentation is dilated cardiomyopathy
- D. Management is with beta-blockers
- E. More common in Asians

Question 214 of 220

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Brugada syndrome

Brugada syndrome is a form of inherited cardiovascular disease with may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

Pathophysiology
- a large number of variants exist
- around 20-40% of cases are caused by a mutation in the SCN5A gene which encodes the myocardial sodium ion channel protein

ECG changes
- convex ST elevation V1-V3
- partial right bundle branch block
- changes may be more apparent following flecainide

Management
- implantable cardioverter-defibrillator

Question 215 of 220

A 55-year-old man is admitted with central chest pain. His ECG shows ST depression in the inferior leads and the chest pain requires intravenous morphine to settle. Past medical history includes a thrombolysed myocardial infarction 2 years ago, asthma and type 2 diabetes mellitus. Treatment with aspirin, clopidogrel and unfractionated heparin is commenced. Which one of the following factors should determine if an intravenous glycoprotein IIb/IIIa receptor antagonist is to be given?

- A. High GRACE (Global Registry of Acute Cardiac Events) risk score + whether a percutaneous coronary intervention is to be performed
- B. Degree of ST depression
- C. High GRACE (Global Registry of Acute Cardiac Events) risk score
- D. Presence of a left ventricular thrombus
- E. The presence of recurrent cardiac chest pain

Question 215 of 220

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- C. High GRACE (Global Registry of Acute Cardiac Events) risk score
- D. Presence of a left ventricular thrombus
- E. The presence of recurrent cardiac chest pain

Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive
- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

Antithrombin treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

Clopidogrel 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

Coronary angiography should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

Aspirin	Antiplatelet - inhibits the production of thromboxane A2
Clopidogrel	Antiplatelet - inhibits ADP binding to its platelet receptor
Enoxaparin	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Fondaparinux	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
Bivalirudin	Reversible direct thrombin inhibitor

Question 216 of 220

What is the main reasons for checking the urea and electrolytes prior to commencing a patient on amiodarone?

A. To detect hyponatraemia

B. To detect impaired renal function

C. To detect a metabolic acidosis

D. To detect hyperkalaemia

E. To detect hypokalaemia

Question 216 of 220

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- B. To detect impaired renal function
- C. To detect a metabolic acidosis
- D. To detect hyperkalaemia
- ✓ E. To detect hypokalaemia

All antiarrhythmic drugs have the potential to cause arrhythmias. Coexistent hypokalaemia significantly increases this risk.

Amiodarone

Amiodarone is a class III antiarrhythmic agent used in the treatment of atrial, nodal and ventricular tachycardias. The main mechanism of action is by blocking potassium channels which inhibits repolarisation and hence prolongs the action potential. Amiodarone also has other actions such as blocking sodium channels (a class I effect)

The use of amiodarone is limited by a number of factors
- long half-life (20-100 days)
- should ideally be given into central veins (causes thrombophlebitis)
- has proarrhythmic effects due to lengthening of the QT interval
- interacts with drugs commonly used concurrently e.g. Decreases metabolism of warfarin
- numerous long-term adverse effects (see below)

Monitoring of patients taking amiodarone
- TFT, LFT, U&E, CXR prior to treatment
- TFT, LFT every 6 months

Adverse effects of amiodarone use
- thyroid dysfunction
- corneal deposits
- pulmonary fibrosis/pneumonitis
- liver fibrosis/hepatitis
- peripheral neuropathy, myopathy
- photosensitivity
- 'slate-grey' appearance
- thrombophlebitis and injection site reactions
- bradycardia

Question 217 of 220

A 62-year-old man is examined in the cardiology clinic. During cardiac auscultation it is noted that the pulmonary component of the second heart sound occurs before the aortic. Which one of the following is associated with this finding?

- A. Pulmonary stenosis
- B. Left bundle branch block
- C. Right bundle branch block
- D. Atrial septal defect
- E. Deep inspiration

Question 217 of 220

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- C. Right bundle branch block
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- E. Deep inspiration

Second heart sound (S2)
- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

Left bundle branch block causes a reversed split second heart sound. Atrial septal defects cause fixed splitting of S2

Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2
- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2
- aortic stenosis

Causes of fixed split S2
- atrial septal defect

Causes of a widely split S2
- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)
- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

Question 218 of 220

A 65-year-old man admitted to the Acute Medical Unit is noted to have cannon 'a' waves of his jugular venous pressure during cardiovascular examination. Which one of the following would not cause this finding?

- A. Tricuspid stenosis
- B. Complete heart block
- C. Ventricular tachycardia
- D. Single chamber ventricular pacing
- E. Nodal rhythm

Question 218 of 220

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- ✓ A. Tricuspid stenosis
- B. Complete heart block
- C. Ventricular tachycardia
- D. Single chamber ventricular pacing
- E. Nodal rhythm

Whilst tricuspid stenosis may cause large 'a' waves it does not cause cannon 'a' waves

Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis

'a' wave = atrial contraction
- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves
- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave
- closure of tricuspid valve
- not normally visible

'v' wave
- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Question 219 of 220

A 45-year-old man presents with pleuritic central chest pain. Which one of the following ECG findings is most specific for pericarditis?

- A. PR depression
- B. T wave inversion
- C. Short PR interval
- D. U waves
- E. ST elevation

Question 219 of 220

A 45-year-old man presents with pleuritic central chest pain. Which one of the following ECG findings is most specific for pericarditis?

- ✓ A. PR depression
- B. T wave inversion
- C. Short PR interval
- D. U waves
- E. ST elevation

ST elevation is seen but is not specific as it may also indicate ischaemia

Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

Features
- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

Causes
- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma
- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

ECG changes
- widespread 'saddle-shaped' ST elevation
- PR depression

Question 220 of 220

Which one of the following clinical signs would best indicate severe aortic stenosis?

- A. Valvular gradient of less than 30 mmHg
- B. Soft second heart sound
- C. Quiet first heart sound
- D. Development of an opening snap
- E. Carotid radiation of ejection systolic murmur

Question 220 of 220

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Aortic stenosis

Features of severe aortic stenosis
- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis
- degenerative calcification (most common cause in elderly patients)
- bicuspid aortic valve (most common cause in younger patients)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management
- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Question 1 of 331

Which one of the following would cause a metabolic acidosis with a normal anion gap?

- A. Renal tubular acidosis
- B. Acute renal failure
- C. Diabetic ketoacidosis
- D. Mesenteric ischaemia
- E. Aspirin overdose

Question 1 of 331

Which one of the following would cause a metabolic acidosis with a normal anion gap?

- ✓ A. Renal tubular acidosis
- B. Acute renal failure
- C. Diabetic ketoacidosis
- D. Mesenteric ischaemia
- E. Aspirin overdose

Renal tubular acidosis causes a normal anion gap

Renal tubular acidosis is the correct answer as all the other four possible options cause a metabolic acidosis with a raised anion gap

Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by: $(Na^+ + K^+) - (Cl- + HCO-3)$. If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap (= hyperchloraemic metabolic acidosis)
- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Raised anion gap
- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:
- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Question 2 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR4?

- A. Ankylosing spondylitis
- B. Behcet's disease
- C. Reiter's syndrome
- D. Rheumatoid arthritis
- E. Coeliac disease

Question 2 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR4?

- A. Ankylosing spondylitis
- B. Behcet's disease
- C. Reiter's syndrome
- ✓ D. Rheumatoid arthritis
- E. Coeliac disease

Rheumatoid arthritis - HLA DR4

Around 70% of patients with rheumatoid arthritis are HLA-DR4. Patients with Felty's syndrome (a triad of rheumatoid arthritis, splenomegaly and neutropaenia) are even more strongly associated with 90% being HLA-DR4

HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

HLA-A3
- haemochromatosis

HLA-B5
- Behcet's disease

HLA-B27
- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DR2
- narcolepsy
- Goodpasture's

HLA-DR3
- coeliac disease
- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4
- type 1 diabetes mellitus*
- rheumatoid arthritis

*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Question 3 of 331

A 22-year-old male with a history of familial adenomatous polyposis (FAP) has a total colectomy. What is the mode of inheritance of FAP?

- A. Uniparental disomy of chromosome 12
- B. Autosomal recessive
- C. Uniparental disomy of chromosome 14
- D. Autosomal dominant
- E. X-linked recessive

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Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are often poorly differentiated and highly aggressive. Currently four gene mutations have been identified (including in the hMLH1 and hMSH2 genes). The Amsterdam criteria are sometimes used to aid diagnosis:

Amsterdam criteria for HNPCC

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Question 4 of 331

A 12-year-old girl develops facial swelling and an erythematous itchy rash shortly after being administed the first dose of the HPV vaccine. On arrival the paramedics note a bilateral expiratory wheeze and blood pressure of 80/50 mmHg. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

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- E. Type V reaction

Anaphylaxis = type I hypersensitivity reaction

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 5 of 331

Which one of the following would shift the oxygen dissociation curve to the left?

- A. Carboxyhaemoglobin
- B. Acidosis
- C. Raised pCO2
- D. Pyrexia
- E. Raised 2,3-DPG levels

Question 5 of 331

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D. Pyrexia

E. Raised 2,3-DPG levels

Oxygen dissociation curve
- shifts **L**eft - **L**ower oxygen delivery - **L**ower acidity, temp, 2-3 DPG - also HbF, carboxy/methaemoglobin
- shifts **R**ight - **R**aised oxygen delivery - **R**aised acidity, temp, 2-3 DPG

Oxygen dissociation curve

The oxygen dissociation curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood. It is not affected by haemoglobin concentration

Basics
- shifts to left = for given oxygen tension there is increased saturation of Hb with oxygen i.e. decreased oxygen delivery to tissues
- shifts to right = for given oxygen tension there is reduced saturation of Hb with oxygen i.e. enhanced oxygen delivery to tissues

Shifts to Left = Lower oxygen delivery	**Shifts to Right = Raised oxygen delivery**
• HbF,methaemoglobin, carboxyhaemoglobin • low [H+] (alkali) • low pCO2 • low 2,3-DPG • low temperature	• raised [H+] (acidic) • raised pCO2 • raised 2,3-DPG* • raised temperature

*2,3-diphosphoglycerate

Question 6 of 331

Which one of the following would cause a rise in the carbon monoxide transfer factor (TLCO)?

- A. Emphysema
- B. Pulmonary embolism
- C. Pulmonary haemorrhage
- D. Pneumonia
- E. Pulmonary fibrosis

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Transfer factor
- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

Where alveolar haemorrhage occurs the TLCO tends to increase due to the enhanced uptake of carbon monoxide by intra-alveolar haemoglobin

Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	Causes of a lower TLCO
• asthma • pulmonary haemorrhage (Wegener's, Goodpasture's) • left-to-right cardiac shunts • polycythaemia • hyperkinetic states • male gender, exercise	• pulmonary fibrosis • pneumonia • pulmonary emboli • pulmonary oedema • emphysema • anaemia • low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO
- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

Question 7 of 331

Which one of the following causes of primary immunodeficiency is a T-cell disorder?

- A. Chediak-Higashi syndrome
- B. Chronic granulomatous disease
- C. Common variable immunodeficiency
- D. DiGeorge syndrome
- E. Wiskott-Aldrich syndrome

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DiGeorge syndrome - a T-cell disorder

DiGeorge syndrome is a primary immunodeficiency disorder caused by T-cell deficiency and dysfunction. It is an example of a microdeletion syndrome. Patients are consequently at increased risk of viral and fungal infections.

Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders
- DiGeorge syndrome

Combined B- and T-cell disorders
- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Question 8 of 331

A 64-year-old female with a history of rheumatoid arthritis presents with increased difficulty in walking. On examination there is weakness of ankle dorsiflexion and of the extensor hallucis longus associated with loss of sensation on the lateral aspect of the lower leg. What is the most likely diagnosis?

- A. Tibial nerve palsy
- B. Obturator nerve
- C. Common peroneal nerve palsy
- D. Lateral cutaneous nerve
- E. Pudendal nerve palsy

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Common peroneal nerve lesion

The sciatic nerve divides into the tibial and common peroneal nerves. Injury often occurs at the neck of the fibula

The most characteristic feature of a common peroneal nerve lesion is foot drop

Other features include:

- weakness of foot dorsiflexion
- weakness of foot eversion
- weakness of extensor hallucis longus
- sensory loss over the dorsum of the foot and the lower lateral part of the leg
- wasting of the anterior tibial and peroneal muscles

Question 9 of 331

Which one of the following would invalidate the use of the Student's t-test when performing a significance test?

- A. Using it with unpaired data
- B. Using it with data that is not normally distributed
- C. Using it with data that has a small sample size
- D. Using it to test whether the slope of a regression line differs significantly from 0
- E. Using it to test a null hypothesis

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Data must be parametric, i.e. follows a normal distribution

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests

- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 10 of 331

A 72-year-old woman presents with polyuria and polydipsia. Investigations reveal the following:

Fasting glucose	4.5 mmol/l
Calcium	2.88 mmol/l
Phosphate	0.75 mmol/l
Parathyroid hormone	6 pmol/L (normal range = 0.8 - 8.5)

What is the most likely underlying diagnosis?

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- B. Sarcoidosis
- C. Primary hyperparathyroidism
- D. Vitamin D excess
- E. Osteomalacia

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The PTH level in primary hyperparathyroidism may be normal

Despite a raised calcium level the parathyroid hormone level is inappropriately normal. This points towards a diagnosis of primary hyperparathyroidism and the other causes (such as myeloma) would lead to a suppression of parathyroid hormone

Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism
- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'
- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations
- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations
- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment
- total parathyroidectomy

Question 11 of 331

Which of the following is true regarding rheumatoid factor?

- A. It is usually an IgM molecule reacting against patient's own IgG
- B. High titres are not associated with severe disease
- C. Rose-Waaler test involves agglutination of IgG coated latex particles
- D. 80% of SLE patients are RF positive
- E. 50% of patients with Sjogren's syndrome are RF positive

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- E. 50% of patients with Sjogren's syndrome are RF positive

Rheumatoid factor is an IgM antibody against IgG

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either
- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:
- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

Question 12 of 331

A 79-year-old man is admitted with congestive cardiac failure. Bloods on admission show:
BNP 354 pg/ml

Which one of the following would result from elevated BNP levels?

- A. Decreased sodium diuresis
- B. Vasoconstriction of the coronary arteries
- C. Inhibition of the renin-angiotensin-aldosterone system
- D. Vasoconstriction of the pulmonary vessels
- E. Increased sympathetic tone

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BNP - actions:
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

B-type natriuretic peptide

B-type natriuretic peptide (BNP) hormone produced mainly by the left ventricular myocardium in response to strain

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

Clinical uses of BNP
Diagnosing patients with acute dyspnoea
- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

Prognosis in patients with chronic heart failure
- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure
- effective treatment lowers BNP levels

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 13 of 331

Which one of the following causes of primary immunodeficiency is due to a defect in both B-cell and T-cell function?

- A. Common variable immunodeficiency
- B. Chronic granulomatous disease
- C. Wiskott-Aldrich syndrome
- D. Chediak-Higashi syndrome
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Combined B- and T-cell disorders: SCID WAS ataxic (SCID, Wiskott-Aldrich syndrome, ataxic telangiectasia)

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene. Features include recurrent bacterial infections (e.g. chest), eczema and thrombocytopenia

Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
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Question 14 of 331

A randomised controlled trial compares two drugs used in the initial management of rheumatoid arthritis. After being assigned to the randomised groups a number of patients drop out due to adverse effects of the medication. How should the data be analysed?

- A. Recruit more patients
- B. For each patient who drops out, remove a patient from the other randomised group
- C. Include the patients who drop out in the final data set
- D. Remove patients who drop out from final data set
- E. Abandon the trial if more than 5% of patients drop out

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Intention to treat analysis

Intention to treat analysis is a method of analysis for randomized controlled trials in which all patients randomly assigned to one of the treatments are analysed together, regardless of whether or not they completed or received that treatment

Intention to treat analysis is done to avoid the effects of crossover and drop-out, which may affect the randomization to the treatment groups

Question 15 of 331

Doxazosin is a:

- A. Alpha-1 antagonist
- B. Alpha-1 agonist
- C. Non-selective alpha antagonist
- D. Alpha-2 agonist
- E. Alpha-2 antagonist

Question 15 of 331

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Doxazosin is an alpha-1 adrenoceptor antagonist used in the treatment of hypertension and benign prostatic hypertrophy

Adrenoceptor antagonists

Alpha antagonists
- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists
- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

Question 16 of 331

A patient is seen in clinic complaining of abdominal pain. Routine bloods show:

Na^+	142 mmol/l
K^+	4.0 mmol/l
Chloride	104 mmol/l
Bicarbonate	19 mmol/l
Urea	7.0 mmol/l
Creatinine	112 µmol/l

What is the anion gap?

- A. 4 mmol/L
- B. 14 mmol/L
- C. 20 mmol/L
- D. 21 mmol/L
- E. 23 mmol/L

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- D. 21 mmol/L
- ✓ E. 23 mmol/L

The anion gap may be calculated by using (sodium + potassium) - (bicarbonate + chloride)

= (142 + 4.0) - (104 + 19) = 23 mmol/L

Anion gap

The anion gap is calculated by:

(sodium + potassium) - (bicarbonate + chloride)

A normal anion gap is 8-14 mmol/L

It is useful to consider in patients with a metabolic acidosis:

Causes of a normal anion gap or hyperchloraemic metabolic acidosis
- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Causes of a raised anion gap metabolic acidosis
- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Question 17 of 331

Patients with deficiencies of which one of the following complement proteins are most predisposed to disseminated meningococcal infection?

- A. C1
- B. C2
- C. C3
- D. C4
- E. C5

Question 17 of 331

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- C. C3
- D. C4
- ✓ E. C5

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection

Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency
- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 18 of 331

Which cell organelle is involved in the breakdown of oligopeptides?

- A. Golgi apparatus
- B. Rough endoplasmic reticulum
- C. Peroxisome
- D. Lysosome
- E. Smooth endoplasmic reticulum

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Protein degradation in eukaryotes is also carried out by protein complexes called proteasomes

Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Energy production. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide

Question 19 of 331

Which one of the following statements best describes a type II statistical error?

- A. The p value fails to reach statistical significance
- B. A study fails to reach an appropriate power
- C. The null hypothesis is rejected when it is true
- D. The null hypothesis is accepted when it is false
- E. The alternative hypothesis is rejected when it is false

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Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example
- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis
- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false
- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 20 of 331

In the Gell and Coombs classification of hypersensitivity reactions Grave's disease is an example of a:

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Hypersensitivity

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Type IV - Delayed hypersensitivity
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In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 21 of 331

Which one of the following statements regarding nitric oxide is incorrect?

- A. Promotes platelet aggregation
- B. Raises intracellular cGMP levels
- C. An inducible form of NOS is present in macrophages
- D. In sepsis increased levels of NO contribute to septic shock
- E. Causes venodilation

Question 21 of 331

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- E. Causes venodilation

Nitric oxide - inhibits platelet aggregation + vasodilation

Nitric oxide inhibits, rather than promotes, platelet aggregation

Nitric oxide

Previously known as endothelium derived relaxation factor, nitric oxide (NO) has emerged as a molecule which is integral to many physiological and pathological processes. It is formed from L-arginine and oxygen by nitric oxide synthetase (NOS). An inducible form of NOS has been shown to be present in macrophages. Nitric oxide has a very short half-life (seconds), being inactivated by oxygen free radicals

Effects

- acts on guanylate cyclase leading to raised intracellular cGMP levels and therefore decreasing Ca2+ levels
- vasodilation, mainly venodilation
- inhibits platelet aggregation

Clinical relevance

- underproduction of NO is implicated in hypertrophic pyloric stenosis
- lack of NO is thought to promote atherosclerosis
- in sepsis increased levels of NO contribute to septic shock
- organic nitrates (metabolism produces NO) is widely used to treat cardiovascular disease (e.g. angina, heart failure)
- sildenafil is thought to potentiate the action of NO on penile smooth muscle and is used in the treatment of erectile dysfunctions

Question 22 of 331

Which one of the following statements regarding mitochondrial inheritance is true?

- A. Friedreich's ataxia is caused by defects in mitochondrial DNA
- B. There is a 50% chance that the female offspring of an affected male will inherit the disease
- C. Affected females cannot pass on the disease
- D. Most cases of spinocerebellar ataxia are caused by defects in mitochondrial DNA
- E. Poor genotype:phenotype correlation

Question 22 of 331

Which one of the following statements regarding mitochondrial inheritance is true?

- A. Friedreich's ataxia is caused by defects in mitochondrial DNA
- B. There is a 50% chance that the female offspring of an affected male will inherit the disease
- C. Affected females cannot pass on the disease
- D. Most cases of spinocerebellar ataxia are caused by defects in mitochondrial DNA
- ✓ E. Poor genotype:phenotype correlation

Mitochondrial diseases

Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria. It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

- inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote
- all children of affected males will not inherit the disease
- all children of affected females will inherit it
- generally encode rare neurological diseases
- poor genotype:phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

Histology

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:

- Leber's optic atrophy
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

Question 23 of 331

A study looks at the chance of having a myocardial infarction (MI) in patients with known ischaemic heart disease. Group A are given standard treatment. After 5 years 20 of the 100 patients have had a MI. Group B have standard treatment plus a new cardiac drug. After 5 years 10 of the 60 patients have had an MI. What is the odds ratio of having a MI whilst taking the new drug compared to those who do not?

- A. 0.8
- B. 0.83
- C. 2
- D. 1.2
- E. 1.25

Question 23 of 331

A study looks at the chance of having a myocardial infarction (MI) in patients with known ischaemic heart disease. Group A are given standard treatment. After 5 years 20 of the 100 patients have had a MI. Group B have standard treatment plus a new cardiac drug. After 5 years 10 of the 60 patients have had an MI. What is the odds ratio of having a MI whilst taking the new drug compared to those who do not?

- ✓ A. 0.8
- B. 0.83
- C. 2
- D. 1.2
- E. 1.25

Odds - remember a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

NOT a ratio of the number of people who incur a particular outcome to the total number of people

Odds of MI in group B = 10/50 = 1/5

Odds of MI in group A = 20/80 = 1/4

Odds ratio of having a MI = 1/5 divided by 1/4 = 0.8

Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	**Achieved = 50% pain relief**
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol = 40 / 20 = 2

The odds of achieving significant pain relief with placebo = 30 / 60 = 0.5

Therefore the odds ratio = 2 / 0.5 = 4

Question 24 of 331

Each one of the following is associated with hyperkalaemia, except:

- A. Rhabdomyolysis
- B. Carbenoxolone
- C. Acute renal failure
- D. Ciclosporin
- E. Addison's

Question 24 of 331

Each one of the following is associated with hyperkalaemia, except:

- A. Rhabdomyolysis
- ✓ B. Carbenoxolone
- C. Acute renal failure
- D. Ciclosporin
- E. Addison's

Hyperkalaemia

Plasma potassium levels are regulated by a number of factors including aldosterone, acid-base balance and insulin levels. Metabolic acidosis is associated with hyperkalaemia as hydrogen and potassium ions compete with each other for exchange with sodium ions across cell membranes and in the distal tubule. ECG changes seen in hyperkalaemia include tall-tented T waves, small P waves, widened QRS leading to a sinusoidal pattern and asystole

Causes of hyperkalaemia:

- acute renal failure
- drugs*: potassium sparing diuretics, ACE inhibitors, angiotensin 2 receptor blockers, spironolactone, ciclosporin
- metabolic acidosis
- Addison's
- rhabdomyolysis
- massive blood transfusion

Foods that are high in potassium:

- salt substitutes (i.e. Contain postassium rather than sodium)
- bananas, oranges, kiwi fruit, avocado, spinach, tomatoes

*beta-blockers interfere with potassium transport into cells and can potentially cause hyperkalaemia in renal failure patients - remember beta-agonists, e.g. Salbutamol, are sometimes used as emergency treatment

Question 25 of 331

Vitamin D causes which one of the following:

- A. Increased plasma phosphate
- B. Decreased plasma calcium
- C. Decreased osteoclastic activity
- D. Decreased gut absorption of calcium
- E. Decreased renal tubular absorption of calcium

Question 25 of 331

Vitamin D causes which one of the following:

- ✓ A. Increased plasma phosphate
- B. Decreased plasma calcium
- C. Decreased osteoclastic activity
- D. Decreased gut absorption of calcium
- E. Decreased renal tubular absorption of calcium

Vitamin D increases plasma calcium and plasma phosphate levels by promoting renal tubular absorption and gut absorption of calcium and increasing renal phosphate reabsorption

Calcium metabolism

The two hormones which primarily control calcium metabolism are:
- parathyroid hormone (PTH)
- vitamin D

Other hormones include
- calcitonin: secreted from the C cells of the thyroid gland
- thyroxine
- growth hormone

Actions of parathyroid hormone
- increases plasma calcium, decreases plasma phosphate
- increases renal tubular reabsorption of calcium
- increases osteoclastic activity
- increases renal conversion of 25-hydroxy vitamin D to 1,25 dihydroxy vitamin D
- decreases renal phosphate reabsorption

Actions of vitamin D
- increases plasma calcium and plasma phosphate
- increases renal tubular reabsorption and gut absorption of calcium
- increases osteoclastic activity
- increases renal phosphate reabsorption

Question 26 of 331

Which of the following conditions is inherited in an autosomal recessive fashion?

- A. Hypokalaemic periodic paralysis
- B. Adult polycystic disease
- C. Huntington's disease
- D. Friedreich's ataxia
- E. Ehlers-Danlos syndrome

Question 26 of 331

Which of the following conditions is inherited in an autosomal recessive fashion?

- A. Hypokalaemic periodic paralysis
- B. Adult polycystic disease
- C. Huntington's disease
- ✓ D. Friedreich's ataxia
- E. Ehlers-Danlos syndrome

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's
- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Question 27 of 331

A new oral-hypoglycaemic is being developed. A number of different study types are considered to demonstrate efficacy in reducing the HbA1c. Which one of the following study designs would require the most patients to produce a significant result?

- A. Equivalence trial
- B. Non-inferiority trial
- C. Superiority trial
- D. Placebo-controlled trial
- E. Study design would not affect the number of patients required

Question 27 of 331

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- ✓ C. Superiority trial
- D. Placebo-controlled trial
- E. Study design would not affect the number of patients required

As a superiority trial compares the new drug with an existing treatment, which would also lower HbA1c, a large sample size is required to demonstrate a significant difference.

Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined (-delta to +delta) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e. -delta). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

Question 28 of 331

Which one of the following electrolyte disturbances is most associated with the development of a prolonged QT interval on ECG?

- A. Hyponatraemia
- B. Hypocalcaemia
- C. Hyperkalaemia
- D. Hypercalcaemia
- E. Hypophosphataemia

Question 28 of 331

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- D. Hypercalcaemia
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Long QT syndrome

Long QT syndrome (LQTS) is associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than 440 ms in males and 450 ms in females.

Congenital
- Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)
- Romano-Ward syndrome (no deafness)

Drugs
- amiodarone
- sotalol
- class 1a antiarrhythmic drugs
- tricyclic antidepressants
- chloroquine
- terfenadine*
- erythromycin

Other causes
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- acute MI
- myocarditis
- hypothermia
- subarachnoid haemorrhage

Management
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 29 of 331

A 65-year-old man presents with bilateral leg pain that is brought on by walking. His past medical history includes peptic ulcer disease and osteoarthritis. He can typically walk for around 5 minutes before it develops. The pain subsides when he sits down. He has also noticed that leaning forwards or crouching improves the pain. Musculoskeletal and vascular examination of his lower limbs is unremarkable. What is the most likely diagnosis?

- A. Inflammatory arachnoiditis
- B. Peripheral arterial disease
- C. Raised intracranial pressure
- D. Spinal stenosis
- E. Lumbar vertebral crush fracture

Question 29 of 331

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- C. Raised intracranial pressure
- ✓ D. Spinal stenosis
- E. Lumbar vertebral crush fracture

This is a classic presentation of spinal stenosis. Whilst peripheral arterial disease is an obvious differential the characteristic relieving factors of the pain and normal vascular examination point away from this diagnosis.

Lower back pain

Lower back pain (LBP) is one of the most common presentations seen in practice. Whilst the majority of presentations will be of a non-specific muscular nature it is worth keeping in mind possible causes which may need specific treatment.

Red flags for lower back pain
- age < 20 years or > 50 years
- history of previous malignancy
- night pain
- history of trauma
- systemically unwell e.g. weight loss, fever

The table below indicates some specific causes of LBP:

Facet joint	May be acute or chronic Pain worse in the morning and on standing On examination there may be pain over the facets. The pain is typically worse on extension of the back
Spinal stenosis	Usually gradual onset Unilateral or bilateral leg pain (with or without back pain), numbness, and weakness which is worse on walking. Resolves when sits down. Pain may be described as 'aching', 'crawling'. Relieved by sitting down, leaning forwards and crouching down Clinical examination is often normal Requires MRI to confirm diagnosis
Ankylosing spondylitis	Typically a young man who presents with lower back pain and stiffness Stiffness is usually worse in morning and improves with activity Peripheral arthritis (25%, more common if female)
Peripheral arterial disease	Pain on walking, relieved by rest Absent or weak foot pulses and other signs of limb ischaemia Past history may include smoking and other vascular diseases

Question 30 of 331

Which one of the following is least associated with hypercalcaemia?

- A. Sarcoidosis
- B. Primary hyperparathyroidism
- C. Thiazide diuretics
- D. Squamous cell lung cancer
- E. Monoclonal gammopathy of uncertain significance

Question 30 of 331

Which one of the following is least associated with hypercalcaemia?

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- B. Primary hyperparathyroidism
- C. Thiazide diuretics
- D. Squamous cell lung cancer
- ✓ E. Monoclonal gammopathy of uncertain significance

One of the key differentiating features between monoclonal gammopathy of uncertain significance (MGUS) and myeloma is the absence of complications such as immune paresis, hypercalcaemia and bone pain

Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, Ca2+ containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

*other causes of granulomas may lead to hypercalcaemia e.g. tuberculosis and histoplasmosis

**usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 31 of 331

The nicotinic acetylcholine receptor is an example of a:

- A. Ligand-gated ion channel
- B. Tyrosine kinase receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Intracellular receptor

Question 31 of 331

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- ✓ A. Ligand-gated ion channel
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- D. G protein-coupled receptor
- E. Intracellular receptor

Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel
- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 32 of 331

A new test to screen for pulmonary embolism (PE) is used in 100 patients who present to the Emergency Department. The test is positive in 30 of the 40 patients who are proven to have a PE. Of the remaining 60 patients, only 5 have a positive test. What is the sensitivity of the new test?

- A. 8.33%
- B. 30%
- C. 40%
- D. 66.66%
- E. 75%

Question 32 of 331

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- A. 8.33%
- B. 30%
- C. 40%
- D. 66.66%
- ✓ E. 75%

A contingency table can be constructed from the above data, as shown below:

	PE diagnosed	**No PE**
Test positive	30	5
Test negative	10	55

The sensitivity is therefore 30 / (30 + 10) = 75%

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 33 of 331

Which one of the following statements regarding glucagon-like peptide-1 (GLP-1) is incorrect?

- A. Secreted in response to an oral glucose load
- B. Increased levels are seen in type 2 diabetes mellitus
- C. Slows gastric emptying
- D. Secreted by the small intestine
- E. Responsible for the incretin effect

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Decreased levels of GLP-1 are seen in type 2 diabetes mellitus

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 34 of 331

Which one of the following statements regarding gastrin is true?

- A. Secreted by D cells in the stomach
- B. Secretion is inhibited by high antral pH
- C. Reduces acid secretion in the stomach
- D. Increases gastric motility
- E. Distension of the stomach inhibits secretion

Question 34 of 331

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Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
Gastrin	G cells in antrum of the stomach	Distension of stomach, extrinsic nerves Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
CCK	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
Secretin	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
VIP	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion
Somatostatin	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Question 35 of 331

In the Gell and Coombs classification of hypersensitivity reactions scabies is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

Question 35 of 331

In the Gell and Coombs classification of hypersensitivity reactions scabies is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- ✓ D. Type IV reaction
- E. Type V reaction

Scabies produces a delayed type IV hypersensitivity reaction approximately one month after infestation. This produces the characteristic intense itching

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 36 of 331

Which one of the following clotting factors is not affected by warfarin?

- A. Factor II
- B. Factor VII
- C. Factor XII
- D. Factor IX
- E. Factor X

Question 36 of 331

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- A. Factor II
- B. Factor VII
- ✓ C. Factor XII
- D. Factor IX
- E. Factor X

Warfarin - clotting factors affected mnemonic - 1972 (**10**, **9**, **7**, **2**)

Factor XII is not affected by warfarin

Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C

Factors that may potentiate warfarin
- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

Side-effects
- haemorrhage
- teratogenic
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

Question 37 of 331

Which one of the following occurs during reverse transcriptase polymerase chain reaction?

- A. Proteins are converted to DNA
- B. DNA is converted to RNA
- C. Used to amplify DNA
- D. RNA is converted to DNA
- E. Proteins are converted to RNA

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PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep
- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place
- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR
- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

Question 38 of 331

Each one of the following may raise ESR, except:

- A. Female sex
- B. Systemic lupus erythematous
- C. Polycythaemia
- D. Myeloma
- E. Increasing age

Question 38 of 331

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Erythrocyte sedimentation rate (ESR)

The ESR is a non-specific marker of inflammation and depends on both the size, shape and number of red blood cells and the concentration of plasma proteins such as fibrinogen, alpha2-globulins and gamma globulins

Causes of a high ESR
- temporal arteritis
- myeloma
- other connective tissue disorders e.g. systemic lupus erythematosus
- other malignancies
- infection
- other factors which raise ESR: increasing age, female sex, anaemia

Causes of a low ESR
- polycythaemia
- afibrinogenaemia/hypofibrinogenaemia

Question 39 of 331

A new drug designed to prevent exacerbations of genital herpes undergoes clinical trials. One hundred patients are given the new drug. During a three month period 10 of the patients have an episode of genital herpes. In the control group there are 300 patients who are given a placebo. In this group 50 people have an exacerbation during the same time period. What is the relative risk of having an exacerbation of genital herpes whilst taking the new drug?

- A. 0.8
- B. 0.2
- C. 1.66
- D. 0.6
- E. 0.06

Question 39 of 331

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- A. 0.8
- B. 0.2
- C. 1.66
- ✓ D. 0.6
- E. 0.06

Experimental event rate, EER = 10 / 100 = 0.10
Control event rate, CER = 50 / 300 = 0.166
Therefore the relative risk = EER / CER = 0.1 / 0.166 = 0.6

Relative risk

Relative risk (RR) is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER)

To recap
- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	**Experienced significant pain relief**
Paracetamol	100	60
Placebo	80	20

Experimental event rate, EER = 60 / 100 = 0.6

Control event rate, CER = 20 / 80 = 0.25

Therefore the relative risk = EER / CER = 0.6 / 0.25 = 2.4

If the risk ratio is > 1 then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is < 1 then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

Relative risk reduction (RRR) or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data, RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140%

Question 40 of 331

Which of the following statements is true regarding hyponatraemia?

A. In a dehydrated patient with urinary sodium < 20mmol/L it may be due to the diuretic stage of renal failure

B. SIADH typically leads to urine osmolality of < 500 mmol/kg

C. Hyperlipidaemia may cause pseudohyponatraemia

D. Cardiac failure and liver cirrhosis may lead to primary hyperaldosteronism

E. It is known to cause a long QT interval

Question 40 of 331

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- D. Cardiac failure and liver cirrhosis may lead to primary hyperaldosteronism
- E. It is known to cause a long QT interval

Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolarity levels aid making a diagnosis

Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)
- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic
- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss
- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)
- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Question 41 of 331

Which one of the following serum proteins is most likely to increase in a patient with severe pneumococcal pneumonia?

- A. Transferrin
- B. Transthyretin
- C. Ferritin
- D. Albumin
- E. Cortisol binding protein

Question 41 of 331

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- D. Albumin
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Acute phase proteins

Acute phase proteins
- CRP
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:
- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

*plays a more significant role in other mammals such as mice

Question 42 of 331

A 19-year-old female with a history of anorexia nervosa is admitted to hospital. Her BMI has dropped to 16. She has agreed to be fed by nasogastric tube. Which one of the following electrolyte disturbances is most likely to occur?

- A. Hyperkalaemia
- B. Hypocalcaemia
- C. Metabolic acidosis
- D. Hypophosphataemia
- E. Hypermagnesemia

Question 42 of 331

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- C. Metabolic acidosis
- ✓ D. Hypophosphataemia
- E. Hypermagnesemia

This patient is at risk of refeeding syndrome, which can lead to profound hypophosphataemia

Hypophosphataemia

Causes
- alcohol excess
- acute liver failure
- diabetic ketoacidosis
- refeeding syndrome
- primary hyperparathyroidism
- osteomalacia

Consequences
- red blood cell haemolysis
- white blood cell and platelet dysfunction
- muscle weakness and rhabdomyolysis
- central nervous system dysfunction

Question 43 of 331

A 61-year-old woman is admitted to the Acute Medical Unit as she is generally unwell with muscle twitching. Blood pressure is recorded at 114/78 mmHg, pulse 84/min and she is apyrexial. Blood tests reveal the following:

Calcium 1.94 mmol/l

Albumin 38 g/l

Which one of the following tests is most useful in elucidating the cause of her symptoms?

- A. Urea
- B. Vitamin D
- C. Phosphate
- D. Parathyroid hormone
- E. Magnesium

Question 43 of 331

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- C. Phosphate
- ✓ D. Parathyroid hormone
- E. Magnesium

Parathyroid hormone is the single most useful test in determining the cause of hypocalcaemia

Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Question 44 of 331

A study is to be performed to assess whether the combined oral contraceptive pill is protective against pelvic inflammatory disease. What is the most appropriate type of study design to provide robust evidence?

- A. Cohort study
- B. Placebo-controlled randomised controlled trial
- C. Case-control study
- D. Cross-sectional survey
- E. Cross-over trial

Question 44 of 331

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- D. Cross-sectional survey
- E. Cross-over trial

Whilst a case-control study may be used it would provide inferior evidence to that of a cohort study. It is of course not ethical to give women placebo contraceptive pills, as would be required with a randomised control trial

Study design

The following table highlights the main features of the different types of study

Randomised controlled trial	Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo) • Practical or ethical problems may limit use
Cohort study	Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome • Examples include Framingham Heart Study
Case-control study	Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition • Inexpensive, produce quick results • Useful for studying rare conditions • Prone to confounding
Cross-sectional survey	Provide a 'snapshot', sometimes called prevalence studies • Provide weak evidence of cause and effect

Question 45 of 331

Which one of the following types of thyroid cancer is associated with the RET oncogene?

- A. Anaplastic
- B. Lymphoma
- C. Follicular
- D. Medullary
- E. All types of thyroid cancer

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The RET oncogene encodes a receptor tyrosine kinase and is associated with MEN type 2. Papillary thyroid cancer also appears to be associated with the RET oncogene

Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	**MEN type IIa**	**MEN type IIb**
Mnemonic 'three P's': • parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia • pituitary (70%) • pancreas (50%, e.g. insulinoma, gastrinoma) • also: adrenal and thyroid	• phaeochromocytoma (95%, e.g. Phaeochromocytoma) • medullary thyroid cancer (70%) • parathyroid (60%)	• medullary thyroid cancer • phaeochromocytoma • marfanoid body habitus • neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene

MEN is inherited as an autosomal dominant disorder

Question 46 of 331

One of your colleagues confides in you that he has just been diagnosed with hepatitis C. He has not told anyone else as he is worried he may lose his job. He does not undertake any form of surgery but regularly takes blood from patients. You try to persuade him to inform occupational health but he refuses. What is the most appropriate action?

- A. Keep confidentiality but ask him to stop taking blood
- B. Send an anonymous letter to his employer
- C. Keep confidentiality
- D. Inform your colleague's employing body
- E. Contact the police

Question 46 of 331

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- A. Keep confidentiality but ask him to stop taking blood
- B. Send an anonymous letter to his employer
- C. Keep confidentiality
- ✓ D. Inform your colleague's employing body
- E. Contact the police

Whilst this may seem harsh patient safety has to be paramount. Please see the updated GMC guidelines for further details.

GMC guidance: confidentiality

We will not try to replicate the extensive guidance given by the General Medical Council here. There is a link available for more detailed information.

Question 47 of 331

Which one of the following is the most common cause of recurrent first trimester spontaneous miscarriage?

- A. Factor V Leiden gene mutation
- B. Polycystic ovarian syndrome
- C. Hyperprolactinaemia
- D. Antithrombin III deficiency
- E. Antiphospholipid syndrome

Question 47 of 331

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- ✓ E. Antiphospholipid syndrome

Antiphospholipid antibodies (aPL) are present in 15% of women with recurrent miscarriage, but in comparison, the prevalence of aPL in women with a low risk obstetric history is less than 2%

Antiphospholipid syndrome: pregnancy

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

Question 49 of 331

What level of evidence does a randomised control trial offer?

- A. Ia
- B. Ib
- C. IIa
- D. IIb
- E. IV

Question 49 of 331

What level of evidence does a randomised control trial offer?

- A. Ia
- ✓ B. Ib
- C. IIa
- D. IIb
- E. IV

Study design: evidence and recommendations

Levels of evidence

- Ia - evidence from meta-analysis of randomised controlled trials
- Ib - evidence from at least one randomised controlled trial
- IIa - evidence from at least one well designed controlled trial which is not randomised
- IIb - evidence from at least one well designed experimental trial
- III - evidence from case, correlation and comparative studies
- IV - evidence from a panel of experts

Grading of recommendation

- Grade A - based on evidence from at least one randomised controlled trial (i.e. Ia or Ib)
- Grade B - based on evidence from non-randomised controlled trials (i.e. IIa, IIb or III)
- Grade C - based on evidence from a panel of experts (i.e. IV)

Question 50 of 331

Which one of the following foods is the best source of folic acid?

- A. Cheese
- B. Red meat
- C. Liver
- D. Fish
- E. Milk

Question 50 of 331

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- A. Cheese
- B. Red meat
- ✓ C. Liver
- D. Fish
- E. Milk

Folic acid is also present in green vegetables and nuts

Folate metabolism

Drugs which interfere with metabolism
- trimethoprim
- methotrexate
- pyrimethamine

Drugs which can reduce absorption
- phenytoin

Question 51 of 331

Which one of the following may be used to calculate the number needed to treat?

- A. 1 / (Absolute risk reduction)
- B. (Absolute Risk Reduction) / (Number of people in trial)
- C. ((Control event rate) - (Experimental event rate)) / (Control event rate)
- D. 1 / (Relative risk)
- E. 1 / (Hazard ratio)

Question 51 of 331

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- D. 1 / (Relative risk)
- E. 1 / (Hazard ratio)

NNT = 1 / (EER - CER), or 1 / Absolute Risk Reduction

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 52 of 331

Which one of the following is associated with increased lung compliance?

- A. Kyphosis
- B. Pulmonary oedema
- C. Emphysema
- D. Pulmonary fibrosis
- E. Pneumonectomy

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Respiratory physiology: lung compliance

Lung compliance is defined as change in lung volume per unit change in airway pressure

Causes of increased compliance
- age
- emphysema

Causes of decreased compliance
- pulmonary oedema
- pulmonary fibrosis
- pneumonectomy
- kyphosis

Question 53 of 331

What is the mode of inheritance of vitamin D-resistant rickets?

- A. X-linked dominant
- B. Autosomal recessive
- C. Autosomal dominant
- D. Mitochondrial inheritance
- E. X-linked recessive

Question 53 of 331

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- D. Mitochondrial inheritance
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Vitamin D-resistant rickets

Vitamin D-resistant rickets is a X-linked dominant condition which usually presents in infancy with failure to thrive. It is caused by impaired phosphate reabsorption in the renal tubules

Features
- failure to thrive
- normal serum calcium, low phosphate, elevated alkaline phosphotase
- x-ray changes: cupped metaphyses with widening of the epiphyses

Diagnosis is made by demonstrating increased urinary phosphate

Management
- high-dose vitamin D supplements
- oral phosphate supplements

Question 54 of 331

Which one of the following best describes rheumatoid factor?

- A. IgG against the Fc portion of IgM
- B. IgM against the Fc portion of IgA
- C. IgM against the Fc portion of IgM
- D. IgM against the Fc portion of IgG
- E. IgG against the Fc portion of IgA

Question 54 of 331

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- C. IgM against the Fc portion of IgM
- ✓ D. IgM against the Fc portion of IgG
- E. IgG against the Fc portion of IgA

Rheumatoid factor is an IgM antibody against IgG

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either
- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:
- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

Question 55 of 331

A 17-year-old man is investigated for recurrent infections and easy bruising. In the past year he has had four episodes of pneumonia. Other than the bruising he is noted to have severe eczema on his trunk and arms. A full blood count is ordered and reported as follows:

Hb 14.1 g/dl

Plt 82 * 10^9/l

WBC 5.9 * 10^9/l

Neuts 4.4 * 10^9/l

Further bloods show low immunoglobulin G levels. What is the most likely diagnosis?

- A. Bruton's congenital agammaglobulinaemia
- B. Wiskott-Aldrich syndrome
- C. Ataxic telangiectasia
- D. Chediak-Higashi syndrome
- E. DiGeorge syndrome

Question 55 of 331

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- C. Ataxic telangiectasia
- D. Chediak-Higashi syndrome
- E. DiGeorge syndrome

Wiskott-Aldrich syndrome
- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia

Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene.

Features
- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia

Question 56 of 331

Which one of the following statements regarding hypersensitivity reactions is false?

- A. Delayed hypersensitivity is responsible for graft versus host disease
- B. Anaphylaxis is a type I reaction
- C. Type II reactions are caused by circulating antibodies reacting with antigen on cell surface
- D. Type IV reactions are T cell mediated
- E. Goodpasture's syndrome is an example of a type III reaction

Question 56 of 331

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- D. Type IV reactions are T cell mediated
- ✓ E. Goodpasture's syndrome is an example of a type III reaction

Goodpasture's syndrome is actually an example of a type II reaction. The other statements are true

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 57 of 331

Which layer of the epidermis are melanocytes found in?

- A. Stratum lucidum
- B. Stratum germinativum
- C. Stratum spinosum
- D. Stratum corneum
- E. Stratum granulosum

Question 57 of 331

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- A. Stratum lucidum
- ✓ B. Stratum germinativum
- C. Stratum spinosum
- D. Stratum corneum
- E. Stratum granulosum

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

Epidermis

The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina

It may be divided in to five layers:

Layer	Description
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

Question 58 of 331

The muscarinic acetylcholine receptor is an example of a:

- A. Ligand-gated ion channel
- B. Tyrosine kinase receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Intracellular receptor

Question 58 of 331

The muscarinic acetylcholine receptor is an example of a:

- A. Ligand-gated ion channel
- B. Tyrosine kinase receptor
- C. Guanylate cyclase receptor
- ✓ D. G protein-coupled receptor
- E. Intracellular receptor

Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel
- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 59 of 331

A 34-year-old man is climbing Mount Kilimanjaro. For the past two days he has complained of nausea and a headache. The climbing team is now at an altitude of 4,500m when he develops shortness of breath and a pink frothy cough. Examination reveals bibasal crackles. What is the most appropriate treatment, other than descent?

- A. Nifedipine
- B. Frusemide
- C. Mannitol
- D. Hydralazine
- E. Third-generation cephalosporin

Question 59 of 331

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- ✓ A. Nifedipine
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- C. Mannitol
- D. Hydralazine
- E. Third-generation cephalosporin

This man has developed high altitude pulmonary oedema (HAPE) and should to be treated with prompt descent, oxygen and nifedipine if it is available. Other options for treating HAPE include dexamethasone, acetazolamide and phosphodiesterase type V inhibitors.

Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

Management of HACE

- descent
- dexamethasone

Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors*
- oxygen if available

*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

Question 60 of 331

Immunoglobulin therapy may be indicated in each of the following except:

- A. Dermatomyositis
- B. Guillain-Barre syndrome
- C. Kawasaki disease
- D. Idiopathic thrombocytopenic purpura
- E. Thrombotic thrombocytopenic purpura

Question 60 of 331

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- B. Guillain-Barre syndrome
- C. Kawasaki disease
- D. Idiopathic thrombocytopenic purpura
- ✓ E. Thrombotic thrombocytopenic purpura

The management of management thrombotic thrombocytopenic purpura involves steroids and immunosuppressants. Plasma exchange is also commonly used

Immunoglobulins: therapeutics

The Department of Health issued guidelines on the use of intravenous immunoglobulins in May 2008

Uses

- primary and secondary immunodeficiency
- idiopathic thrombocytopenic purpura
- myasthenia gravis
- Guillain-Barre syndrome
- Kawasaki disease
- toxic epidermal necrolysis
- pneumonitis induced by CMV following transplantation
- low serum IgG levels following haematopoietic stem cell transplant for malignancy
- dermatomyositis
- chronic inflammatory demyelinating polyradiculopathy

Basics

- formed from large pool of donors (e.g. 5,000)
- IgG molecules with a subclass distribution similar to that of normal blood
- half-life of 3 weeks

Question 61 of 331

A 43-year-old man has a routine medical for insurance purposes. The following result is obtained:

Uric acid 622 µmol/l (210 - 480)

He is well with no significant past medical history. What is the most appropriate test to perform next?

- A. Lipid profile
- B. Thyroid function test
- C. Calcium
- D. Parathyroid hormone
- E. Pyrophosphate levels

Question 61 of 331

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Hyperuricaemia may be associated with both hyperlipidaemia and hypertension. It may also be seen in conjunction with the metabolic syndrome

Hyperuricaemia

Increased levels of uric acid may be seen secondary to either increased cell turnover or reduced renal excretion of uric acid. Hyperuricaemia may be found in asymptomatic patients who have not experienced attacks of gout

Hyperuricaemia may be associated with hyperlipidaemia and hypertension. It may also be seen in conjunction with the metabolic syndrome

Increased synthesis
- Lesch-Nyhan disease
- myeloproliferative disorders
- diet rich in purines
- exercise
- psoriasis
- cytotoxics

Decreased excretion
- drugs: low-dose aspirin, diuretics, pyrazinamide
- pre-eclampsia
- alcohol
- renal failure
- lead

Question 62 of 331

A 66-year-old comes for review. He had a prosthetic aortic valve replacement five years for which he is warfarinised. Over the past three months he has been complaining of fatigue and a full blood count was requested:

Hb	10.3 g/dl
MCV	68 fl
Plt	356 * 10^9/l
WBC	5.2 * 10^9/l
Blood film	Hypochromia
INR	3.0

An upper GI endoscopy was reported as normal. What is the most appropriate next investigation?

- A. Transthoracic echocardiogram
- B. Colonoscopy
- C. Three sets of blood cultures
- D. Transoesophageal echocardiogram
- E. Reticulocyte count

Question 62 of 331

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- C. Three sets of blood cultures
- D. Transoesophageal echocardiogram
- E. Reticulocyte count

Any patient of this age with an unexplained microcytic anaemia should have a lower gastrointestinal tract investigation to exclude colorectal cancer

Colorectal cancer: referral guidelines

NICE recommend the following patients are referred urgently (i.e. within 2 weeks) to colorectal services for investigation:

- patients > 40 years old, reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more
- patients > 60 years old, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms
- patients > 60 years old, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding
- any patient presenting with a right lower abdominal mass consistent with involvement of the large bowel
- any patient with a palpable rectal mass
- unexplained iron deficiency anaemia in men or non-menstruating women (Hb < 11 g/dl in men, < 10 g/dl in women)

Question 63 of 331

A new blood test to screen patients for heart failure is trialled on 500 patients. The test was positive in 40 of the 50 patients shown to have heart failure by echocardiography. It was also positive in 20 patients who were shown not to have heart failure. What is the positive predictive value of the test?

- A. 0.8
- B. 0.66
- C. 0.33
- D. 0.1
- E. Cannot be calculated

Question 63 of 331

A new blood test to screen patients for heart failure is trialled on 500 patients. The test was positive in 40 of the 50 patients shown to have heart failure by echocardiography. It was also positive in 20 patients who were shown not to have heart failure. What is the positive predictive value of the test?

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- ✓ B. 0.66
- C. 0.33
- D. 0.1
- E. Cannot be calculated

A contingency table can be constructed from the above data, as shown below:

	Heart failure	**No heart failure**
Test positive	40	20
Test negative	10	430

Positive predictive value = TP / (TP + FP) = 40 / (40 + 20) = 0.66

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 64 of 331

A 59-year-old man presents with a severe pain deep within his right ear. He feels dizzy and reports that the room 'is spinning'. Clinical examination shows a partial facial nerve palsy on the right side and vesicular lesions on the anterior two-thirds of his tongue. What is the most likely diagnosis?

- A. Meniere's disease
- B. Herpes zoster ophthalmicus
- C. Ramsay Hunt syndrome
- D. Acoustic neuroma
- E. Trigeminal neuralgia

Question 64 of 331

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- ✓ C. Ramsay Hunt syndrome
- D. Acoustic neuroma
- E. Trigeminal neuralgia

Ramsay Hunt syndrome

Ramsay Hunt syndrome (herpes zoster oticus) is caused by the reactivation of the varicella zoster virus in the geniculate ganglion of the seventh cranial nerve.

Features
- auricular pain is often the first feature
- facial nerve palsy
- vesicular rash around the ear
- other features include vertigo and tinnitus

Management
- oral aciclovir and corticosteroids are usually given

Question 65 of 331

For a patient undergoing an elective splenectomy, when is the optimal time to give the pneumococcal vaccine?

- A. Two weeks before surgery
- B. One week before surgery
- C. Immediately following surgery
- D. Two weeks after surgery
- E. At least one month after surgery

Question 65 of 331

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- ✓ A. Two weeks before surgery
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- D. Two weeks after surgery
- E. At least one month after surgery

The current British National Formulary recommends giving the vaccine at least 2 weeks before elective splenectomy

Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus* infections

Vaccination
- if elective, should be done 2 weeks prior to operation
- pneumococcal, Hib, meningitis A & C and annual influenza vaccination

Antibiotic prophylaxis
- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

*usually from dog bites

Question 66 of 331

Troponin T is a type of:

- A. Contractile protein
- B. Enzyme
- C. Protein kinase C inhibitor
- D. Structural protein
- E. T-tubule membrane wall component

Question 66 of 331

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Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superceded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	**Peak value**	**Returns to normal**
Myoglobin	1-2 hours	6-8 hours	1-2 days
CK-MB	2-6 hours	16-20 hours	2-3 days
CK	4-8 hours	16-24 hours	3-4 days
Trop T	4-6 hours	12-24 hours	7-10 days
AST	12-24 hours	36-48 hours	3-4 days
LDH	24-48 hours	72 hours	8-10 days

Question 67 of 331

Aldosterone is secreted by the:

- A. Juxtaglomerular apparatus
- B. Zona glomerulosa
- C. Posterior pituitary
- D. Zona reticularis
- E. Zona fasciculata

Question 67 of 331

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Adrenal cortex mnemonic: GFR - ACD

Renin-angiotensin-aldosterone system

Adrenal cortex (mnemonic **GFR - ACD**)
- zona **g**lomerulosa (on outside): mineralocorticoids, mainly **a**ldosterone
- zona **f**asciculata (middle): glucocorticoids, mainly **c**ortisol
- zona **r**eticularis (on inside): androgens, mainly **d**ehydroepiandrosterone (DHEA)

Renin
- released by JGA cells in kidney in response to reduced renal perfusion, low sodium
- hydrolyses angiotensinogen to form angiotensin I

Factors stimulating renin secretion
- low BP
- hyponatraemia
- sympathetic nerve stimulation
- catecholamines
- erect posture

Angiotensin
- ACE in lung converts angiotensin I --> angiotensin II
- vasoconstriction leads to raised BP
- stimulates thirst
- stimulates aldosterone and ADH release

Aldosterone
- released by the zona glomerulosa in response to raised angiotensin II, potassium, and ACTH levels
- causes retention of Na^+ in exchange for K^+/H+ in distal tubule

Question 68 of 331

A study is designed to assess a new proton pump inhibitor (PPI) in elderly patients who are taking aspirin. The new PPI is given to 120 patients whilst a control group of 240 is given the standard PPI. Over a five year period 24 of the group receiving the new PPI had an upper GI bleed compared to 60 who received the standard PPI. What is the absolute risk reduction?

- A. 15%
- B. 10%
- C. 12
- D. 5%
- E. 20

Question 68 of 331

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- A. 15%
- B. 10%
- C. 12
- ✓ D. 5%
- E. 20

Absolute risk reduction = (Experimental event rate) - (Control event rate)
Experimental event rate = 24 / 120 = 0.2
Control event rate = 60 / 240 = 0.25
Absolute risk reduction = 0.2 - 0.25 = -0.05 = 5% reduction

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 69 of 331

Which foramen does the maxillary nerve go through?

- A. Jugular foramen
- B. Foramen ovale
- C. Superior orbital fissure
- D. Optic canal
- E. Foramen rotundum

Question 69 of 331

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Foramina of the skull

Questions asking about foramina of the skull have come up in the exam in previous years. Below is a brief summary of the major foramina, please see the Wikipedia link for a full list.

Foramen	Bone	Vessels	Nerves
Optic canal	Sphenoid	Ophthalmic artery	Optic nerve (II)
Superior orbital fissure	Sphenoid	Superior ophthalmic vein Inferior ophthalmic vein	Oculomotor nerve (III) Trochlear nerve (IV) lacrimal, frontal and nasociliary branches of ophthalmic nerve (V1) Abducent nerve (VI)
Inferior orbital fissure	Sphenoid and maxilla	Inferior ophthalmic veins Infraorbital artery Infraorbital vein	Zygomatic nerve and infraorbital nerve of maxillary nerve (V2) Orbital branches of pterygopalatine ganglion
Foramen rotundum	Sphenoid	-	Maxillary nerve (V2)
Foramen ovale	Sphenoid	Accessory meningeal artery	Mandibular nerve (V3)
Jugular foramen	Occipital and temporal	Posterior meningeal artery Ascending pharyngeal artery Inferior petrosal sinus Sigmoid sinus Internal jugular vein	Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI)

Question 70 of 331

Which one of the following is in direct anatomical contact with the left kidney?

- A. Stomach
- B. Distal part of small intestine
- C. Spleen
- D. Pancreas
- E. Duodenum

Question 70 of 331

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Renal anatomy

The tables below show the anatomical relations of the kidneys:

Right kidney

Direct contact	Layer of peritoneum in-between
Right suprarenal gland Duodenum Colon	Liver Distal part of small intestine

Left kidney

Direct contact	Layer of peritoneum in-between
Left suprarenal gland Pancreas Colon	Stomach Spleen Distal part of small intestine

Question 71 of 331

Which one of the following statements regarding the power of a study is correct?

- A. Is the probability of rejecting the null hypothesis when it is false
- B. Decreases with increasing sample size
- C. Lies within 2 standard deviations of the mean
- D. Is the chance a significant p value will be reached
- E. Is equal to 1 - (the probability of a type I error)

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Power = 1 - the probability of a type II error

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example

- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 72 of 331

Which of the following may be used in the treatment of hereditary angioedema?

- A. Anabolic steroids
- B. Oral contraceptive pill
- C. ACE inhibitors
- D. Beta-blockers
- E. Aspirin

Question 72 of 331

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Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues

Investigation
- C1-INH level is low
- low C2 and C4 levels are seen, even between attacks

Symptoms
- attacks may be proceeded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management
- acute: IV C1-inhibitor concentrate
- anabolic steroid Danazol may help

Question 73 of 331

How is the left ventricular ejection fraction calculated?

- A. End systolic LV volume / end diastolic LV volume
- B. End diastolic LV volume / end systolic LV volume
- C. End diastolic LV volume / stroke volume
- D. End systolic LV volume - end diastolic LV volume
- E. Stroke volume / end diastolic LV volume

Question 73 of 331

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- ✓ E. Stroke volume / end diastolic LV volume

Cardiovascular physiology

Left ventricular ejection fraction

Left ventricular ejection fraction = (stroke volume / end diastolic LV volume) * 100%

Stroke volume = end diastolic LV volume - end systolic LV volume

Question 74 of 331

T-Helper cells of the Th2 subset typically secrete:

- A. IL-4, IL-5, IL-6, IL-10, IL-13
- B. IFN-gamma, IL-2, IL-3
- C. IL-1, IL-6, TNF-alpha
- D. IFN-beta, IL-4, IL-8
- E. IL-1

Question 74 of 331

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- D. IFN-beta, IL-4, IL-8
- E. IL-1

T-Helper cells

There are two major subsets of T-Helper cells:

Th1
- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2
- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Question 75 of 331

Where are G protein-coupled receptors located?

- A. Nucleus
- B. Golgi apparatus
- C. Ribosome
- D. Cell membrane
- E. Mitochondria

Question 75 of 331

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G protein-coupled receptors span the cell membrane

Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel
- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 76 of 331

Which one of the following molecules acts as the co-receptor for cells expressing antigens combined with HLA class I molecules?

- A. CD4
- B. CD2b
- C. CD1
- D. CD8
- E. CD2

Question 76 of 331

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- ✓ D. CD8
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Clusters of differentiation

The table below lists the major clusters of differentiation (CD) molecules

CD1	HLA molecule that presents lipid molecules
CD2	Found on thymocytes, T cells, and some natural killer cells that acts as a ligand for CD58 and CD59 and is involved in signal transduction and cell adhesion
CD3	The signalling component of the T cell receptor (TCR) complex
CD4	Co-receptor for HLA class II; also a receptor used by HIV to enter T cells
CD8	Co-receptor for HLA class I; also found on a subset of myeloid dendritic cells

Question 77 of 331

Which one of the following best describes the Bohr effect?

- A. Increase in pO2 means CO2 binds less well to Hb
- B. Decreasing acidity (or pCO2) means oxygen binds less well to Hb
- C. Decrease in pO2 means CO2 binds less well to Hb
- D. Raised 2,3-DPG enhances oxygen delivery to the tissues
- E. Increasing acidity (or pCO2) means oxygen binds less well to Hb

Question 77 of 331

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- D. Raised 2,3-DPG enhances oxygen delivery to the tissues
- ✓ E. Increasing acidity (or pCO2) means oxygen binds less well to Hb

Respiratory physiology

Chloride shift
- CO2 diffuses into RBCs
- CO2 + H20 ---- carbonic anhydrase ---> HCO3- + H+
- H+ combines with Hb
- HCO3- diffuses out of cell,- Cl- replaces it

Bohr effect
- increasing acidity (or pCO2) means O2 binds less well to Hb

Haldane effect
- increase pO2 means CO2 binds less well to Hb

Question 78 of 331

What are funnel plots primarily used for?

- A. Demonstrate the heterogeneity of a meta-analysis
- B. Demonstrate the existence of publication bias in meta-analyses
- C. Provide a graphical representation of the relative risk results in a case-control study
- D. Provide a graphical representation of the relative risk results in a cohort study
- E. Provide a graphical representation of the probability of a patient experiencing a particular adverse effect

Question 78 of 331

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Funnel plots - show publication bias in meta-analyses

Funnel plot

A funnel plot is primarily used to demonstrate the existence of publication bias in meta-analyses. Funnel plots are usually drawn with treatment effects on the horizontal axis and study size on the vertical axis.

Interpretation

- a symmetrical, inverted funnel shape indicates that publication bias is unlikely
- conversely, an asymmetrical funnel indicates a relationship between treatment effect and study size. This indicates either publication bias or a systematic difference between smaller and larger studies ('small study effects')

Question 79 of 331

Which one of the following statements regarding interleukin 1 (IL-1) is true?

- A. It is released mainly by macrophages/monocytes
- B. It causes vasoconstriction
- C. It reduces expression of selectin molecules on the endothelium
- D. IL-1 antagonists are currently licensed for use in colorectal cancer
- E. It inhibits the release of nitric oxide by the endothelium

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IL-1

Interleukin 1 (IL-1) is a key mediator of the immune response. It is secreted mainly by macrophages and monocytes and acts as a costimulator of T cell and B cell proliferation.

Other effects include increasing the expression of adhesion molecules on the endothelium. By stimulating the release by the endothelium of vasoactive factors such as PAF, nitric oxide and prostacyclin it also causes vasodilation and increases vascular permeability. It is therefore one of the mediators of shock in sepsis. Along with IL-6 and TNF, it acts on the hypothalamus causing pyrexia.

Question 80 of 331

Which of the following statements is true regarding the p53 gene?

- A. It is an oncogene
- B. Mutation results in a gain of function
- C. 50% of families with a strong history of breast cancer have a p53 mutation
- D. Li-Fraumeni syndrome predisposes to the development of sarcomas
- E. It is located on chromosome 13

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p53

p53 is a tumour suppressor gene located on chromosome 17p. It is the most commonly mutated gene in breast, colon and lung cancer

p53 is thought to play a crucial role in the cell cycle, preventing entry into the S phase until DNA has been checked and repaired. It may also be a key regulator of apoptosis

Li-Fraumeni syndrome is a rare autosomal dominant disorder characterised by the early onset of a variety of cancers such as sarcomas and breast cancer. It is caused by mutation in the p53 gene

Question 81 of 331

A new drug is trialled for the treatment of lung cancer. Drug A is given to 500 people with early stage non-small cell lung cancer and a placebo is given to 450 people with the same condition. After 5 years 300 people who received drug A had survived compared to 225 who received the placebo. What is the number needed to treat to save one life?

- A. 3.33
- B. 75
- C. 10
- D. 5
- E. 2

Question 81 of 331

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- A. 3.33
- B. 75
- ✓ C. 10
- D. 5
- E. 2

NNT = 1 / (EER - CER), or 1 / Absolute Risk Reduction

Experimental (drug A) event rate = 300 / 500 = 0.6
Control (placebo) event rate = 225 / 450 = 0.5

Absolute risk reduction = 0.6 - 0.5 = 0.1
Number needed to treat = 1 / 0.1 = 10

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 82 of 331

Which of the following conditions is inherited in an autosomal dominant fashion?

- A. Noonan syndrome
- B. Homocystinuria
- C. Cystinuria
- D. Congenital adrenal hyperplasia
- E. Fanconi anaemia

Question 82 of 331

Which of the following conditions is inherited in an autosomal dominant fashion?

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- B. Homocystinuria
- C. Cystinuria
- D. Congenital adrenal hyperplasia
- E. Fanconi anaemia

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias
Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease*

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 83 of 331

Acute intermittent porphyria is due to a defect in:

- A. ALA synthetase
- B. PPG oxidase
- C. Uroporphyrinogen decarboxylase
- D. Ferrochelatase
- E. Porphobilinogen deaminase

Question 83 of 331

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- B. PPG oxidase
- C. Uroporphyrinogen decarboxylase
- D. Ferrochelatase
- ✓ E. Porphobilinogen deaminase

AIP - porphobilinogen de**A**minase; P**C**T - uroporphyrinogen de**C**arboxylase

Porphyrias

Overview
- abnormality in enzymes responsible for the biosynthesis of haem
- results in overproduction of intermediate compounds (porphyrins)
- may be acute or non-acute

Acute intermittent porphyria (AIP)
- autosomal dominant
- defect in porphobilinogen deaminase
- female and 20-40 year olds more likely to be affected
- typically present with abdominal symptoms, neuropsychiatric symptoms
- hypertension and tachycardia common
- urine turns deep red on standing

Porphyria cutanea tarda (PCT)
- most common hepatic porphyria
- defect in uroporphyrinogen decarboxylase
- may be caused by hepatocyte damage e.g. alcohol, oestrogens
- classically photosensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp
- manage with chloroquine

Variegate porphyria
- autosomal dominant
- defect in protoporphyrinogen oxidase
- photosensitive blistering rash
- abdominal and neurological symptoms
- more common in South Africans

Question 84 of 331

Which one of the following adrenoceptors cause vasoconstriction and relaxation of GI muscle in response to sympathetic stimulation?

- A. Alpha-1
- B. Alpha-2
- C. Beta-1
- D. Beta-2
- E. Beta-3

Question 84 of 331

Which one of the following adrenoceptors cause vasoconstriction and relaxation of GI muscle in response to sympathetic stimulation?

- ✓ A. Alpha-1
- B. Alpha-2
- C. Beta-1
- D. Beta-2
- E. Beta-3

Adrenoceptors

Alpha-1
- vasoconstriction
- relaxation of GI smooth muscle
- salivary secretion
- hepatic glycogenolysis

Alpha-2
- mainly presynaptic: inhibition of transmitter release (inc NA, Ach from autonomic nerves)
- inhibits insulin
- platelet aggregation

Beta-1
- mainly located in the heart
- increase heart rate + force

Beta-2
- vasodilation
- bronchodilation
- relaxation of GI smooth muscle

Beta-3
- lipolysis

Pathways
- all are G-protein coupled
- alpha-1:activate phospholipase C --> IP3 --> DAG
- alpha-2: inhibit adenylate cyclase
- beta-1: stimulate adenylate cyclase
- beta-2: stimulate adenylate cyclase
- beta-3: stimulate adenylate cyclase

Question 85 of 331

Where is CCK secreted from?

- A. I cells in upper small intestine
- B. G cells in stomach
- C. K cells in upper small intestine
- D. D cells in the pancreas
- E. S cells in upper small intestine

Question 85 of 331

Where is CCK secreted from?

- ✓ A. I cells in upper small intestine
- B. G cells in stomach
- C. K cells in upper small intestine
- D. D cells in the pancreas
- E. S cells in upper small intestine

Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
Gastrin	G cells in antrum of the stomach	Distension of stomach, extrinsic nerves Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
CCK	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
Secretin	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
VIP	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion
Somatostatin	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Question 86 of 331

An endocrinologist performs a study to assess whether a patient's HbA1c level is correlated to their LDL level. Assuming both HbA1c and LDL are normally distributed, which one of the following statistical tests is it most appropriate to perform?

- A. Chi-squared test
- B. Pearson's product-moment coefficient
- C. Mann-Whitney test
- D. Spearman's rank correlation coefficient
- E. McNemar's test

Question 86 of 331

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- A. Chi-squared test
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- C. Mann-Whitney test
- D. Spearman's rank correlation coefficient
- E. McNemar's test

Correlation
- parametric (normally distributed): Pearson's coefficient
- non-parametric: Spearman's coefficient

Pearson's product-moment coefficient test is most appropriate as the data is parametric and the study is assessing the correlation of two variables

McNemar's test is a non-parametric method used on nominal data to determine whether the row and column marginal frequencies are equal

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 87 of 331

A 65-year-old woman is investigated for a 6 week history of worsening shortness of breath, lethargy and weight loss. Her past medical history includes chronic obstructive pulmonary disease, hypertension and she is an ex-smoker. Clinical examination is unremarkable. Investigation results are as follows:

Chest x-ray
Hyperinflated lung fields, normal heart size

Bloods

Sodium	131 mmol/l
Potassium	3.4 mmol/l
Urea	7.2 mmol/l
Creatinine	101 µmol/l
Hb	10.4 g/dl
MCV	91 fl
Plt	452 * 10^9/l
WBC	3.7 * 10^9/l

What is the most appropriate management?

- A. Screen for depression
- B. Short synacthen test
- C. Urgent referral to the chest clinic
- D. Stop bendroflumethiazide
- E. Urgent gastroscopy

Question 87 of 331

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Despite a normal chest x-ray an ex-smoker with shortness of breath, weight loss and hyponatraemia should be investigated on an urgent basis for lung cancer. This approach is supported by current NICE guidelines. Whilst gastrointestinal cancer is a possibility the normal MCV is not entirely consistent with chronic blood loss

Lung cancer: referral

The 2005 NICE cancer referral guidelines gave the following advice:

Consider immediate referral for patients with:

- signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure)
- stridor

Refer urgently patients with:

- persistent haemoptysis (in smokers or ex-smokers aged 40 years and older)
- a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation)
- a normal chest X-ray where there is a high suspicion of lung cancer
- a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms where a chest x-ray indicates pleural effusion, pleural mass or any suspicious lung pathology

Refer urgently for chest x-ray for patients with any of the following:

- haemoptysis
- unexplained or persistent (longer than 3 weeks): chest and/or shoulder pain, dyspnoea, weight loss, chest signs, hoarseness, finger clubbing, cervical or supraclavicular lymphadenopathy, cough, features suggestive of metastasis from a

lung cancer (for example, secondaries in the brain, bone, liver, skin)

- underlying chronic respiratory problems with unexplained changes in existing symptomS

Question 88 of 331

Which one of the following is the best definition of the p value?

- A. The probability of obtaining a similar result, assuming that the null hypothesis is true
- B. The probability that a replicating experiment would not yield the same conclusion
- C. The probability of obtaining a result at least as extreme, assuming that the null hypothesis is true
- D. The probability that the null hypothesis is true
- E. The probability of obtaining a result at least as extreme, assuming that the null hypothesis is false

Question 88 of 331

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- D. The probability that the null hypothesis is true
- E. The probability of obtaining a result at least as extreme, assuming that the null hypothesis is false

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example

- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 89 of 331

A 25-year-old man who has been morbidly obese for the past five years is reviewed in the endocrinology clinic. In this patient, which one of the following hormones would increase appetite as levels increase?

- A. Leptin
- B. Thyroxine
- C. Adiponectin
- D. Ghrelin
- E. Serotonin

Question 89 of 331

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Obesity hormones
- leptin decreases appetite
- ghrelin increases appetite

Whilst thyroxine can increase appetite it does not fit with the clinical picture being described

Obesity: physiology

Leptin

Leptin is thought to play a key role in the regulation of body weight. It is produced by adipose tissue and acts on satiety centres in the hypothalamus and decreases appetite. More adipose tissue (e.g. in obesity) results in high leptin levels.

Leptin stimulates the release of melanocyte-stimulating hormone (MSH) and corticotrophin-releasing hormone (CRH). Low levels of leptin stimulates the release of neuropeptide Y (NPY)

Ghrelin

Where as leptin induces satiety, ghrelin stimulates hunger. It is produced mainly by the fundus of the stomach and the pancreas. Ghrelin levels increase before meals and decrease after meals

Question 90 of 331

You are asked to review some arterial blood gases (ABGs) done on a patient who has recently been admitted to the Emergency Department. The ABGs shown below were taken on air:

pH 7.53

pCO2 5.1 kPa

pO2 13.9 kPa

Which one of the following is the most likely cause?

- A. Chronic obstructive pulmonary disease
- B. Renal tubular acidosis
- C. Mesenteric ischaemia
- D. Anxiety
- E. Vomiting

Question 90 of 331

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- B. Renal tubular acidosis
- C. Mesenteric ischaemia
- D. Anxiety
- ✓ E. Vomiting

The blood gases show a metabolic alkalosis

Metabolic alkalosis

Metabolic alkalosis may be caused by a loss of hydrogen ions or a gain of bicarbonate. It is due mainly to problems of the kidney or gastrointestinal tract

Causes

- vomiting / aspiration (e.g. peptic ulcer leading to pyloric stenos, nasogastric suction)
- diuretics
- liquorice, carbenoxolone
- hypokalaemia
- primary hyperaldosteronism
- Cushing's syndrome
- Bartter's syndrome
- congenital adrenal hyperplasia

Mechanism of metabolic alkalosis

- activation of renin-angiotensin II-aldosterone (RAA) system is a key factor
- aldosterone causes reabsorption of Na^+ in exchange for H+ in the distal convoluted tubule
- ECF depletion (vomiting, diuretics) --> Na^+ and Cl- loss --> activation of RAA system --> raised aldosterone levels
- in hypokalaemia, K^+ shift from cells --> ECF, alkalosis is caused by shift of H+ into cells to maintain neutrality

Question 91 of 331

What is the main mechanism by which vitamin B12 is absorbed?

- A. Passive absorption in the terminal ileum
- B. Active absorption in the middle to terminal part of jejunum
- C. Active absorption by the parietal cells of the stomach
- D. Active absorption in the terminal ileum
- E. Passive absorption in the proximal ileum

Question 91 of 331

What is the main mechanism by which vitamin B12 is absorbed?

- A. Passive absorption in the terminal ileum
- B. Active absorption in the middle to terminal part of jejunum
- C. Active absorption by the parietal cells of the stomach
- ✓ D. Active absorption in the terminal ileum
- E. Passive absorption in the proximal ileum

Vitamin B12 is actively absorbed in the terminal ileum

A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Vitamin B12 deficiency

Vitamin B12 is mainly used in the body for red blood cell development and also maintenance of the nervous system. It is absorbed after binding to intrinsic factor (secreted from parietal cells in the stomach) and is actively absorbed in the terminal ileum. A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Causes of vitamin B12 deficiency
- pernicious anaemia
- post gastrectomy
- poor diet
- disorders of terminal ileum (site of absorption): Crohn's, blind-loop etc

Features of vitamin B12 deficiency
- macrocytic anaemia
- sore tongue and mouth
- neurological symptoms: e.g. Ataxia
- neuropsychiatric symptoms: e.g. Mood disturbances

Management
- if no neurological involvement 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- if a patient is also deficient in folic acid then it is important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

Question 92 of 331

A 24-year-old female who is 10 weeks in to her first pregnancy presents for review. Her blood pressure today is 126/82 mmHg. What normally happens to blood pressure during pregnancy?

- A. Falls in first half of pregnancy before rising to pre-pregnancy levels before term
- B. Systolic + diastolic rises by < 10 mmHg
- C. Systolic + diastolic falls by < 10 mmHg
- D. Rise in first half of pregnancy before falling to pre-pregnancy levels before term
- E. Doesn't change

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- C. Systolic + diastolic falls by < 10 mmHg
- D. Rise in first half of pregnancy before falling to pre-pregnancy levels before term
- E. Doesn't change

Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy in usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	**Pregnancy-induced hypertension (PIH, also known as gestational hypertension)**	**Pre-eclampsia**
A history of hypertension before pregnancy or an elevated blood pressure > 140/90 mmHg before 20 weeks gestation No proteinuria, no oedema Occurs in 3-5% of pregnancies and is more common in older women	Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks) No proteinuria, no oedema Occurs in around 5-7% of pregnancies Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life	Pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours) Oedema may occur but is now less commonly used as a criteria Occurs in around 5% of pregnancies

Question 93 of 331

Which one of the following karyotypes is associated with short stature?

- A. 45,XO
- B. 46,YO
- C. 46,XO
- D. 47,XYY
- E. 47,XXY

Question 93 of 331

Which one of the following karyotypes is associated with short stature?

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- D. 47,XYY
- E. 47,XXY

Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 94 of 331

In a normal distribution what percentage of values lie within 3 standard deviations of the mean?

- A. 68.3%
- B. 98.3%
- C. 95.4%
- D. 99.7%
- E. 97.2%

Question 94 of 331

In a normal distribution what percentage of values lie within 3 standard deviations of the mean?

- A. 68.3%
- B. 98.3%
- C. 95.4%
- ✓ D. 99.7%
- E. 97.2%

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 95 of 331

A 14-year-old girl presents with a swollen left knee. Her parents state she suffers from haemophilia and has been treated for a right-sided haemarthrosis previously. What other condition is she most likely to have?

- A. Turner's syndrome
- B. Down's syndrome
- C. Ataxia telangiectasia
- D. Hunter's syndrome
- E. Coeliac disease

Question 95 of 331

A 14-year-old girl presents with a swollen left knee. Her parents state she suffers from haemophilia and has been treated for a right-sided haemarthrosis previously. What other condition is she most likely to have?

- ✓ A. Turner's syndrome
- B. Down's syndrome
- C. Ataxia telangiectasia
- D. Hunter's syndrome
- E. Coeliac disease

Haemophilia is a X-linked recessive disorder and would hence be expected only to occur in males. As patients with Turner's syndrome only have one X chromosome however, they may develop X-linked recessive conditions

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 96 of 331

A 37-year-old man with a history of alcohol excess is admitted with alcohol-withdrawal seizures to the acute medical unit. Admission bloods show the following:

Na^+	137 mmol/l
K^+	3.0 mmol/l
Urea	2.0 mmol/l
Creatinine	78 µmol/l
Calcium	2.03 mmol/l

What other blood abnormality is he also most likely to have?

- A. Hypomagnesaemia
- B. Elevated ammonia levels
- C. Hypophosphataemia
- D. Partially compensated metabolic alkalosis
- E. Elevated lactate levels

Question 96 of 331

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- C. Hypophosphataemia
- D. Partially compensated metabolic alkalosis
- E. Elevated lactate levels

Hypomagnesaemia

Cause of low magnesium
- diuretics
- total parenteral nutrition
- diarrhoea
- alcohol
- hypokalaemia, hypocalcaemia

Features
- paraesthesia
- tetany
- seizures
- arrhythmias
- decreased PTH secretion --> hypocalcaemia
- ECG features similar to those of hypokalaemia
- exacerbates digoxin toxicity

Question 97 of 331

Which of the following conditions is inherited in a X-linked recessive fashion?

- A. Androgen insensitivity syndrome
- B. Myotonic dystrophy
- C. von Willebrand's disease
- D. Ehlers-Danlos syndrome
- E. Huntington's disease

Question 97 of 331

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- B. Myotonic dystrophy
- C. von Willebrand's disease
- D. Ehlers-Danlos syndrome
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X-linked conditions: Duchenne/Becker, haemophilia, G6PD

X-linked recessive conditions

The following conditions are inherited in a X-linked recessive fashion:

Androgen insensitivity syndrome
Becker muscular dystrophy
Colour blindness
Duchenne muscular dystrophy
Fabry's disease
G6PD deficiency
Haemophilia A,B
Hunter's disease
Lesch-Nyhan syndrome
Nephrogenic diabetes insipidus
Ocular albinism
Retinitis pigmentosa
Wiskott-Aldrich syndrome

The following diseases have varying patterns of inheritance, with the majority being in an X-linked recessive fashion:

Chronic granulomatous disease (in > 70%)

Question 98 of 331

Which one of the following best describes the characteristics of a negatively skewed distribution?

- A. Median < mode < mean
- B. Mean < median < mode
- C. Mode < mean < median
- D. Median < mean < mode
- E. Mean < mode < median

Question 98 of 331

Which one of the following best describes the characteristics of a negatively skewed distribution?

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- ✓ B. Mean < median < mode
- C. Mode < mean < median
- D. Median < mean < mode
- E. Mean < mode < median

Skewed distributions
- alphabetical order: mean - median - mode
- '>' for positive, '<' for negative

Skewed distributions

Normal distributions: mean = median = mode

Positively skewed distribution: mean > median > mode

Negatively skewed distribution mean < median < mode

To remember the above note how they are in alphabetical order, think positive going forward with '>', whilst negative going backwards '<'

Question 99 of 331

Which one of the following is not associated with hypocalcaemia combined with a raised phosphate level?

- A. Chronic renal failure
- B. Pseudohypoparathyroidism
- C. Hypoparathyroidism
- D. Osteomalacia
- E. Acute rhabdomyolysis

Question 99 of 331

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- B. Pseudohypoparathyroidism
- C. Hypoparathyroidism
- ✓ D. Osteomalacia
- E. Acute rhabdomyolysis

Osteomalacia causes hypocalcaemia associated with a low serum phosphate

Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Question 100 of 331

Which one of the following is secreted only by the adrenal medulla?

- A. Noradrenaline
- B. Aldosterone
- C. Metadrenaline
- D. Cortisol
- E. Adrenaline

Question 100 of 233

Which one of the following is secreted only by the adrenal medulla?

- A. Noradrenaline
- B. Aldosterone
- C. Metadrenaline
- D. Cortisol
- ✓ E. Adrenaline

Adrenal medulla

The adrenal medulla secretes virtually all the adrenaline in the body as well as secreting small amounts of noradrenaline. It essentially represents an enlarged and specialised sympathetic ganglion.

Question 101 of 331

A 40-year-old man presents with pain in his lower back and 'sciatica' for the past three days. He describes bending down to pick up a washing machine when he felt 'something go'. He now has severe pain radiating from his back down the right leg. On examination he describes paraesthesia over the anterior aspect of the right knee and the medial aspect of his calf. Power is intact and the right knee reflex is diminished. The femoral stretch test is positive on the right side. Which nerve root is most likely to be affected?

- A. Common peroneal nerve
- B. Lateral cutaneous nerve of the thigh
- C. L5
- D. L3
- E. L4

Question 101 of 331

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- B. Lateral cutaneous nerve of the thigh
- C. L5
- D. L3
- ✓ E. L4

Lower back pain: prolapsed disc

A prolapsed lumbar disc usually produces clear dermatomal leg pain associated with neurological deficits.

Features
- leg pain usually worse than back
- pain often worse when sitting

The table below demonstrates the expected features according to the level of compression:

L3 nerve root compression	Sensory loss over anterior thigh Weak quadriceps Reduced knee reflex Positive femoral stretch test
L4 nerve root compression	Sensory loss anterior aspect of knee Weak quadriceps Reduced knee reflex Positive femoral stretch test
L5 nerve root compression	Sensory loss dorsum of foot Weakness in foot and big toe dorsiflexion Reflexes intact Positive sciatic nerve stretch test
S1 nerve root compression	Sensory loss posterolateral aspect of leg and lateral aspect of foot Weakness in plantar flexion of foot Reduced ankle reflex Positive sciatic nerve stretch test

Management
- similar to that of other musculoskeletal lower back pain: analgesia, physiotherapy, exercises
- if symptoms persist then referral for consideration of MRI is appropriate

Question 102 of 331

A 54-year-old woman is treated with rituximab for non-Hodgkin's lymphoma. What is the target of rituximab?

- A. CD20
- B. CD52
- C. Epidermal growth factor receptor
- D. CD22
- E. Vascular endothelial growth factor receptor

Question 102 of 331

A 54-year-old woman is treated with rituximab for non-Hodgkin's lymphoma. What is the target of rituximab?

- ✓ A. CD20
- B. CD52
- C. Epidermal growth factor receptor
- D. CD22
- E. Vascular endothelial growth factor receptor

Rituximab - monoclonal antibody against CD20

Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from an human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue

Question 103 of 331

A 64-year-old woman who is reviewed due to multiple non-healing leg ulcers. She reports feeling generally unwell for many months. Examination findings include a blood pressure of 138/72 mmHg, pulse 90 bpm, pale conjunctivae and poor dentition associated with bleeding gums. What is the most likely underlying diagnosis?

- A. Thyrotoxicosis
- B. Vitamin B12 deficiency
- C. Vitamin C deficiency
- D. Diabetes mellitus
- E. Sarcoidosis

Question 103 of 331

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- ✓ C. Vitamin C deficiency
- D. Diabetes mellitus
- E. Sarcoidosis

Vitamin C deficiency

Vitamin C deficiency (scurvy) leads to defective synthesis of collagen resulting in capillary fragility (bleeding tendency) and poor wound healing

Features

- gingivitis, loose teeth
- poor wound healing
- bleeding from gums, haematuria, epistaxis
- general malaise

Question 104 of 331

A 27-year-old man is reviewed in a fertility clinic. Semen analysis has revealed azoospermia. On examination at the previous appointment he was noted to be 1.83 metres tall with a body mass index of 25 kg / m^2. A degree of gynaecomastia is noted, testicular volume is around 10ml bilaterally and his visual fields were normal. Which investigation is likely to be diagnostic?

- A. FISH analysis of DNA
- B. Prolactin level
- C. Karyotype
- D. MRI pituitary
- E. PCR analysis of DNA

Question 104 of 331

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- B. Prolactin level
- ✓ C. Karyotype
- D. MRI pituitary
- E. PCR analysis of DNA

Klinefelter's syndrome

Klinefelter's syndrome is associated with karyotype 47, XXY

Features

- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis

Question 105 of 331

A 23-year-old student is investigated following an anaphylactic reaction suspected to be secondary to a wasp sting. Which one of the following is the most appropriate first-line test to investigate the cause of the reaction?

- A. Hair analysis
- B. Radioallergosorbent test (RAST)
- C. Desensitization therapy
- D. Skin patch test
- E. Skin prick test

Question 105 of 331

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- C. Desensitization therapy
- D. Skin patch test
- E. Skin prick test

Given the history of anaphylaxis it would not be appropriate to perform a skin prick test

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 106 of 331

Which one of the following adrenoceptors causes inhibition of pre-synaptic neurotransmitter release in response to sympathetic stimulation?

- A. Alpha-1
- B. Alpha-2
- C. Beta-1
- D. Beta-2
- E. Beta-3

Question 106 of 331

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- ✓ B. Alpha-2
- C. Beta-1
- D. Beta-2
- E. Beta-3

Adrenoceptors

Alpha-1
- vasoconstriction
- relaxation of GI smooth muscle
- salivary secretion
- hepatic glycogenolysis

Alpha-2
- mainly presynaptic: inhibition of transmitter release (inc NA, Ach from autonomic nerves)
- inhibits insulin
- platelet aggregation

Beta-1
- mainly located in the heart
- increase heart rate + force

Beta-2
- vasodilation
- bronchodilation
- relaxation of GI smooth muscle

Beta-3
- lipolysis

Pathways
- all are G-protein coupled
- alpha-1:activate phospholipase C --> IP3 --> DAG
- alpha-2: inhibit adenylate cyclase
- beta-1: stimulate adenylate cyclase
- beta-2: stimulate adenylate cyclase
- beta-3: stimulate adenylate cyclase

Question 107 of 331

A 55-year-old man with a history of type 2 diabetes mellitus, bipolar disorder and chronic obstructive pulmonary disease has bloods taken as part of his annual diabetic review:

Na^+	129 mmol/l
K^+	3.8 mmol/l
Bicarbonate	24 mmol/l
Urea	3.7 mmol/l
Creatinine	92 µmol/l

Due to his smoking history a chest x-ray is ordered which is reported as normal. Which one of the following medications is most likely to be responsible?

- A. Metformin
- B. Lithium
- C. Carbamazepine
- D. Sodium valproate
- E. Pioglitazone

Question 107 of 331

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- D. Sodium valproate
- E. Pioglitazone

SIADH - drug causes: carbamazepine, sulfonylureas, SSRIs, tricyclics

Lithium only tends to cause raised antidiuretic hormone levels following a severe overdosage. Please see the BNF.

SIADH: causes

Malignancy
- especially small cell lung cancer
- also: pancreas, prostate

Neurological
- stroke
- subarachnoid haemorrhage
- subdural haemorrhage
- meningitis/encephalitis/abscess

Infections
- TB
- pneumonia

Drugs
- sulfonylureas
- SSRIs, tricyclics
- carbamazepine
- vincristine
- cyclophosphamide

Other causes
- positive end-expiratory pressure (PEEP)
- porphyrias

Question 108 of 331

Which one of the following statements regarding leukotrienes is not true?

- A. Secreted by leukocytes
- B. Formed from arachidonic acid
- C. Attract leukocytes
- D. Cause bronchodilation
- E. Increase vascular permeability

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- E. Increase vascular permeability

Leukotrienes

Function
- mediators of inflammation and allergic reactions
- cause bronchoconstriction, mucous production
- increase vascular permeability, attract leukocytes
- leukotriene D4 has been identified as the SRS-A (slow reacting substance of anaphylaxis)

Production
- secreted by leukocytes
- formed from arachidonic acid by action of lipoxygenase
- it is thought that the NSAID induced bronchospasm in asthmatics is secondary to the express production of leukotrienes due to the inhibition of prostaglandin synthetase

Question 109 of 331

A 25-year-old man is counselled regarding the genetics of Huntington's disease. Which one of the following best describes the concept of anticipation?

- A. The psychological effect of a patient knowing they will develop an incurable condition
- B. Earlier age of onset in successive generations
- C. More severe disease in successive generations
- D. Where there is a known history of inherited conditions, patients may attribute symptoms to the onset of the disease
- E. Screening at risk families to allow early intervention and improve outcomes

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- E. Screening at risk families to allow early intervention and improve outcomes

(Anticipation) in trinucleotide repeat disorders = **earlier onset** in successive generations

Difficult question. In the exam both B and C were given as choices. The 'classic' definition of anticipation is earlier onset in successive generations. However, in most cases, an increase in the severity of symptoms is also noted. If both options are presented then B should be chosen, as this represents the more accepted definition of anticipation. What do you think?

Trinucleotide repeat disorders

Trinucleotide repeat disorders are genetic conditions caused by an abnormal number of repeats (expansions) of a repetitive sequence of three nucleotides. These expansions are unstable and may enlarge which may lead to an earlier age of onset in successive generations - a phenomenon known as anticipation*. In most cases, an increase in the severity of symptoms is also noted

Examples - note dominance of neurological disorders

- Fragile X (CGG)
- Huntington's (CAG)
- myotonic dystrophy (CTG)
- Friedreich's ataxia* (GAA)
- spinocerebellar ataxia
- spinobulbar muscular atrophy
- dentatorubral pallidoluysian atrophy

*Friedreich's ataxia is unusual in not demonstrating anticipation

Question 110 of 331

In the Gell and Coombs classification of hypersensitivity reactions idiopathic thrombocytopenic purpura is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

Question 110 of 331

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- A. Type I reaction
- ✓ B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 111 of 331

Which one of the following statements is true regarding the radial nerve?

- A. Damage at the axilla would lead to wrist drop
- B. Damage at the wrist leads to wasting of the thenar muscles
- C. It supplies the lateral 2 lumbricals
- D. It supplies sensation to the lateral one and a half fingers
- E. It is derived from C6-8 and T1

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Radial nerve

Overview
- arises from the posterior cord of the brachial plexus (C5-8)

Motor to
- extensor muscles (forearm, wrist, fingers, thumb)

Sensory to
- dorsal aspect of lateral 3 1/2 fingers
- however, only small area between the dorsal aspect of the 1st and 2nd metacarpals is unique to the radial nerve

Patterns of damage
- wrist drop
- sensory loss to small area between the dorsal aspect of the 1st and 2nd metacarpals

Axillary damage
- as above
- paralysis of triceps

Question 112 of 331

Which of the following conditions is inherited in an autosomal dominant fashion?

- A. Familial Mediterranean Fever
- B. Homocystinuria
- C. Tuberose sclerosis
- D. Ataxia telangiectasia
- E. Friedreich's ataxia

Question 112 of 331

Which of the following conditions is inherited in an autosomal dominant fashion?

- A. Familial Mediterranean Fever
- B. Homocystinuria
- ✓ C. Tuberose sclerosis
- D. Ataxia telangiectasia
- E. Friedreich's ataxia

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease*

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 113 of 331

Southern blotting is used to:

- A. Amplify RNA
- B. Detect DNA
- C. Detect RNA
- D. Detect and quantify proteins
- E. Amplify DNA

Question 113 of 331

Southern blotting is used to:

- A. Amplify RNA
- ✓ B. Detect DNA
- C. Detect RNA
- D. Detect and quantify proteins
- E. Amplify DNA

Molecular biology techniques
- SNOW (**S**outh - **NO**rth - **W**est)
- DROP (**D**NA - **R**NA - **P**rotein)

Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Question 114 of 331

What is the correct formula to calculate the positive predictive value?
TP = true positive; FP = false positive; TN = true negative; FN = false negative

- A. Sensitivity / (1 - specificity)
- B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. TN / (TN + FN)
- E. TP / (TP + FN)

Question 114 of 331

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TP = true positive; FP = false positive; TN = true negative; FN = false negative

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- ✓ B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. TN / (TN + FN)
- E. TP / (TP + FN)

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 115 of 331

What is the site of action of antidiuretic hormone?

- A. Descending loop of Henle
- B. Distal convoluted tubule
- C. Ascending loop of Henle
- D. Proximal convoluted tubule
- E. Collecting ducts

Question 115 of 331

What is the site of action of antidiuretic hormone?

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- B. Distal convoluted tubule
- C. Ascending loop of Henle
- D. Proximal convoluted tubule
- ✓ E. Collecting ducts

Antidiuretic hormone (ADH) - site of action = collecting ducts

Antidiuretic hormone

Antidiuretic hormone (ADH) is secreted from the posterior pituitary gland. It promotes water reabsorption in the collecting ducts of the kidneys by the insertion of aquaporin-2 channels

Question 116 of 331

Which type of secondary messenger system does nitric oxide stimulate?

- A. Cyclic GMP
- B. Cyclic AMP
- C. Phosphoinositide
- D. Protein kinase
- E. Calcium

Question 116 of 331

Which type of secondary messenger system does nitric oxide stimulate?

- ✓ A. Cyclic GMP
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- C. Phosphoinositide
- D. Protein kinase
- E. Calcium

Second messengers

Overview
- many different types
- allow amplification of external stimulus

Cyclic AMP
- e.g. adrenaline, noradrenaline, glucagon, LH, FSH, TSH, calcitonin, parathyroid hormone

Protein kinase activity
- e.g. insulin, growth hormone, prolactin, oxytocin, erythropoietin, growth factors

Calcium and/or phosphoinositides
- e.g. ADH, GnRH, TRH

Cyclic GMP
- e.g. ANP, nitric oxide

Question 117 of 331

A 23-year-old female with Down's syndrome is reviewed in clinic. Which one of the following features is least associated with her condition?

- A. Infertility
- B. Hypothyroidism
- C. Alzheimer's disease
- D. Short stature
- E. Ventricular septal defect

Question 117 of 331

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- B. Hypothyroidism
- C. Alzheimer's disease
- D. Short stature
- E. Ventricular septal defect

As this patient is female she is likely to be subfertile rather than infertile - please see the notes below

Down syndrome: features

Clinical features
- face: upslanting palpebral fissures, epicanthic folds, Brushfield spots in iris, protruding tongue, small ears, round/flat face
- flat occiput
- single palmar crease, pronounced 'sandal gap' between big and first toe
- hypotonia
- congenital heart defects (40-50%, see below)
- duodenal atresia
- Hirschsprung's disease

Cardiac complications
- multiple cardiac problems may be present
- endocardial cushion defect (c. 40%, also known as atrioventricular septal canal defects)
- ventricular septal defect (c. 30%)
- secundum atrial septal defect (c. 10%)
- tetralogy of Fallot (c. 5%)
- isolated patent ductus arteriosus (c. 5%)

Later complications
- subfertility: males are almost always infertile due to impaired spermatogenesis. Females are usually subfertile, and have an increased incidence of problems with pregnancy and labour
- learning difficulties
- short stature
- repeated respiratory infections (+hearing impairment from glue ear)
- acute lymphoblastic leukaemia
- hypothyroidism
- Alzheimer's
- atlantoaxial instability

Question 118 of 331

A 31-year-old woman presents for review. For the past few months she has been feeling generally tired and has not had a normal period for around 4 months. Prior to this she had a regular 30 day cycle. A pregnancy test is negative, pelvic examination is normal and routine bloods are ordered:

FBC	Normal
U&E	Normal
TFT	Normal
Follicle-stimulating hormone	41 iu/l (< 35 iu/l)
Luteinizing hormone	33 miu/l (< 20 miu/l)
Oestradiol	70 pmol/l (> 100 pmol/l)

What is the most likely diagnosis?

- A. Ovarian cancer
- B. Gonadotropin-producing pituitary adenoma
- C. Turner syndrome
- D. Premature ovarian failure
- E. Aromatase enzyme deficiency

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- E. Aromatase enzyme deficiency

Premature ovarian failure

Premature ovarian failure is defined as the onset of menopausal symptoms and elevated gonadotrophin levels before the age of 40 years.

Causes
- idiopathic - the most common cause
- chemotherapy
- autoimmune
- radiation

Features are similar to those of the normal climateric but the actual presenting problem may differ
- climateric symptoms: hot flushes etc
- infertility
- secondary amenorrhoea
- raised FSH, LH levels

Question 119 of 331

A 72-year-old woman is admitted for investigation of hyponatraemia. Which one of the following features is most consistent with syndrome of inappropriate ADH secretion?

- A. Peripheral oedema
- B. Recent lisinopril therapy
- C. Urine osmolality of 325 mmol/kg
- D. Serum sodium of 115 mmol/l
- E. Urinary sodium of 40 mmol/l

Question 119 of 331

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Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolarity levels aid making a diagnosis

Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)
- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic
- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss
- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)
- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Question 120 of 331

A 24-year-old man is planning an expedition to the Andes. He asks for advice on preventing acute mountain sickness (AMS), other than gradual ascent. What is the most appropriate advice?

- A. Carbonic anhydrase inhibitor
- B. Non-steroid anti-inflammatories
- C. Ensure maximal physical fitness prior to trip
- D. Dexamethasone starting 2 days prior to arrival
- E. There is no evidence of any effective intervention to prevent AMS

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C. Ensure maximal physical fitness prior to trip

D. Dexamethasone starting 2 days prior to arrival

E. There is no evidence of any effective intervention to prevent AMS

Acetazolamide, a carbonic anhydrase inhibitor, has an evidence to support its use in preventing AMS. Interestingly, there actually appears to be a positive correlation between physical fitness and the risk of developing AMS

Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

Management of HACE

- descent
- dexamethasone

Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors*
- oxygen if available

*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

Question 121 of 331

The commonest chromosomal defect in Down's syndrome is:

- A. Trinucleotide repeat disorder
- B. Autosomal dominant
- C. Translocation
- D. Mosaicism
- E. Non-dysjunction

Question 121 of 331

The commonest chromosomal defect in Down's syndrome is:

- A. Trinucleotide repeat disorder
- B. Autosomal dominant
- C. Translocation
- D. Mosaicism
- ✓ E. Non-dysjunction

Down's syndrome: epidemiology and genetics

Risk of Down's syndrome with increasing maternal age
- risk at 30 years = 1/1000
- 35 years = 1/350
- 40 years = 1/100
- 45 years = 1/30

One way of remembering this is by starting at 1/1,000 at 30 years and then dividing by 3 (i.e. 3 times more common) for every extra 5 years of age

Cytogenetics

Mode	% of cases	Risk of recurrence
Non-disjunction	94%	1 in 100 if under mother < 35 years
Robertsonian translocation (usually onto 14)	5%	10-15% if mother is translocation carrier 2.5% if father is translocation carrier
Mosaicism	1%	

The chance of a further child with Down's syndrome is approximately 1 in 100 if the mother is less than 35 years old. If the trisomy 21 is a result of a translocation the risk is much higher

Question 122 of 331

A 60-year-old man who is currently receiving chemotherapy for non-small cell lung cancer presents for review. He is currently being treated with oral calcium supplements as hypocalcaemia was detected during a recent admission. Bloods taken two days ago reveal the following:

Calcium 2.01 mmol/l

Which one of the following tests may help determine why his calcium level remains low despite calcium supplementation?

- A. Vitamin D
- B. Parathyroid hormone
- C. Phosphate
- D. Alkaline phosphatase
- E. Magnesium

Question 122 of 331

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- D. Alkaline phosphatase
- ✓ E. Magnesium

Cisplatin, often used in the management of non-small cell lung cancer, is a well known cause of magnesium deficiency. Without first correcting magnesium levels it is difficult to reverse hypocalcaemia

Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Question 123 of 331

A new antihypertensive is in phase III development. A study is designed where a margin is defined (-delta to +delta) on mean blood pressure reduction. If the confidence interval of the difference between the new drug and ramipril lies within this margin then the trial can be said to have produced a positive result. What is this an example of?

- A. Non-inferiority trial
- B. Superiority trial
- C. Placebo-controlled trial
- D. Delta-controlled trial
- E. Equivalence trial

Question 123 of 331

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Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined (-delta to +delta) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e. -delta). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

Question 124 of 331

Which one of the following foodstuffs contains the most calories per unit weight?

- A. White bread
- B. Butter
- C. Pasta
- D. Sugar
- E. Red meat

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Energy from food

The amount of energy that may be derived from 1 gram of food is as follows:

- carbohydrates: 4 kcal
- protein: 4 kcal
- fat: 9 kcal

Question 125 of 331

The serum potassium is measured in a 1,000 patients taking an ACE inhibitors. The mean potassium is 4.6 mmol/l with a standard deviation of 0.3 mmol/l. Which one of the following statements is correct?

- A. 95% of values lie between 4.5 and 4.75 mmol/l
- B. 95.4% of values lie between 4.3 and 4.9 mmol/l
- C. 99.7% of values lie between 4.0 and 5.2 mmol/l
- D. 68.3% of values lie between 4.5 and 4.75 mmol/l
- E. 68.3% of values lie between 4.3 and 4.9 mmol/l

Question 125 of 331

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- ✓ E. 68.3% of values lie between 4.3 and 4.9 mmol/l

We know that 68.3% of values of a normally distributed variable lie within 1 standard deviation of the mean. This means the range is 4.3 to 4.9 mmol/l.

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 126 of 331

A 54-year-old man is brought to the Emergency Department after being found collapsed in the street. He is known to have a history of alcoholic liver disease. Blood tests reveal the following:

Calcium 1.62 mmol/l

Albumin 33 g/l

Which one of the following is the most appropriate management of the calcium result?

- A. 10ml of 10% calcium chloride over 10 minutes
- B. 20% albumin infusion
- C. 10ml of 10% calcium gluconate over 10 minutes
- D. No action
- E. 10ml of 10% calcium chloride over 4 hours

Question 126 of 331

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- E. 10ml of 10% calcium chloride over 4 hours

Even after correction for the low albumin level this patient has significant hypocalcaemia which should be corrected

Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
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- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
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Question 127 of 331

Which one of the following reduces the secretion of renin?

- A. Erect posture
- B. Adrenaline
- C. Hyponatraemia
- D. Hypotension
- E. Beta-blockers

Question 127 of 331

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- D. Hypotension
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Renin

Renin is secreted by juxtaglomerular cells and hydrolyses angiotensinogen to produce angiotensin I

Factors stimulating renin secretion
- hypotension causing reduced renal perfusion
- hyponatraemia
- sympathetic nerve stimulation
- catecholamines
- erect posture

Factors reducing renin secretion
- drugs: beta-blockers, NSAIDs

Question 128 of 331

A small study is designed to look at the link between drinking alcohol and liver cirrhosis. One hundred patients with liver cirrhosis were questioned and it was found that 80 of them drank excessive alcohol. As a control, one hundred patients without liver cirrhosis were questioned and only 20 of these patients drank excessively. What is the odds ratio of developing liver cirrhosis for people who drink excessively compared to those who do not?

- A. 2
- B. 4
- C. 0.25
- D. 16
- E. 3

Question 128 of 331

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- A. 2
- B. 4
- C. 0.25
- ✓ D. 16
- E. 3

The odds of a patient with liver cirrhosis having a history of excessive drinking is 80/20 = 4.

The odds of a patient without liver cirrhosis having a history of excessive drinking is 20/80 = 0.25.

Therefore the odds ratio = 4 / 0.25 = 16

Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	**Achieved = 50% pain relief**
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol = 40 / 20 = 2

The odds of achieving significant pain relief with placebo = 30 / 60 = 0.5

Therefore the odds ratio = 2 / 0.5 = 4

Question 129 of 331

A study measures a patients serum cholesterol before and after a new lipid-lowering therapy has been given. What type of significance test should be used to analyse the data?

- A. Student's paired t-test
- B. Student's unpaired t-test
- C. Chi-squared test
- D. Pearson's test
- E. Spearman test

Question 129 of 331

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- C. Chi-squared test
- D. Pearson's test
- E. Spearman test

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 130 of 331

A 67-year-old woman who is taking long-term prednisolone for polymyalgia rheumatica presents with progressive pain in her right hip joint. A diagnosis of avascular necrosis is suspected. Which investigation is most likely to be diagnostic?

- A. Radionuclide bone scan
- B. MRI
- C. Plain x-ray
- D. CT
- E. DEXA scan

Question 130 of 331

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- ✓ B. MRI
- C. Plain x-ray
- D. CT
- E. DEXA scan

Avascular necrosis

Avascular necrosis (AVN) may be defined as death of bone tissue secondary to loss of the blood supply. This leads to loss of bone destruction and loss of joint function. It most commonly affects the epiphysis of long bones such as the femur.

Causes
- long-term steroid use
- alcohol excess
- trauma

Features
- initially asymptomatic
- pain in the affected joint

Investigation
- plain x-ray findings may be normal initially
- MRI is the investigation of choice. It is more sensitive than radionuclide bone scanning

Question 131 of 331

Which of the following statements is true regarding autosomal recessive inheritance?

- A. Disease is manifest in every generation
- B. There is a 25% chance of two heterozygote parents having a carrier child
- C. Conditions tend to be less severe than autosomal dominant conditions
- D. All offspring of an affected individual and a non-affected individual (i.e. not a carrier or affected) will be heterozygote carriers
- E. Examples include Huntingdon's disease

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- E. Examples include Huntingdon's disease

Autosomal recessive

In autosomal recessive inheritance
- only homozygotes are affected
- males and females are equally likely to be affected
- not manifest in every generation - may 'skip a generation'

If two heterozygote parents
- 25% chance of having an affected (homozygote) child
- 50% chance of having a carrier (heterozygote) child
- 25% chance of having an unaffected (i.e. genotypical) child

If one affected parent (i.e. homozygote for gene) and one unaffected (i.e. not a carrier or affected)
- all the children will be carriers

Autosomal recessive disorders are often metabolic in nature and are generally more life-threatening compared to autosomal dominant conditions

Question 132 of 331

Tamsulosin is a:

- A. Alpha-1b agonist
- B. Alpha-1a agonist
- C. Non-selective alpha antagonist
- D. Alpha-1a antagonist
- E. Alpha-1b antagonist

Question 132 of 331

Tamsulosin is a:

- A. Alpha-1b agonist
- B. Alpha-1a agonist
- C. Non-selective alpha antagonist
- ✓ D. Alpha-1a antagonist
- E. Alpha-1b antagonist

Adrenoceptor antagonists

Alpha antagonists
- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists
- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

Question 133 of 331

Which one of the following clinical features would be least consistent with a diagnosis of severe pre-eclampsia?

- A. Headache
- B. Epigastric pain
- C. Reflexes difficult to elicit
- D. Low platelet count
- E. Papilloedema

Question 133 of 331

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- A. Headache
- B. Epigastric pain
- ✓ C. Reflexes difficult to elicit
- D. Low platelet count
- E. Papilloedema

Severe pre-eclampsia is associated with hyperreflexia and clonus. A low platelet count may indicate the patient is developing HELLP syndrome

Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m^2
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count < 100 * 10^6/l, abnormal liver enzymes or HELLP syndrome

Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral methyldopa is often used first-line with oral labetalol, nifedipine and hydralazine also being used
- for severe hypertension IV labetalol and IV hydralazine are used in addition to the above
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Question 134 of 331

Which one of the following best describes the main action of the polymerase chain reaction?

- A. DNA identification using RNA
- B. DNA amplification
- C. RNA translation to protein
- D. RNA amplification
- E. DNA to RNA conversion

Question 134 of 331

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PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep
- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place
- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR
- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

Question 135 of 331

You are a ST1 doctor in medicine. A 67-year-old man has been investigated for anaemia and weight loss. Endoscopy shows a gastric tumour which is confirmed as an adenocarcinoma on biopsy. On discussing the diagnosis the patient states that he has had 'a good life' and doesn't want any treatment. Clinical examination is unremarkable. He is able to retain and understand the information you give to him, including the likely curative nature of surgery. What is the most appropriate action?

- A. Respect his wishes and book a follow-up appointment for four weeks
- B. Arrange a CT head and check bloods to exclude cerebral metastases and hypercalcaemia
- C. Arrange an appointment with a psychiatrist
- D. Detain him under the Mental Health Act
- E. Ask to speak to his wife alone to find out why he is refusing surgery

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- D. Detain him under the Mental Health Act
- E. Ask to speak to his wife alone to find out why he is refusing surgery

This question is ultimately about autonomy. By being able to understand and retain the information you give him the patient has demonstrated that he is competent to make decisions. It should be noted that the Mental Capacity Act 2005 states that *'a person is not to be treated as unable to make a decision merely because he makes an unwise decision'*.

A CT head and bloods may exclude causes that would impair judgement but would you override his decision even if you noticed evidence of a cerebral metastase? As there is no evidence that this man is suffering from a mental illness referral to a psychiatrist would be inappropriate.

By speaking to the wife alone you are risking breaching confidentiality. Detaining him under the Mental Health Act simply because you disagree with his decision is clearly wrong

Question 136 of 331

A 67-year-old man presents with shortness-of-breath. He has a past history of aortic stenosis but is otherwise well. On examination he has a systolic murmur and a clear chest. Routine bloods are as follows:

Hb 8.7 g/dl

MCV 71 fl

Plt 277 * 10^9/l

WBC 6.4 * 10^9/l

Which one of the following investigations is most likely to explain his anaemia?

- A. Colonoscopy
- B. Renal biopsy
- C. Duodenal biopsy
- D. Gastroscopy
- E. Echocardiogram

Question 136 of 331

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- B. Renal biopsy
- C. Duodenal biopsy
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- E. Echocardiogram

This patient most likely has angiodysplasia which has a known association with aortic stenosis.

Angiodysplasia

Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia. It is associated with aortic stenosis

Diagnosis
- colonoscopy
- mesenteric angiography if acutely bleeding

Management
- endoscopic cautery or argon plasma coagulation
- antifibrinolytics e.g. tranexamic acid
- oestrogens may also be used

Question 137 of 331

A 10-year-old boy is found to have haemophilia A following investigation for a haemoarthrosis. Which one of his relatives is most likely to have the condition?

- A. Father
- B. Mother's brother
- C. Father's sister
- D. Mother
- E. Father's brother

Question 137 of 331

A 10-year-old boy is found to have haemophilia A following investigation for a haemoarthrosis. Which one of his relatives is most likely to have the condition?

- A. Father
- ✓ B. Mother's brother
- C. Father's sister
- D. Mother
- E. Father's brother

X-linked recessive conditions are only seen in males which therefore excludes two of the options. As male to male transmission is not seen this means the answer is mother's brother.

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 138 of 331

In terms of the cell cycle, mitosis takes place in:

- A. M
- B. M0
- C. G1
- D. S
- E. G2

Question 138 of 331

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Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

Question 139 of 331

Which one of the following is involved in the translation of RNA into proteins?

- A. Golgi apparatus
- B. Rough endoplasmic reticulum
- C. Ribosome
- D. Smooth endoplasmic reticulum
- E. Lysosome

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Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Energy production. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide

Question 140 of 331

Which of the following is not a tumour suppressor gene?

- A. p53
- B. APC
- C. NF-1
- D. Rb
- E. myc

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- A. p53
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- C. NF-1
- D. Rb
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myc is an oncogene which encodes a transcription factor

Tumour suppressor genes

Basics
- genes which normally control the cell cycle
- exhibit a recessive effect - both copies must be mutated before cancer occurs

Examples
- p53
- APC: colorectal cancer
- NF-1: neurofibromatosis
- Rb: retinoblastoma

Question 141 of 331

What is the underlying problem in methaemoglobinaemia?

- A. The oxidation of Fe2+ in haemoglobin to Fe3+
- B. The reduction of Fe2+ in haemoglobin to Fe+
- C. The oxidation of Fe3+ in haemoglobin to Fe2+
- D. The reduction of Fe2+ in haemoglobin to Fe3+
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Question 141 of 331

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- E. The reduction of Fe3+ in haemoglobin to Fe2+

Methaemoglobinaemia = oxidation of Fe2+ in haemoglobin to Fe3+

Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes
- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes
- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features
- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO2 but decreased oxygen saturation

Management
- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

Question 142 of 331

A 65-year-old Asian female presents with generalised bone pain and muscle weakness. Investigations show:

Calcium	2.07 mmol/l
Phosphate	0.66 mmol/l
ALP	256 U/l

What is the most likely diagnosis?

- A. Bone tuberculosis
- B. Hypoparathyroidism
- C. Myeloma
- D. Osteomalacia
- E. Paget's disease

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- B. Hypoparathyroidism
- C. Myeloma
- ✓ D. Osteomalacia
- E. Paget's disease

The low calcium and phosphate combined with the raised alkaline phosphatase point towards osteomalacia

Osteomalacia

Basics
- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

Types
- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis

Features
- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

Investigation
- low Ca2+, PO34-, 25(OH) vitamin D
- raised ALP
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser’s zones or pseudofractures)

Treatment
- calcium with vitamin D tablets

Question 143 of 331

Which one of the following statements is not correct regarding hypertension in pregnancy?

A. An increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic suggests hypertension

B. Pre-eclampsia occurs in around 5% of pregnancies

C. Urine dipstick showing protein + is consistent with gestational hypertension

D. Rise in blood pressure before 20 weeks suggests pre-existing hypertension

E. With gestational hypertension blood pressure rises in the second half of pregnancy

Question 143 of 331

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- ✓ C. Urine dipstick showing protein + is consistent with gestational hypertension
- D. Rise in blood pressure before 20 weeks suggests pre-existing hypertension
- E. With gestational hypertension blood pressure rises in the second half of pregnancy

Proteinuria suggests pre-eclampsia

Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy in usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	**Pregnancy-induced hypertension (PIH, also known as gestational hypertension)**	**Pre-eclampsia**
A history of hypertension before pregnancy or an elevated blood pressure > 140/90 mmHg before 20 weeks gestation No proteinuria, no oedema Occurs in 3-5% of pregnancies and is more common in older women	Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks) No proteinuria, no oedema Occurs in around 5-7% of pregnancies Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life	Pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours) Oedema may occur but is now less commonly used as a criteria Occurs in around 5% of pregnancies

Question 144 of 331

A new test to screen for ovarian cancer in patients with a positive family history is tested on 920 patients. The test is positive in 16 of the 20 patients who are proven to have ovarian cancer. Of the remaining patients, only 10 have a positive test. What is the negative predictive value of the new test?

- A. 900/920 = 97.8%
- B. 890/900 = 98.9%
- C. 10/900 = 1.1%
- D. 890/894 = 99.6%
- E. 890/920 = 96.7%

Question 144 of 331

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- C. 10/900 = 1.1%
- ✓ D. 890/894 = 99.6%
- E. 890/920 = 96.7%

A contingency table can be constructed from the above data, as shown below:

	Ovarian cancer	**No ovarian cancer**
Test positive	16	10
Test negative	4	890

The negative predictive value = TN / (TN + FN) = 890 / (890 + 4) = 890/894

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 145 of 331

Which of the following is most likely to cause hypokalaemia associated with acidosis?

- A. Cushing's syndrome
- B. Vomiting
- C. Conn's syndrome
- D. Diuretics
- E. Acetazolamide

Question 145 of 331

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- A. Cushing's syndrome
- B. Vomiting
- C. Conn's syndrome
- D. Diuretics
- ✓ E. Acetazolamide

Hypokalaemia and acid-base balance

Potassium and hydrogen can be thought of as competitors. Hyperkalaemia tends to be associated with acidosis because as potassium levels rise fewer hydrogen ions can enter the cells

Hypokalaemia with alkalosis
- vomiting
- diuretics
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)

Hypokalaemia with acidosis
- diarrhoea
- renal tubular acidosis
- acetazolamide
- partially treated diabetic ketoacidosis

Question 146 of 331

A 43-year-old man is suspected of having a common peroneal nerve palsy following a fracture of his fibula. Each one of the following features may be seen in such lesions, except:

- A. Wasting of the anterior tibial and peroneal muscles
- B. Weakness of foot dorsiflexion
- C. Weakness of extensor hallucis longus
- D. Weakness of foot eversion
- E. Sensory loss over the medial aspect of the lower limb

Question 146 of 331

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- B. Weakness of foot dorsiflexion
- C. Weakness of extensor hallucis longus
- D. Weakness of foot eversion
- ✓ E. Sensory loss over the medial aspect of the lower limb

Sensory loss over the dorsum of the foot and the lower lateral part of the leg is seen in a common peroneal nerve palsy. The degree of wasting would of course depend on how long the nerve palsy had been present

Common peroneal nerve lesion

The sciatic nerve divides into the tibial and common peroneal nerves. Injury often occurs at the neck of the fibula

The most characteristic feature of a common peroneal nerve lesion is foot drop

Other features include:

- weakness of foot dorsiflexion
- weakness of foot eversion
- weakness of extensor hallucis longus
- sensory loss over the dorsum of the foot and the lower lateral part of the leg
- wasting of the anterior tibial and peroneal muscles

Question 147 of 331

Which one of the following cardiac tissue types has the highest conduction velocity?

- A. Atrial myocardial tissue
- B. Ventricular myocardial tissue
- C. Purkinje fibres
- D. Atrioventricular node
- E. Sinoatrial node

Question 147 of 331

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- E. Sinoatrial node

Electrical activity of the heart

Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by Na^+/K^+ ATPase There is slow entry of Na^+ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles

Question 148 of 331

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

- A. Acute asthma
- B. Wegener's granulomatosis
- C. Polycythaemia
- D. Exercise
- E. Emphysema

Question 148 of 331

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- A. Acute asthma
- B. Wegener's granulomatosis
- C. Polycythaemia
- D. Exercise
- ✓ E. Emphysema

Transfer factor
- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	Causes of a lower TLCO
• asthma • pulmonary haemorrhage (Wegener's, Goodpasture's) • left-to-right cardiac shunts • polycythaemia • hyperkinetic states • male gender, exercise	• pulmonary fibrosis • pneumonia • pulmonary emboli • pulmonary oedema • emphysema • anaemia • low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO
- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

Question 149 of 331

Each one of the following statements regarding atrial natriuretic peptide are true, except:

- A. Lowers blood pressure
- B. Degraded by endopeptidases
- C. Promotes excretion of sodium
- D. Secreted mainly by the left atrium
- E. Antagonises actions of angiotensin II and aldosterone

Question 149 of 331

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- B. Degraded by endopeptidases
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- ✓ D. Secreted mainly by the left atrium
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Atrial natriuretic peptide

Basics
- secreted mainly from myocytes of right atrium and ventricle in response to increased blood volume
- secreted by both the right and left atria (right >> left)
- 28 amino acid peptide hormone, which acts via cGMP
- degraded by endopeptidases

Actions
- natriuretic, i.e. promotes excretion of sodium
- lowers BP
- antagonises actions of angiotensin II, aldosterone

Question 150 of 331

The Framingham Heart Study is an example of a:

- A. Cross-sectional survey
- B. Cohort study
- C. Case-control study
- D. Randomised controlled trial
- E. Meta-analysis

Question 150 of 331

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- A. Cross-sectional survey
- ✓ B. Cohort study
- C. Case-control study
- D. Randomised controlled trial
- E. Meta-analysis

Study design

The following table highlights the main features of the different types of study

Randomised controlled trial	Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo) • Practical or ethical problems may limit use
Cohort study	Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome • Examples include Framingham Heart Study
Case-control study	Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition • Inexpensive, produce quick results • Useful for studying rare conditions • Prone to confounding
Cross-sectional survey	Provide a 'snapshot', sometimes called prevalence studies • Provide weak evidence of cause and effect

Question 151 of 331

Which one of the following enzymes is mainly responsible for breaking starch down into sugars?

- A. Amylase
- B. Sucrase
- C. Alpha-glucosidase
- D. Maltase
- E. Lactase

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Amylase: breaks starch down to sugars

Gastrointestinal physiology: enzymes

Amylase is present in saliva and pancreatic secretions. It breaks starch down into sugar

The following brush border enzymes are involved in the breakdown of carbohydrates:

- maltase: cleaves disaccharide maltose to glucose + glucose
- sucrase: cleaves sucrose to fructose and glucose
- lactase: cleaves disaccharide lactose to glucose + galactose

Question 152 of 331

Which one of the following causes of primary immunodeficiency is due to a defect in neutrophil function?

- A. Wiskott-Aldrich syndrome
- B. Common variable immunodeficiency
- C. Bruton's congenital agammaglobulinaemia
- D. Di George syndrome
- E. Chronic granulomatous disease

Question 152 of 331

Which one of the following causes of primary immunodeficiency is due to a defect in neutrophil function?

A. Wiskott-Aldrich syndrome

B. Common variable immunodeficiency

C. Bruton's congenital agammaglobulinaemia

D. Di George syndrome

✓ E. Chronic granulomatous disease

Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders
- DiGeorge syndrome

Combined B- and T-cell disorders
- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Question 153 of 331

Osteogenesis imperfecta is due to a defect in which one of the following proteins?

- A. Fibrillin
- B. Elastin
- C. Type I collagen
- D. Type IV collagen
- E. Polycystin-1

Question 153 of 331

Osteogenesis imperfecta is due to a defect in which one of the following proteins?

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- D. Type IV collagen
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Osteogenesis imperfecta

Osteogenesis imperfecta (more commonly known as brittle bone disease) is a group of disorders of collagen metabolism resulting in bone fragility and fractures. The most common, and milder, form of osteogenesis imperfecta is type 1

Overview
- autosomal dominant
- abnormality in type 1 collagen due to decreased synthesis of pro-alpha 1 or pro-alpha 2 collagen polypeptides

Features
- presents in childhood
- fractures
- blue sclera
- deafness secondary to otosclerosis

Question 154 of 331

What chromosome abnormality is associated with Klinefelter's syndrome?

- A. 47, XO
- B. 47, XXY
- C. 46, XXY
- D. 47, XYY
- E. 47, XXO

Question 154 of 331

What chromosome abnormality is associated with Klinefelter's syndrome?

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- C. 46, XXY
- D. 47, XYY
- E. 47, XXO

Klinefelter's syndrome

Klinefelter's syndrome is associated with karyotype 47, XXY

Features
- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis

Question 155 of 331

An 18-year-old male presents is reviewed in the endocrinology clinic due to concerns about delayed pubertal development, despite being 1.77m tall. On examination he has scant pubic hair and reduced testicular volume. The following blood results are obtained:

Testosterone	6.7 nmol/l (9 - 30)
LH	3 .1 mu/l (3 - 10)
FSH	5.7 mu/l (3 - 10)

What is the most likely diagnosis?

- A. Klinefelter's syndrome
- B. Acute lymphoblastic leukaemia
- C. Testicular feminisation syndrome
- D. Primary testicular failure
- E. Kallman's syndrome

Question 155 of 331

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- A. Klinefelter's syndrome
- B. Acute lymphoblastic leukaemia
- C. Testicular feminisation syndrome
- D. Primary testicular failure
- ✓ E. Kallman's syndrome

Klinefelter's - LH & FSH raised Kallman's - LH & FSH low-normal

The LH and FSH levels are inappropriately low-normal given the low testosterone concentration, which points towards a diagnosis of hypogonadotrophic hypogonadism. In Klinefelter's syndrome the LH and FSH levels are raised

Kallman's syndrome

Kallman's syndrome is a recognised cause of delayed puberty secondary to hypogonadotrophic hypogonadism. It is usually inherited as an X-linked recessive trait. Kallman's syndrome is thought to be caused by failure of GnRH-secreting neurons to migrate to the hypothalamus.

The clue given in many questions is lack of smell (anosmia) in a boy with delayed puberty

Features

- 'delayed puberty'
- hypogonadism, cryptorchidism
- anosmia
- sex hormone levels are low
- LH, FSH levels are inappropriately low/normal
- patients are typically of normal or above average height

Cleft lip/palate and visual/hearing defects are also seen in some patients

Question 156 of 331

Which of the following conditions is inherited in an autosomal recessive fashion?

- A. Familial adenomatous polyposis
- B. Noonan syndrome
- C. Malignant hyperthermia
- D. Antithrombin III deficiency
- E. Congenital adrenal hyperplasia

Question 156 of 331

Which of the following conditions is inherited in an autosomal recessive fashion?

- A. Familial adenomatous polyposis
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- D. Antithrombin III deficiency
- ✓ E. Congenital adrenal hyperplasia

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's
- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Question 157 of 331

Whilst reviewing a patient's drug card you notice that you prescribed the wrong dose of atenolol when the patient was initially clerked. Instead of 25mg atenolol od you prescribed 50mg atenolol od. She has received the incorrect dose on two occasions. On examining Mrs Smith you note her blood pressure and pulse are normal. Mrs Smith has a past history of anxiety and describes herself as a 'worrier'. What is the most appropriate action?

- A. Complete an entry in your e-portfolio
- B. Apologise to the patient + complete a clinical incident form
- C. Complete a clinical incident form + avoid telling patient to prevent unnecessary anxiety
- D. Fill out a 'yellow card'
- E. Keep her on the higher dose as she is suffering no ill effects

Question 157 of 331

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- E. Keep her on the higher dose as she is suffering no ill effects

In this scenario the patient appears to have come to no harm following the error. This should not however change your approach to the situation. The patient should be informed of what has happened, an apology should be made and reassurance give that there appears to be no ill effects. By completing a clinical incident form you add to a body of data which may in the long term change to practice.

An entry to your e-portfolio at least shows that you both acknowledge and are willing to learn from the error. The yellow card system is intended to report side-effects from drugs rather than prescription errors and hence is fairly pointless.

The dose of a drug a patient takes should be based on clinical need rather than a reluctance to acknowledge an error.

Question 158 of 331

A study is performed looking at the chance of stroke in high-risk patients taking a new oral antithrombotic drug compared to warfarin. The following results are obtained:

	Total number of patients	**Number who had a stroke within a 3 year period**
New drug	200	10
Warfarin	600	12

What is the relative risk of having a stroke within a 3 year period for patients taking the new drug compared to warfarin?

- A. 3.33
- B. 0.66
- C. 1.2
- D. 2.5
- E. Cannot calculate from above data

Question 158 of 331

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- A. 3.33
- B. 0.66
- C. 1.2
- ✓ D. 2.5
- E. Cannot calculate from above data

Relative risk = EER / CER

Experimental event rate, EER = 10 / 200 = 0.05
Control event rate, CER = 12 / 600 = 0.02
Therefore the relative risk = EER / CER = 0.05 / 0.02 = 2.5

Relative risk

Relative risk (RR) is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER)

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate, EER = 60 / 100 = 0.6
Control event rate, CER = 20 / 80 = 0.25
Therefore the relative risk = EER / CER = 0.6 / 0.25 = 2.4

If the risk ratio is > 1 then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is < 1 then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

Relative risk reduction (RRR) or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data, RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140%

Question 159 of 331

A study looks at the benefits of adding a new antiplatelet drug to aspirin following a myocardial infarction. The following results are obtained:

	Percentage of patients having further MI within 3 months
Aspirin	4%
Aspirin + new drug	3%

What is the number needed to treat to prevent one patient having a further myocardial infarction within 3 months?

- A. 0.75
- B. 0.33
- C. Cannot calculate without more data
- D. 1
- E. 100

Question 159 of 331

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Aspirin	4%
Aspirin + new drug	3%

What is the number needed to treat to prevent one patient having a further myocardial infarction within 3 months?

- A. 0.75
- B. 0.33
- C. Cannot calculate without more data
- D. 1
- ✓ E. 100

NNT = 1 / (EER - CER), or 1 / Absolute Risk Reduction

NNT = 1 / (experimental event rate - control event rate)= 1 / (0.03-0.04) = 1 / (-0.01) = 100

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 160 of 331

A randomised controlled trial is performed to look at a new drug to prevent hip fractures in postmenopausal women. Group A consists of 1,000 women who take the new drug whilst group B contains 1,400 women taking a placebo. The hip fracture rate in group A is 2% and in group B is 4%. What is the number needed to treat to prevent one hip fracture?

- A. 10
- B. 50
- C. 6
- D. 12
- E. 2

Question 160 of 331

A randomised controlled trial is performed to look at a new drug to prevent hip fractures in postmenopausal women. Group A consists of 1,000 women who take the new drug whilst group B contains 1,400 women taking a placebo. The hip fracture rate in group A is 2% and in group B is 4%. What is the number needed to treat to prevent one hip fracture?

- A. 10
- ✓ B. 50
- C. 6
- D. 12
- E. 2

NNT = 1 / (EER - CER), or 1 / Absolute Risk Reduction

They key to answering this question is to ignore irrelevant data, the number of patients in each group

Experimental event rate = 2% = 0.02
Control event rate = 4% = 0.04
Absolute risk reduction = 0.02 - 0.04 = -0.02
Number needed to treat = 1 / 0.02 = 50

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 161 of 331

Which one of the following features is least likely to be seen in a patient with pellagra?

- A. Diarrhoea
- B. Depression
- C. Dysphagia
- D. Dermatitis
- E. Dementia

Question 161 of 331

Which one of the following features is least likely to be seen in a patient with pellagra?

- A. Diarrhoea
- B. Depression
- ✓ C. Dysphagia
- D. Dermatitis
- E. Dementia

Depression is quite a common early finding in patients with pellagra

Pellagra

Pellagra is a caused by nicotinic acid (niacin) deficiency. The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin)

Features

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

Question 162 of 331

Which one of the following statements best describes a type I statistical error?

- A. The null hypothesis is rejected when it is true
- B. The null hypothesis is accepted when it is false
- C. The p value fails to reach statistical significance
- D. The alternative hypothesis is rejected when it is true
- E. A study fails to reach an appropriate power

Question 162 of 331

Which one of the following statements best describes a type I statistical error?

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- C. The p value fails to reach statistical significance
- D. The alternative hypothesis is rejected when it is true
- E. A study fails to reach an appropriate power

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example
- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis
- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false
- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 163 of 331

Which one of the following immunoglobulins are present in the lowest concentration in blood?

- A. IgA
- B. IgE
- C. IgG
- D. IgM
- E. IgD

Question 163 of 331

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- ✓ B. IgE
- C. IgG
- D. IgM
- E. IgD

Whilst the majority of IgA is found in secretions there is a significant quantity present in blood. IgE makes up less than 0.1% of immunoglobulins

Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

IgG	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
IgA	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
IgM	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
IgD	1%	Monomer	Involved in activation of B cells
IgE	0.1%	Monomer	Involved in allergic reactions

Question 164 of 331

At which point in the menstrual cycle do progesterone levels peak?

- A. Luteal phase
- B. Ovulation
- C. Follicular phase
- D. Levels remain constant throughout cycle
- E. Menstruation

Question 164 of 331

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Progesterone is secreted by the corpus luteum following ovulation.

Menstrual cycle

The menstrual cycle may be divided into the following phases:

	Days
Menstruation	1-4
Follicular phase (proliferative phase)	5-13
Ovulation	14
Luteal phase (secretory phase)	15-28

Further details are given in the table below

	Follicular phase (proliferative phase)	**Luteal phase (secretory phase)**
Ovarian histology	A number of follicles develop. One follicle will become dominant around the mid-follicular phase	Corpus luteum
Endometrial histology	Proliferation of endometrium	Endometrium changes to secretory lining under influence of progesterone
Hormones	A rise in FSH results in the development of follicles which in turn secrete oestradiol When the egg has matured, it secretes enough oestradiol to trigger the acute release of LH. This in turn leads to ovulation	Progesterone secreted by corpus luteum rises through the luteal phase. If fertilisation does not occur the corpus luteum will demise and progesterone levels fall Oestradiol levels also rise again during the luteal phase
Cervical mucus	Following menstruation the mucus is thick and forms a plug across the external os Just prior to ovulation the mucus becomes clear, acellular, low viscosity. It also becomes 'stretchy' - a quality termed spinnbarkeit	Under the influence of progesterone it becomes thick, scant, and tacky
Basal body temperature	Falls prior to ovulation due to the influence of oestradiol	Rises following ovulation in response to higher progesterone levels

Question 165 of 331

Which one of the following hormones is under continuous inhibition?

- A. Growth hormone
- B. Prolactin
- C. Gonadotropin releasing hormone
- D. Thyroid releasing hormone
- E. Adrenocorticotrophic hormone

Question 165 of 331

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- E. Adrenocorticotrophic hormone

Prolactin is unique amongst the pituitary hormones in being tonically inhibited by the hypothalamus

Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin
- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin
- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin
- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

Question 166 of 331

Each one of the following is an acute phase protein, except:

- A. Haptoglobin
- B. Alpha-1 antitrypsin
- C. CRP
- D. Ferritin
- E. ESR

Question 166 of 331

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Acute phase proteins

Acute phase proteins
- CRP
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:
- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

*plays a more significant role in other mammals such as mice

Question 167 of 331

Patients with deficiencies of which one of the following complement proteins are predisposed to Leiner disease?

- A. C1
- B. C2
- C. C3
- D. C4
- E. C5

Question 167 of 331

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- B. C2
- C. C3
- D. C4
- ✓ E. C5

Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency
- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 168 of 331

Where is the majority of iron found in the body?

- A. Bone
- B. Haemoglobin
- C. Ferritin and haemosiderin
- D. Myoglobin
- E. Plasma iron

Question 168 of 331

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Iron metabolism

Absorption
- upper small intestine
- about 10% of dietary iron absorbed
- Fe2+ (ferrous iron) much better absorbed than Fe3+ (ferric iron)
- absorption is regulated according to bodies need
- increased by vitamin C, gastric acid
- decreased by proton pump inhibitors, tetracycline, gastric achlorhydia, tannin (found in tea)

Distribution in body
- total body iron = 4g
- haemoglobin = 70%
- ferritin and haemosiderin = 25%
- myoglobin = 4%
- plasma iron = 0.1%

Transport
- carried in plasma as Fe3+ bound to transferrin

Storage
- stored as ferritin in tissues

Excretion
- lost via intestinal tract following desquamination

Question 169 of 331

Which one of the following statements regarding the standard error of the mean is correct?

- A. Is the square root of standard deviation
- B. It is independent of sample size
- C. Is a measure of correlation between two variables
- D. Confidence intervals cannot be applied to the standard error of the mean
- E. Gets smaller as the sample size increases

Question 169 of 331

Which one of the following statements regarding the standard error of the mean is correct?

- A. Is the square root of standard deviation
- B. It is independent of sample size
- C. Is a measure of correlation between two variables
- D. Confidence intervals cannot be applied to the standard error of the mean
- ✓ E. Gets smaller as the sample size increases

Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- SEM = SD / square root (n)
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation i.e. the 95% confidence interval = mean - (1.96 *SEM) to the mean + (1.96 * SEM)

Question 170 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR2?

- A. Behcet's disease
- B. Type 1 diabetes mellitus
- C. Coeliac disease
- D. Haemochromatosis
- E. Narcolepsy

Question 170 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR2?

- A. Behcet's disease
- B. Type 1 diabetes mellitus
- C. Coeliac disease
- D. Haemochromatosis
- ✓ E. Narcolepsy

HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

HLA-A3
- haemochromatosis

HLA-B5
- Behcet's disease

HLA-B27
- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DR2
- narcolepsy
- Goodpasture's

HLA-DR3
- coeliac disease
- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4
- type 1 diabetes mellitus*
- rheumatoid arthritis

*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Question 171 of 331

How many protein-coding genes does a haploid human genome contain?

- A. 50,000
- B. 25,000
- C. 275.000
- D. 10,000
- E. 3 billion

Question 171 of 331

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Human genome - 25,000 protein-coding genes

Human genome

The human genome is stored on 23 chromosome pairs. The haploid human genome has a total of 3 billion DNA base pairs, making up an estimated 20,000-25,000 protein-coding genes

Question 172 of 331

Which one of the following diseases would give a positive cyanide-nitroprusside test?

- A. Bartter's syndrome
- B. Cryoglobulinaemia
- C. Cystinuria
- D. Paroxysmal nocturnal haemoglobinuria
- E. Cystinosis

Question 172 of 331

Which one of the following diseases would give a positive cyanide-nitroprusside test?

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- B. Cryoglobulinaemia
- ✓ C. Cystinuria
- D. Paroxysmal nocturnal haemoglobinuria
- E. Cystinosis

The cyanide-nitroprusside test would also be positive in homocystinuria

Cystinuria

Cystinuria is an autosomal recessive disorder characterised by the formation of recurrent renal stones. It is due to a defect in the membrane transport of cystine, ornithine, lysine, arginine (mnemonic = COLA)

Genetics
- chromosome 2: SLC3A1 gene, chromosome 19: SLC7A9

Features
- recurrent renal stones
- are classically yellow and crystalline, appearing semi-opaque on x-ray

Diagnosis
- cyanide-nitroprusside test

Management
- hydration
- D-penicillamine
- urinary alkalinization

Question 173 of 331

Each one of the following promotes the release of endothelin, except:

- A. Prostacyclin
- B. ADH
- C. Angiotensin II
- D. Hypoxia
- E. Mechanical shearing force

Question 173 of 331

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- E. Mechanical shearing force

Endothelin

Endothelin is a potent, long-acting vasoconstrictor and bronchoconstrictor. It is secreted initially as a prohormone by the vascular endothelium and later converted to ET-1 by the action of endothelin converting enzyme. It acts via interaction with a G-protein linked to phospholipase C leading to calcium release. Endothelin is thought to be important in the pathogenesis of many diseases including primary pulmonary hypertension (endothelin antagonists are now used), cardiac failure, hepatorenal syndrome and Raynaud's

Promotes release
- angiotensin II
- ADH
- hypoxia
- mechanical shearing forces

Inhibits release
- nitric oxide
- prostacyclin

Raised levels in
- MI
- heart failure
- ARF
- asthma
- primary pulmonary hypertension

Question 174 of 331

What level of evidence does a study offer which is obtained from a meta-analysis of randomised controlled trials?

- A. Ia
- B. Ib
- C. IIa
- D. IIb
- E. IV

Question 174 of 331

What level of evidence does a study offer which is obtained from a meta-analysis of randomised controlled trials?

- ✓ A. Ia
- B. Ib
- C. IIa
- D. IIb
- E. IV

Study design: evidence and recommendations

Levels of evidence

- Ia - evidence from meta-analysis of randomised controlled trials
- Ib - evidence from at least one randomised controlled trial
- IIa - evidence from at least one well designed controlled trial which is not randomised
- IIb - evidence from at least one well designed experimental trial
- III - evidence from case, correlation and comparative studies
- IV - evidence from a panel of experts

Grading of recommendation

- Grade A - based on evidence from at least one randomised controlled trial (i.e. Ia or Ib)
- Grade B - based on evidence from non-randomised controlled trials (i.e. IIa, IIb or III)
- Grade C - based on evidence from a panel of experts (i.e. IV)

Question 175 of 331

The chance of a 45-year-old mother giving birth to a child with Down's syndrome is approximately:

- A. 1 in 5
- B. 1 in 10
- C. 1 in 30
- D. 1 in 100
- E. 1 in 500

Question 175 of 331

The chance of a 45-year-old mother giving birth to a child with Down's syndrome is approximately:

- A. 1 in 5
- B. 1 in 10
- ✓ C. 1 in 30
- D. 1 in 100
- E. 1 in 500

Down's syndrome risk - 1/1,000 at 30 years then divide by 3 for every 5 years

Down's syndrome: epidemiology and genetics

Risk of Down's syndrome with increasing maternal age
- risk at 30 years = 1/1000
- 35 years = 1/350
- 40 years = 1/100
- 45 years = 1/30

One way of remembering this is by starting at 1/1,000 at 30 years and then dividing by 3 (i.e. 3 times more common) for every extra 5 years of age

Cytogenetics

Mode	% of cases	Risk of recurrence
Non-disjunction	94%	1 in 100 if under mother < 35 years
Robertsonian translocation (usually onto 14)	5%	10-15% if mother is translocation carrier 2.5% if father is translocation carrier
Mosaicism	1%	

The chance of a further child with Down's syndrome is approximately 1 in 100 if the mother is less than 35 years old. If the trisomy 21 is a result of a translocation the risk is much higher

Question 176 of 331

Which one of the following statements regarding growth hormone is incorrect?

- A. Doesn't act directly on chondrocytes or osteoblasts
- B. Is an anabolic hormone
- C. Is responsible for changes in protein, lipid, and carbohydrate metabolism
- D. Is secreted by the somatotroph cells
- E. Acts on a transmembrane receptor

Question 176 of 331

Which one of the following statements regarding growth hormone is incorrect?

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- B. Is an anabolic hormone
- C. Is responsible for changes in protein, lipid, and carbohydrate metabolism
- D. Is secreted by the somatotroph cells
- E. Acts on a transmembrane receptor

Growth hormone acts both directly on tissues (e.g. stimulates division and multiplication of cartilage chondrocytes) and also indirectly following the secretion of insulin-like growth factor 1

Growth hormone

Growth hormone (GH) is an anabolic hormone secreted by the somatotroph cells of the anterior lobe of the pituitary gland. It has actions on multiple organ systems and is important in postnatal growth and development. Growth hormone is also responsible for changes in protein, lipid, and carbohydrate metabolism

Mechanism of action
- acts on a transmembrane receptor for growth
- binding of GH to the receptor leads to receptor dimerization
- acts directly on tissues and also indirectly via insulin-like growth factor 1 (IGF-1), primarily secreted by the liver

Conditions associated with GH disorders
- excess GH: acromegaly
- GH deficiency: resulting in short stature

Question 177 of 331

Which one of the following causes of primary immunodeficiency is due to a defect in both B-cell and T-cell function?

- A. Di George syndrome
- B. Chronic granulomatous disease
- C. Bruton's congenital agammaglobulinaemia
- D. Leukocyte adhesion deficiency
- E. Ataxic telangiectasia

Question 177 of 331

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- B. Chronic granulomatous disease
- C. Bruton's congenital agammaglobulinaemia
- D. Leukocyte adhesion deficiency
- ✓ E. Ataxic telangiectasia

Combined B- and T-cell disorders: SCID WAS ataxic (SCID, Wiskott-Aldrich syndrome, ataxic telangiectasia)

Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders
- DiGeorge syndrome

Combined B- and T-cell disorders
- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Question 178 of 331

A 47-year-old man is seen in the respiratory clinic. He has been referred due to progressive shortness of breath. A CT scan showed emphysematous changes in the lungs. As he has never smoked alpha 1-antitrypsin levels were ordered and reported to be 10% of normal. What is the most likely genotype of this patient?

- A. PiZZ
- B. PiSS
- C. PiMS
- D. PiMM
- E. PiMZ

Question 178 of 331

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- ✓ A. PiZZ
- B. PiSS
- C. PiMS
- D. PiMM
- E. PiMZ

Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver

Genetics
- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

Features
- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

Investigations
- A1AT concentrations

Management
- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

*trusted sources are split on which is a more accurate description

Question 179 of 331

A new anti-epileptic drug is trialled for children with absence seizures. There are 250 children in the control group and 150 children assigned to take the new drug. After 4 months 100 children in the control group had had a seizure compared to 15 children in the group taking the new medication. What is the relative risk reduction?

- A. 4
- B. 30%
- C. 3.33
- D. 75%
- E. 40%

Question 179 of 331

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- A. 4
- B. 30%
- C. 3.33
- ✓ D. 75%
- E. 40%

Relative risk reduction = (EER - CER) / CER

Experimental event rate, EER = 15 / 150 = 0.1
Control event rate, CER = 100 / 250 = 0.4
Relative risk reduction = (EER - CER) / CER = (0.1 - 0.4) / 0.4 = -0.75 or a 75% reduction

Relative risk

Relative risk (RR) is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER)

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	**Experienced significant pain relief**
Paracetamol	100	60
Placebo	80	20

Experimental event rate, EER = 60 / 100 = 0.6
Control event rate, CER = 20 / 80 = 0.25
Therefore the relative risk = EER / CER = 0.6 / 0.25 = 2.4

If the risk ratio is > 1 then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is < 1 then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

Relative risk reduction (RRR) or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data, RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140%

Question 180 of 331

A 64-year-old man is having a dual chamber pacemaker inserted. The ventricular lead is to be inserted via the coronary sinus. Where does the coronary sinus drain into?

- A. Right atrium
- B. Left ventricle
- C. Right ventricle
- D. Inferior vena cava
- E. Left atrium

Question 180 of 331

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- ✓ A. Right atrium
- B. Left ventricle
- C. Right ventricle
- D. Inferior vena cava
- E. Left atrium

Coronary circulation

Arterial supply of the heart
- posterior aortic sinus --> left coronary artery (LCA)
- anterior aortic sinus --> right coronary artery (RCA)
- LCA --> LAD + circumflex
- RCA --> posterior descending
- RCA supplies SA node in 60%, AV node in 90%

Venous drainage of the heart
- coronary sinus drains into the right atrium

Question 181 of 331

Interferon-alpha may be used in the management of each one of the following, except:

- A. Metastatic renal cell cancer
- B. Hepatitis B
- C. Kaposi's sarcoma
- D. Hepatitis C
- E. Chronic granulomatous disease

Question 181 of 331

Interferon-alpha may be used in the management of each one of the following, except:

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Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha
- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

IFN-beta
- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

IFN-gamma
- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

Question 182 of 331

A new blood test which can show signs of myocardial damage within one hour of the onset of chest pain is developed. In a trial of 100 patients presenting with chest pain, 40 of the patients are later proven to have had myocardial ischaemia by conventional troponin tests. Of these patients the new test was positive in 20 cases. The new test was also positive in 20 of the remaining 60 patients later shown to have a negative troponin. What is the negative predictive value of the new test for myocardial ischaemia?

- A. 0.5
- B. 0.66
- C. 0.8
- D. Cannot calculate
- E. 0.33

Question 182 of 331

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- A. 0.5
- ✓ B. 0.66
- C. 0.8
- D. Cannot calculate
- E. 0.33

The new test was negative in 20 of the patients later shown to have myocardial ischaemia (false negative) and negative in 40 patients confirmed not to have myocardial ischaemia (true negative)

Negative predictive value = TN / (TN + FN) = 40 / (40 + 20) = 0.66

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 183 of 331

A study is designed to see whether the degree of chest pain is linked to the troponin I value for patients admitted following a myocardial infarction. The pain is assessed using a scale of 1-10, with 10 representing the worst pain that the patient has ever experienced. Which one of the following significance tests is it most appropriate to use to investigate this link?

- A. Student's t-test
- B. Chi-squared test
- C. Spearman's rank correlation coefficient
- D. Pearson's product-moment coefficient
- E. Mann-Whitney test

Question 183 of 331

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- ✓ C. Spearman's rank correlation coefficient
- D. Pearson's product-moment coefficient
- E. Mann-Whitney test

This scenario looks at whether the values are correlated. As the data is non-parametric, particularly the observation based pain scale, Spearman's rank correlation coefficient should be used.

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 184 of 331

Each one of the following is a feature of pseudohypoparathyroidism, except:

- A. Short fourth and fifth metacarpals
- B. Round face
- C. Normal calcium and phosphate levels
- D. Cognitive impairment
- E. Short stature

Question 184 of 331

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- A. Short fourth and fifth metacarpals
- B. Round face
- ✓ C. Normal calcium and phosphate levels
- D. Cognitive impairment
- E. Short stature

Pseudohypoparathyroidism

Pseudohypoparathyroidism is caused by target cell insensitivity to parathyroid hormone (PTH) due to a mutation in a G-protein. In type I pseudohypoparathyroidism there is a complete receptor defect whereas in type II the cell receptor is intact. Pseudohypoparathyroidism is typically inherited in an autosomal dominant fashion*

Bloods
- PTH: high
- calcium: low
- phosphate: high

Features
- short fourth and fifth metacarpals
- short stature
- cognitive impairment
- obesity
- round face

Investigation
- infusion of PTH followed by measurement of urinary phosphate and cAMP measurement - this can help differentiate between type I (neither phosphate or cAMP levels rise) and II (cAMP rises but phosphate levels do not change)

*it was previously thought to be an X-linked dominant condition

Question 185 of 331

Which one of the following features is characteristic of acute intermittent porphyria?

- A. Photosensitivity
- B. Increased urinary porphobilinogen between acute attacks
- C. Hypernatraemia during attacks
- D. Autosomal recessive inheritance
- E. Increased faecal protoporphyrin excretion

Question 185 of 331

Which one of the following features is characteristic of acute intermittent porphyria?

- A. Photosensitivity
- ✓ B. Increased urinary porphobilinogen between acute attacks
- C. Hypernatraemia during attacks
- D. Autosomal recessive inheritance
- E. Increased faecal protoporphyrin excretion

Acute intermittent porphyria

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Features
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

Diagnosis
- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

Question 186 of 331

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

- A. Goodpasture's syndrome
- B. Left-to-right cardiac shunts
- C. Anaemia
- D. Hyperkinetic states
- E. Exercise

Question 186 of 331

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

- A. Goodpasture's syndrome
- B. Left-to-right cardiac shunts
- ✓ C. Anaemia
- D. Hyperkinetic states
- E. Exercise

Transfer factor
- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	Causes of a lower TLCO
• asthma • pulmonary haemorrhage (Wegener's, Goodpasture's) • left-to-right cardiac shunts • polycythaemia • hyperkinetic states • male gender, exercise	• pulmonary fibrosis • pneumonia • pulmonary emboli • pulmonary oedema • emphysema • anaemia • low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO
- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

Question 187 of 331

A 15-year-old girl presents with abdominal pain. She is normally fit and well and currently takes a combined oral contraceptive pill. The patient is accompanied by her mother, who is known to have hereditary spherocytosis. The pain is located in the upper abdomen and is episodic in nature, but has become severe today. There has been no change to her bowel habit and no nausea or vomiting. What is the most likely diagnosis?

- A. Inferior vena cava thrombosis
- B. Acute pancreatitis
- C. Renal vein thrombosis
- D. Gastritis
- E. Biliary colic

Question 187 of 331

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- C. Renal vein thrombosis
- D. Gastritis
- ✓ E. Biliary colic

This patient has hereditary spherocytosis resulting in chronic haemolysis and gallstone formation. An important differential in a poorly patient with hereditary spherocytosis would be splenic rupture

Hereditary spherocytosis

Basics
- most common hereditary haemolytic anaemia in northern Europeans
- autosomal dominant defect of RBC cytoskeleton
- biconcave disc --> spherocyte
- red cell survival reduced, destroyed by spleen

Presentation
- e.g. failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

Diagnosis
- osmotic fragility test

Management
- folate replacement
- splenectomy

Question 188 of 331

A 29-year-old man presents with a productive cough, fever and pleuritic chest pain. A chest x-ray shows lobar consolidation and a sputum culture grows *Haemophilus influenzae*. This is his fourth chest infection in the past seven months. *Streptococcus pneumoniae* has been grown from the sputum of the previous three episodes. Six-weeks following the latest infection a full blood count, urea and electrolytes, CRP and chest x-ray are all reported as normal. What is the most appropriate next investigation?

- A. Serum immunoglobulins
- B. Spirometry
- C. HIV test
- D. Colonscopy
- E. Urinanalysis

Question 188 of 331

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- ✓ A. Serum immunoglobulins
- B. Spirometry
- C. HIV test
- D. Colonscopy
- E. Urinanalysis

This patient has had repeated infections with encapsulated bacteria which should raise the suspicion of immunoglobulin deficiency. HIV would be suggested by infections associated with impaired cellular immunity.

Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

IgG	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
IgA	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
IgM	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
IgD	1%	Monomer	Involved in activation of B cells
IgE	0.1%	Monomer	Involved in allergic reactions

Question 189 of 331

The nitric oxide receptor is an example of a:

- A. Ligand-gated ion channel
- B. Intracellular receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Tyrosine kinase receptor

Question 189 of 331

The nitric oxide receptor is an example of a:

- A. Ligand-gated ion channel
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- D. G protein-coupled receptor
- E. Tyrosine kinase receptor

The nitric oxide receptor is a soluble, intracellular guanylate cyclase

Nitric oxide

Previously known as endothelium derived relaxation factor, nitric oxide (NO) has emerged as a molecule which is integral to many physiological and pathological processes. It is formed from L-arginine and oxygen by nitric oxide synthetase (NOS). An inducible form of NOS has been shown to be present in macrophages. Nitric oxide has a very short half-life (seconds), being inactivated by oxygen free radicals

Effects

- acts on guanylate cyclase leading to raised intracellular cGMP levels and therefore decreasing Ca2+ levels
- vasodilation, mainly venodilation
- inhibits platelet aggregation

Clinical relevance

- underproduction of NO is implicated in hypertrophic pyloric stenosis
- lack of NO is thought to promote atherosclerosis
- in sepsis increased levels of NO contribute to septic shock
- organic nitrates (metabolism produces NO) is widely used to treat cardiovascular disease (e.g. angina, heart failure)
- sildenafil is thought to potentiate the action of NO on penile smooth muscle and is used in the treatment of erectile dysfunctions

Question 190 of 331

A patient presents with an inability to abduct his right shoulder. Which nerve supplies the deltoid muscle?

- A. Lateral cutaneous
- B. Suprascapular
- C. Musculocutaneous
- D. Axillary
- E. Median

Question 190 of 331

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Upper limb anatomy

The information below contains select facts which commonly appear in examinations:

Deltoid muscle
- supplied by the axillary nerve (C5,C6)
- actions: mainly shoulder abduction

Question 191 of 331

A 31-year-old woman is diagnosed with familial hypercholesterolaemia. You discuss the possibility of screening her relatives. What is the chance her brother will also be affected?

- A. 50%
- B. 66%
- C. 25%
- D. 100%
- E. 0%

Question 191 of 331

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- ✓ A. 50%
- B. 66%
- C. 25%
- D. 100%
- E. 0%

As familial hypercholesterolaemia is autosomal dominant there is a 50% chance her brother will be affected.

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the hepatic proteins involved in clearance of LDL-cholesterol from the circulation

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Question 192 of 331

A man with glucose-6-phosphate dehydrogenase deficiency asks for advice regarding his son. What is the chance his son will also develop the disease?

- A. 2 in 3
- B. No increased risk
- C. Will definitely be affected
- D. 1 in 2
- E. 1 in 4

Question 192 of 331

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X-linked recessive conditions - no male-to-male transmission

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 193 of 331

You are a ST1 doctor on a gastroenterology ward. The F2 doctor has asked you to supervise him putting in an ascitic drain for a patient with liver cirrhosis. He is keen to get it signed off for his portfolio. He has never seen one put in before but has read around the subject. What is the most appropriate action?

- A. You do the procedure but sign him off as you know he will do many more over the next 3 months
- B. Get the F2 doctor to insert the drain under your careful guidance, avoid telling the patient to prevent unnecessary anxiety
- C. Suggest it would be better if he watches you insert the drain before attempting one himself
- D. If he is confident ask him to do it so you can spend your time more efficiently on other ward jobs and sign him off
- E. Ask the patient if he minds the F2 doctor doing the procedure and get the F2 doctor to insert the drain under your careful guidance

Question 193 of 331

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- D. If he is confident ask him to do it so you can spend your time more efficiently on other ward jobs and sign him off
- E. Ask the patient if he minds the F2 doctor doing the procedure and get the F2 doctor to insert the drain under your careful guidance

It used to be said that for procedures 'see one, do one, teach one'. These days have long gone. Doctors are now expected to show proof of competency before performing procedures alone. In this scenario the F2 doctor has never seen one previously so it is not appropriate for him to insert the drain today. The best option is for him to watch you.

If you are going to let the F2 doctor insert the drain you should be honest with the patient about his lack of experience.

Signing him off without seeing him perform the procedure is a very poor option which could result in a GMC referral if found out. It also puts future patients at risk

Letting him insert the drain today without supervision is again a very poor option as it puts the patient at risk.

Question 194 of 331

A follow-up study is performed looking at the height of 100 adults who were given steroids during childhood. The average height of the adults is 169cm, with a standard deviation of 16cm. What is the standard error of the mean?

- A. Cannot be calculated
- B. 1.69
- C. 0.16
- D. 1.6
- E. 1.3

Question 194 of 331

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- C. 0.16
- ✓ D. 1.6
- E. 1.3

Standard error of the mean = standard deviation / square root (number of patients)

The standard error of the mean is calculated by the standard deviation / square root (number of patients) = 16 / square root (100) = 16 / 10 = 1.6

Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- SEM = SD / square root (n)
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation i.e. the 95% confidence interval = mean - (1.96 *SEM) to the mean + (1.96 * SEM)

Question 195 of 331

A 54-year-old woman is admitted to the Emergency Department following what sounds like an episode of vasovagal syncope. Blood gases on admission show a metabolic acidosis. Blood tests are reported as follows:

Na^+	141 mmol/l
K^+	5.0 mmol/l
Chloride	116 mmol/l
Bicarbonate	18 mmol/l
Urea	4.0 mmol/l
Creatinine	88 µmol/l

Which one of the following is most likely to explain the metabolic acidosis?

- A. Lithium overdose
- B. Aspirin overdose
- C. Recent myocardial infarction
- D. Alcoholic ketoacidosis
- E. Ureterosigmoidostomy

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- ✓ E. Ureterosigmoidostomy

The anion gap is normal, (141 + 5.0) - (116 + 18) = 12 mmol/l, which is consistent with a ureterosigmoidostomy. Aspirin overdose, myocardial infarction and alcoholic ketoacidosis would cause a raised anion gap

Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by: (Na^+ + K^+) - (Cl- + HCO-3). If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap (= hyperchloraemic metabolic acidosis)
- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Raised anion gap
- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:
- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Question 196 of 331

Which of the following is least recognised as a cause of macroglossia?

- A. Amyloidosis
- B. Turner's syndrome
- C. Duchenne muscular dystrophy
- D. Acromegaly
- E. Hurler syndrome

Question 196 of 331

Which of the following is least recognised as a cause of macroglossia?

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Macroglossia

Causes
- hypothyroidism
- acromegaly
- amyloidosis
- Duchenne muscular dystrophy
- mucopolysaccharidosis (e.g. Hurler syndrome)

Patients with Down's syndrome are now thought to have apparent macroglossia due to a combination of mid-face hypoplasia and hypotonia

Question 197 of 331

Each one of the following is seen in Klinefelter's syndrome, except:

- A. Small, firm testes
- B. Lack of secondary sexual characteristics
- C. Infertility
- D. Increased incidence of breast cancer
- E. Reduced gonadotrophin levels

Question 197 of 331

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Klinefelter's syndrome

Klinefelter's syndrome is associated with karyotype 47, XXY

Features
- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis

Question 198 of 331

A study is designed to compare the calcium levels of males and females who developed inflammatory bowel disease in childhood. Which one of the following statistical tests is it most appropriate to use?

- A. Pearson's test
- B. Mann-Whitney test
- C. Chi-squared test
- D. Student's unpaired t-test
- E. Student's paired t-test

Question 198 of 331

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- A. Pearson's test
- B. Mann-Whitney test
- C. Chi-squared test
- ✓ D. Student's unpaired t-test
- E. Student's paired t-test

As the data is parametric and compares two independent sample from the same population an unpaired t-test is the most appropriate test to use

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 199 of 331

Which one of the following best describes the Hering-Bruer reflex?

- A. Lung distension causing slowing of the respiratory rate
- B. Raised hydrogen ion concentration in the ECF stimulating respiration
- C. Low pO2 stimulating the carotid and aortic bodies
- D. Lung distension causing increase of the respiratory rate
- E. Decreased hydrogen ion concentration in the ECF stimulating respiration

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Respiratory physiology: control

Control of respiration
- central regulatory centres
- central and peripheral chemoreceptors
- pulmonary receptors

Central regulatory centres
- medullary respiratory centre
- apneustic centre (lower pons)
- pneumotaxic centre (upper pons)

Central and peripheral chemoreceptors
- central: raised [H+] in ECF stimulates respiration
- peripheral: carotid + aortic bodies, respond to raised pCO2 & [H+], lesser extent low pO2

Pulmonary receptors
- stretch receptors, lung distension causes slowing of respiratory rate (Hering-Bruer reflex)
- irritant receptor, leading to bronchoconstriction
- juxtacapillary receptors, stimulated by stretching of the microvasculature

Question 200 of 331

You are asked to design a study to assess whether living near electricity pylons is a risk factor for childhood leukaemia. What is the most appropriate type of study design?

- A. Cross-over trial
- B. Cohort study
- C. Cross-sectional survey
- D. Case-control study
- E. Randomised controlled trial

Question 200 of 331

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- C. Cross-sectional survey
- ✓ D. Case-control study
- E. Randomised controlled trial

As the outcome (childhood leukaemia) is relatively rare a cohort study would take an extremely long time to provide significant results

Study design

The following table highlights the main features of the different types of study

Randomised controlled trial	Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo) • Practical or ethical problems may limit use
Cohort study	Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome • Examples include Framingham Heart Study
Case-control study	Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition • Inexpensive, produce quick results • Useful for studying rare conditions • Prone to confounding
Cross-sectional survey	Provide a 'snapshot', sometimes called prevalence studies • Provide weak evidence of cause and effect

Question 201 of 331

Which one of the following statements regarding significance tests is incorrect?

A. Parametric data is usually normally distributed

B. Student's t-test may be paired on unpaired

C. Pearson's product-moment coefficient is used to assess correlation between two variables

D. Chi-squared test is used to compare parametric data

E. Paired data refers to data obtained from a single group of patients

Question 201 of 331

Which one of the following statements regarding significance tests is incorrect?

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- C. Pearson's product-moment coefficient is used to assess correlation between two variables
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Question 202 of 331

Which one of the following is least associated with Reye's syndrome?

- A. Hypoglycaemia
- B. Preceding aspirin use
- C. Purpuric skin lesions
- D. Seizures
- E. Preceding viral infection

Question 202 of 331

Which one of the following is least associated with Reye's syndrome?

- A. Hypoglycaemia
- B. Preceding aspirin use
- ✓ C. Purpuric skin lesions
- D. Seizures
- E. Preceding viral infection

Reye's syndrome
- viral/aspirin use may trigger
- features include encephalopathy, fatty infiltration and hypoglycaemia

Reye's syndrome

Reye's syndrome is a severe, progressive encephalopathy affecting children that is accompanied by fatty infiltration of the liver, kidneys and pancreas. The aetiology of Reye's syndrome is not fully understood although there is a known association with aspirin use and a viral cause has been postulated

The peak incidence is 2 years of age, features include:
- may be history of preceding viral illness
- encephalopathy: confusion, seizures, cerebral oedema, coma
- fatty infiltration of the liver, kidneys and pancreas
- hypoglycaemia

Management is supportive

Prognosis is poor - 30-40% mortality

Question 203 of 331

Which one of the following causes of hyponatraemia is least associated with a urinary sodium > 20 mmol/L?

- A. Diuretics
- B. Addison's
- C. Psychogenic polydipsia
- D. Syndrome of inappropriate ADH
- E. Hypothyroidism

Question 203 of 331

Which one of the following causes of hyponatraemia is least associated with a urinary sodium > 20 mmol/L?

- A. Diuretics
- B. Addison's
- ✓ C. Psychogenic polydipsia
- D. Syndrome of inappropriate ADH
- E. Hypothyroidism

Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolarity levels aid making a diagnosis

Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)
- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic
- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss
- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)
- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Question 204 of 331

Chronic lymphocytic leukaemia is mostly due to a:

- A. Polyclonal proliferation of B-cell lymphocytes
- B. Monoclonal proliferation of B-cell lymphocytes
- C. Monoclonal proliferation of large granular lymphocytes
- D. Monoclonal proliferation of T-cell lymphocytes
- E. Polyclonal proliferation of T-cell lymphocytes

Question 204 of 331

Chronic lymphocytic leukaemia is mostly due to a:

- A. Polyclonal proliferation of B-cell lymphocytes
- ✓ B. Monoclonal proliferation of B-cell lymphocytes
- C. Monoclonal proliferation of large granular lymphocytes
- D. Monoclonal proliferation of T-cell lymphocytes
- E. Polyclonal proliferation of T-cell lymphocytes

CLL is caused by a monoclonal proliferation of B-cell lymphocytes

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 205 of 331

Marfan's syndrome is primarily due to a defect in which one of the following proteins?

- A. Polycystin-1
- B. Fibrillin
- C. Type IV collagen
- D. Type I collagen
- E. Elastin

Question 205 of 331

Marfan's syndrome is primarily due to a defect in which one of the following proteins?

- A. Polycystin-1
- ✓ B. Fibrillin
- C. Type IV collagen
- D. Type I collagen
- E. Elastin

Although fibrillin is the primary protein affected (due to a defect in the fibrillin-1 gene) it should be noted that fibrillin is used as a substrate of elastin

Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 patients.

Features

- tall stature with arm span to height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Question 206 of 331

Which one of the following conditions is usually inherited in a X-linked dominant fashion?

- A. Albinism
- B. Hurler's syndrome
- C. Ataxia telangiectasia
- D. Homocystinuria
- E. Alport's syndrome

Question 206 of 331

Which one of the following conditions is usually inherited in a X-linked dominant fashion?

- A. Albinism
- B. Hurler's syndrome
- C. Ataxia telangiectasia
- D. Homocystinuria
- ✓ E. Alport's syndrome

Alport's syndrome is inherited in a X-linked dominant fashion in around 85% of cases

X-linked dominant

The following conditions are inherited in a X-linked dominant fashion*:

Alport's syndrome (in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing)
Rett syndrome
Vitamin D resistant rickets

*pseudohypoparathyroidism was previously classified as an X-linked dominant condition but has now been shown to be inherited in an autosomal dominant fashion in the majority of cases

Question 207 of 331

Which one of the following is least recognised to cause a clubbed appearance of the fingers?

- A. Graves' disease
- B. Empyema
- C. Cyanotic congenital heart disease
- D. Coeliac disease
- E. Cystic fibrosis

Question 207 of 331

Which one of the following is least recognised to cause a clubbed appearance of the fingers?

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- B. Empyema
- C. Cyanotic congenital heart disease
- ✓ D. Coeliac disease
- E. Cystic fibrosis

Whether thyroid acropachy is a true cause of clubbing is a moot point. The question asks about a 'clubbed appearance of the fingers'

Clubbing

The causes of clubbing may be divided into cardiac, respiratory and other

Cardiac causes
- cyanotic congenital heart disease (Fallot's, TGA)
- bacterial endocarditis
- atrial myxoma

Respiratory causes
- lung cancer
- pyogenic conditions: cystic fibrosis, bronchiectasis, abscess, empyema
- asbestosis, mesothelioma
- fibrosing alveolitis

Other causes
- Crohn's, to a lesser extent UC
- cirrhosis, primary biliary cirrhosis
- Graves' disease (thyroid acropachy)
- rare: Whipple's disease

Question 208 of 331

A 6-year-old boy is referred to clinic due to recurrent renal calculi. His grandmother also had a similar problem. What is the most likely diagnosis?

- A. Marfan's syndrome
- B. Familial gout nephropathy
- C. Homocystinuria
- D. Cystinuria
- E. Cystinosis

Question 208 of 331

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- C. Homocystinuria
- ✓ D. Cystinuria
- E. Cystinosis

Cystinuria

Cystinuria is an autosomal recessive disorder characterised by the formation of recurrent renal stones. It is due to a defect in the membrane transport of cystine, ornithine, lysine, arginine (mnemonic = COLA)

Genetics
- chromosome 2: SLC3A1 gene, chromosome 19: SLC7A9

Features
- recurrent renal stones
- are classically yellow and crystalline, appearing semi-opaque on x-ray

Diagnosis
- cyanide-nitroprusside test

Management
- hydration
- D-penicillamine
- urinary alkalinization

Question 209 of 331

Where is secretin secreted from?

- A. I cells in upper small intestine
- B. G cells in stomach
- C. K cells in upper small intestine
- D. D cells in the pancreas
- E. S cells in upper small intestine

Question 209 of 331

Where is secretin secreted from?

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- C. K cells in upper small intestine
- D. D cells in the pancreas
- ✓ E. S cells in upper small intestine

Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
Gastrin	G cells in antrum of the stomach	Distension of stomach, extrinsic nerves Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
CCK	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
Secretin	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
VIP	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion
Somatostatin	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Question 210 of 331

A new screening test is developed for colorectal cancer. It is a blood test which detects a protein; the higher the level of the protein, the more likely a patient is to have colorectal cancer. If the cut-off for a positive test is increased, which one of the following will also be increased?

- A. The p value
- B. Specificity
- C. Likelihood ratio for a negative test result
- D. Sensitivity
- E. Negative predictive value

Question 210 of 331

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- C. Likelihood ratio for a negative test result
- D. Sensitivity
- E. Negative predictive value

Increasing the cut-off of a positive test result will decrease the number of false positives and hence increase the specificity

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 211 of 331

Which one of the following statements regarding the normal distribution is correct?

- A. Is a discrete probability distribution
- B. 99.7% of values lie within 2 standard deviations of the mean
- C. Mean = mode = median
- D. Standard deviation = mean / square root (variance)
- E. Is also referred to as the binomial distribution

Question 211 of 331

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The Normal distribution is a continuous probability distribution

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 212 of 331

Which type of secondary messenger system does adrenaline stimulate?

- A. Calcium
- B. Protein kinase
- C. Phosphoinositide
- D. Cyclic AMP
- E. Cyclic GMP

Question 212 of 331

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- ✓ D. Cyclic AMP
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Second messengers

Overview
- many different types
- allow amplification of external stimulus

Cyclic AMP
- e.g. adrenaline, noradrenaline, glucagon, LH, FSH, TSH, calcitonin, parathyroid hormone

Protein kinase activity
- e.g. insulin, growth hormone, prolactin, oxytocin, erythropoietin, growth factors

Calcium and/or phosphoinositides
- e.g. ADH, GnRH, TRH

Cyclic GMP
- e.g. ANP, nitric oxide

Question 213 of 331

Which one of the following immunological changes is seen in progressive HIV infection?

- A. Increase in IL-2 production
- B. Increase in B2-microglobulin levels
- C. Increased type IV hypersensitivity responses
- D. Increased natural killer (NK) cell function
- E. A rise in the CD4/CD8 ratio

Question 213 of 331

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HIV: immunology

The following immunological changes are seen in progressive HIV:

- reduction in CD4 count
- increase B2-microglobulin
- decreased IL-2 production
- polyclonal B-cell activation
- decrease NK cell function
- reduced delayed hypersensitivity responses

Question 214 of 331

Cystic fibrosis is due to a gene defect on:

- A. Chromosome 3
- B. Chromosome 7
- C. Chromosome 11
- D. Chromosome 14
- E. Chromosome 15

Question 214 of 331

Cystic fibrosis is due to a gene defect on:

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- ✓ B. Chromosome 7
- C. Chromosome 11
- D. Chromosome 14
- E. Chromosome 15

Cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder causing increased viscosity of secretions (e.g. lungs and pancreas). It is due to a defect in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which codes a cAMP-regulated chloride channel

In the UK 80% of CF cases are due to a deletion at delta F508 on the long arm of chromosome 7. Cystic fibrosis affects 1 per 2500 births, and the carrier rate is c. 1 in 25

Organisms which may colonise CF patients

- Staph aureus
- *Pseudomonas aeruginosa*
- Burkholderia cepacia*
- Aspergillus

*previously known as *Pseudomonas* cepacia

Question 215 of 331

Which one of the following is not a recognised cause of hypocalcaemia?

- A. Hypoparathyroidism
- B. Bendroflumethiazide
- C. Pseudohypoparathyroidism
- D. Acute pancreatitis
- E. Acute rhabdomyolysis

Question 215 of 331

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- D. Acute pancreatitis
- E. Acute rhabdomyolysis

Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Question 216 of 331

The atrial natriuretic peptide receptor is an example of a:

- A. Ligand-gated ion channel
- B. Intracellular receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Tyrosine kinase receptor

Question 216 of 331

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Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel
- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 217 of 331

Which one of the following is equivalent to the pre-test probability?

- A. Post test odds / (1 + post-test odds)
- B. Pre-test odds x likelihood ratio
- C. The prevalence of a condition
- D. The incidence of a condition
- E. Post-test odds / likelihood ratio

Question 217 of 331

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- ✓ C. The prevalence of a condition
- D. The incidence of a condition
- E. Post-test odds / likelihood ratio

The prevalence is the proportion of a population that have the condition at a point in time whilst the incidence is the rate at which new cases occur in a population during a specified time period.

Pre- and post- test odds and probability

Pre-test probability

The proportion of people with the target disorder in the population at risk at a specific time (point prevalence) or time interval (period prevalence)

For example, the prevalence of rheumatoid arthritis in the UK is 1%

Post-test probability

The proportion of patients with that particular test result who have the target disorder

Post-test probability = post test odds / (1 + post-test odds)

Pre-test odds

The odds that the patient has the target disorder before the test is carried out

Pre-test odds = pre-test probability / (1 - pre-test probability)

Post-test odds

The odds that the patient has the target disorder after the test is carried out

Post-test odds = pre-test odds x likelihood ratio

where the likelihood ratio for a positive test result = sensitivity / (1 - specificity)

Question 218 of 331

Vital capacity may be defined as:

- A. Volume inspired or expired with each breath at rest
- B. Volume of air remaining after maximal expiration
- C. Maximum volume of air that can be inspired at the end of a normal tidal inspiration
- D. Maximum volume of air that can be expired at the end of a normal tidal expiration
- E. Maximum volume of air that can be expired after a maximal inspiration

Question 218 of 331

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- ✓ E. Maximum volume of air that can be expired after a maximal inspiration

Respiratory physiology: lung volumes

Tidal volume (TV)
- volume inspired or expired with each breath at rest
- 500ml in males, 350ml in females

Inspiratory reserve volume (IRV) = 2-3 L
- maximum volume of air that can be inspired at the end of a normal tidal inspiration
- inspiratory capacity = TV + IRV

Expiratory reserve volume (ERV) = 750ml
- maximum volume of air that can be expired at the end of a normal tidal expiration

Residual volume (RV) = 1.2L
- volume of air remaining after maximal expiration
- increases with age
- RV = FRC - ERV

Vital capacity (VC) = 5L
- maximum volume of air that can be expired after a maximal inspiration
- 4,500ml in males, 3,500 mls in females
- decreases with age
- VC = IC + ERV

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

Question 219 of 331

Which one of the following features is least commonly seen in patients with pseudoxanthoma elasticum?

- A. Increased risk of ischaemic heart disease
- B. Retinitis pigmentosa
- C. Gastrointestinal haemorrhage
- D. Autosomal recessive inheritance
- E. 'Plucked chicken skin' appearance

Question 219 of 331

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- D. Autosomal recessive inheritance
- E. 'Plucked chicken skin' appearance

Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is an inherited condition (usually autosomal recessive*) characterised by an abnormality in elastic fibres

Features

- retinal angioid streaks
- 'plucked chicken skin' appearance - small yellow papules on the neck, antecubital fossa and axillae
- cardiac: mitral valve prolapse, increased risk of ischaemic heart disease
- gastrointestinal haemorrhage

*there are reports of autosomal dominant inheritance in a minority of cases

Question 220 of 331

Which one of the following types of blood vessel is first to vasoconstrict in the presence of hypoxia?

- A. Muscle arteries
- B. Skin arteries
- C. Hepatic arteries
- D. Renal arteries
- E. Pulmonary arteries

Question 220 of 331

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- A. Muscle arteries
- B. Skin arteries
- C. Hepatic arteries
- D. Renal arteries
- ✓ E. Pulmonary arteries

Pulmonary arteries vasoconstrict in the presence of hypoxia

Respiratory physiology: hypoxia

A fall in the partial pressure of oxygen in the blood leads to vasoconstriction of the pulmonary arteries. This allows blood to be diverted to better aerated areas of the lung and improves the efficiency of gaseous exchange

Question 221 of 331

Which one of the following is not a recognised feature of methaemoglobinaemia?

- A. Dyspnoea
- B. 'Chocolate' cyanosis
- C. Anxiety
- D. Reduced pO2 but normal oxygen saturation on pulse oximetry
- E. Acidosis

Question 221 of 331

Which one of the following is not a recognised feature of methaemoglobinaemia?

- A. Dyspnoea
- B. 'Chocolate' cyanosis
- C. Anxiety
- ✓ D. Reduced pO2 but normal oxygen saturation on pulse oximetry
- E. Acidosis

Normal pO2 but decreased oxygen saturation is characteristic of methaemoglobinaemia

Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes
- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes
- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features
- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO2 but decreased oxygen saturation

Management
- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

Question 222 of 331

Dobutamine is an example of:

- A. Alpha-1 agonist
- B. Alpha-2 agonist
- C. Beta-1 antagonist
- D. Beta-2 antagonist
- E. Beta-1 agonist

Question 222 of 331

Dobutamine is an example of:

- A. Alpha-1 agonist
- B. Alpha-2 agonist
- C. Beta-1 antagonist
- D. Beta-2 antagonist
- ✓ E. Beta-1 agonist

Adrenoceptor agonists

Alpha-1 agonists
- phenylephrine

Alpha-2 agonists
- clonidine

Beta-1 agonists
- dobutamine

Beta-2 agonists
- salbutamol

Beta-3 agonists
- being developed, may have a role in preventing obesity (stimulation causes lipolysis)

Question 223 of 331

A patient receives vincristine to help treat non-Hodgkin's lymphoma. What stage in the cell cycle does vincristine act?

- A. G1
- B. M0
- C. M
- D. G2
- E. S

Question 223 of 331

A patient receives vincristine to help treat non-Hodgkin's lymphoma. What stage in the cell cycle does vincristine act?

- A. G1
- B. M0
- ✓ C. M
- D. G2
- E. S

Vincristine inhibits formation of microtubules and arrests mitosis

Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

Question 224 of 331

A 14-year-old girl is admitted to hospital following a ruptured ectopic pregnancy. She comes from a family of Jehovah's Witnesses. Her haemoglobin on admission is 6.9 g/dl. She consents to a blood transfusion but her mother refuses. What is the most appropriate course of action?

- A. Advise the parents she will have to get a High Court injunction in order to stop the transfusion
- B. Give the blood transfusion
- C. Transfer the patient to a hospital run by Jehovah's Witnesses
- D. Respect parental wishes and withhold the blood transfusion
- E. Ask the hospital lawyer to come in and decide upon the correct course of action

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- D. Respect parental wishes and withhold the blood transfusion
- E. Ask the hospital lawyer to come in and decide upon the correct course of action

The GMC gives the following guidance:

'You should encourage young people to involve their parents in making important decisions, but you should usually abide by any decision they have the capacity to make themselves'

With respect to Jehovah's witnesses:
'You should not make assumptions about the decisions that a Jehovah's Witness patient might make about treatment with blood or blood products. You should ask for and respect their views and answer their questions honestly and to the best of your ability. You may also wish to contact the hospital liaison committees established by the Watch Tower Society (the governing body of Jehovah's Witnesses) to support Jehovah's Witnesses faced with treatment decisions involving blood. These committees can advise on current Society policy regarding the acceptability or otherwise of particular blood products. They also keep details of hospitals and doctors who are experienced in 'bloodless' medical procedures.'

A blood transfusion is clearly in the patient's best interests and in the scenario described above may potentially be life-saving. Whilst a child cannot refuse treatment they are able to provide consent. Giving the blood transfusion is therefore both clinically and ethically the right course of action.

Not giving the blood transfusion not only fails to respect the patient's wishes but also causes potential harm.

Question 225 of 331

When establishing a screening programme, which one of the following is not a key criteria as defined by Wilson and Junger?

- A. There should be a recognised latent or early symptomatic stage
- B. The condition should be an important public health problem
- C. The test or examination should be acceptable to the population
- D. There should be agreed policy on whom to treat as patients
- E. The condition should be potentially curable

Question 225 of 331

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Screening: Wilson and Junger criteria

1. The condition should be an important public health problem

2. There should be an acceptable treatment for patients with recognised disease

3. Facilities for diagnosis and treatment should be available

4. There should be a recognised latent or early symptomatic stage

5. The natural history of the condition, including its development from latent to declared disease should be adequately understood

6. There should be a suitable test or examination

7. The test or examination should be acceptable to the population

8. There should be agreed policy on whom to treat

9. The cost of case-finding (including diagnosis and subsequent treatment of patients) should be economically balanced in relation to the possible expenditure as a whole

10. Case-finding should be a continuous process and not a 'once and for all' project

Question 226 of 331

Each one of the following is associated with Noonan's syndrome, except:

- A. Webbed neck
- B. Short stature
- C. Factor XI deficiency
- D. Pulmonary valve stenosis
- E. Abnormal karyotype

Question 226 of 331

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- A. Webbed neck
- B. Short stature
- C. Factor XI deficiency
- D. Pulmonary valve stenosis
- ✓ E. Abnormal karyotype

In contrast to Turner's syndrome, the karyotype is normal

Noonan's syndrome

Often thought of as the 'male Turner's', Noonan's syndrome is an autosomal condition associated with a normal karyotype. It is thought to be caused by a defect in a gene on chromosome 12

As well as features similar to Turner's syndrome (webbed neck, widely-spaced nipples, short stature, pectus carinatum and excavatum), a number of characteristic clinical signs may also be seen:

- cardiac: pulmonary valve stenosis
- ptosis
- triangular-shaped face
- low-set ears
- coagulation problems: factor XI deficiency

Question 227 of 331

You are a ST1 doctor in medicine. Whilst on-call you review a 60-year-old woman who is known to have COPD. She has been admitted with an infective exacerbation and has not responded to nebulisers and intravenous aminophylline. Her most recent blood gases show a worsening respiratory acidosis. You feel that non-invasive ventilation (NIV) is needed and bleep the on-call physio. After discussing the blood gas results over the phone she says that NIV is not indicated in her opinion and refuses to set it up. What is the most appropriate action?

- A. Phone her back in 30 minutes and exaggerate the clinical picture to persuade her to come in
- B. Accept her professional opinion and reassess the situation in 30 minutes
- C. Set-up the NIV equipment yourself to avoid any further delay
- D. As there is a disagreement on management speak to the consultant on-call
- E. Transfer the patient to another hospital

Question 227 of 331

You are a ST1 doctor in medicine. Whilst on-call you review a 60-year-old woman who is known to have COPD. She has been admitted with an infective exacerbation and has not responded to nebulisers and intravenous aminophylline. Her most recent blood gases show a worsening respiratory acidosis. You feel that non-invasive ventilation (NIV) is needed and bleep the on-call physio. After discussing the blood gas results over the phone she says that NIV is not indicated in her opinion and refuses to set it up. What is the most appropriate action?

- A. Phone her back in 30 minutes and exaggerate the clinical picture to persuade her to come in
- B. Accept her professional opinion and reassess the situation in 30 minutes
- C. Set-up the NIV equipment yourself to avoid any further delay
- ✓ D. As there is a disagreement on management speak to the consultant on-call
- E. Transfer the patient to another hospital

By far the best option here is to speak to the consultant on-call. The physio may be experienced in providing NIV but it is ultimately a medical decision about whether to start a treatment.

Accepting her opinion is a poor option as she has not reviewed the patient herself and is only giving an opinion on the basis of blood gases.

Setting up NIV equipment requires training. If done incorrectly it could potentially harm a patient. Transferring an acutely unwell patient simply because the physio won't come in is not appropriate. Lying about clinical information is a very poor option.

Question 228 of 331

Fragile X is associated with each one of the following, except:

- A. Small, firm testes
- B. Mental retardation
- C. Hypotonia
- D. Short stature
- E. Large low set ears

Question 228 of 331

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- C. Hypotonia
- D. Short stature
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Fragile X

Fragile X is a trinucleotide repeat disorder

Features in males
- learning difficulties
- large low set ears, long thin face, high arched palate
- macroorchidism
- hypotonia
- autism is more common
- mitral valve prolapse

Features in females (who have one fragile chromosome and one normal X chromosome) range from normal to mild

Diagnosis
- can be made antenatally by chorionic villus sampling or amniocentesis
- analysis of the number of CGG repeats using restriction endonuclease digestion and Southern blot analysis

Question 229 of 331

Which one of the following cells secretes the majority of tumour necrosis factor in humans?

- A. Neutrophils
- B. Macrophages
- C. Natural killer cells
- D. Killer-T cells
- E. Helper-T cells

Question 229 of 331

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Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of bodies response to Gram negative septicaemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF-alpha binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also cause activation of NFkB

Endothelial effects include increase expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

TNF blockers

- infliximab: monoclonal antibody, IV administration
- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

Question 230 of 331

Which one of the following is least associated with hypercalcaemia?

- A. Thyrotoxicosis
- B. Secondary hyperparathyroidism
- C. Tertiary hyperparathyroidism
- D. Thiazide diuretics
- E. Primary hyperparathyroidism

Question 230 of 331

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- D. Thiazide diuretics
- E. Primary hyperparathyroidism

Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, Ca2+ containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

*other causes of granulomas may lead to hypercalcaemia e.g. tuberculosis and histoplasmosis

**usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 231 of 331

A new drug which may reduce the chance of patients with chronic kidney disease developing gout is introduced. In one study of 2,000 patients 1,200 received the new drug of which 120 patients develop gout. The remaining 800 patients received a placebo of which 200 developed gout. What is the absolute risk reduction of developing gout?

- A. 0.1
- B. 15%
- C. 120
- D. 25%
- E. 6.66

Question 231 of 331

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- C. 120
- D. 25%
- E. 6.66

Absolute risk reduction = (Experimental event rate) - (Control event rate)

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Experimental event rate = 120 / 1,200 = 0.1
Control event rate = 200 / 800 = 0.25

Absolute risk reduction = 0.1 - 0.25 = -0.15 = 15% reduction

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 232 of 331

Which one of the following cell organelles contains double-stranded circular DNA?

- A. Nucleus
- B. Ribosome
- C. Nucleolus
- D. Golgi apparatus
- E. Mitochondria

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Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Energy production. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide

Question 233 of 331

Which one of the following statements regarding the normal menstrual cycle is incorrect?

- A. A number of follicles develop in the follicular phase under the influence of FSH
- B. The luteal phase is also known as the secretory phase
- C. The follicular phase follows menstruation and occurs around day 5 - 13
- D. A surge of FSH causes ovulation
- E. Progesterone levels are low in the follicular phase

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LH surge causes ovulation

Menstrual cycle

The menstrual cycle may be divided into the following phases:

	Days
Menstruation	1-4
Follicular phase (proliferative phase)	5-13
Ovulation	14
Luteal phase (secretory phase)	15-28

Further details are given in the table below

	Follicular phase (proliferative phase)	**Luteal phase (secretory phase)**
Ovarian histology	A number of follicles develop. One follicle will become dominant around the mid-follicular phase	Corpus luteum
Endometrial histology	Proliferation of endometrium	Endometrium changes to secretory lining under influence of progesterone
Hormones	A rise in FSH results in the development of follicles which in turn secrete oestradiol When the egg has matured, it secretes enough oestradiol to trigger the acute release of LH. This in turn leads to ovulation	Progesterone secreted by corpus luteum rises through the luteal phase. If fertilisation does not occur the corpus luteum will demise and progesterone levels fall Oestradiol levels also rise again during the luteal phase
Cervical mucus	Following menstruation the mucus is thick and forms a plug across the external os Just prior to ovulation the mucus becomes clear, acellular, low viscosity. It also becomes 'stretchy' - a quality termed spinnbarkeit	Under the influence of progesterone it becomes thick, scant, and tacky
Basal body temperature	Falls prior to ovulation due to the influence of oestradiol	Rises following ovulation in response to higher progesterone levels

Question 234 of 331

A 69-year-old female with a history of multiple myeloma is admitted with confusion. The following results are obtained:

Na^+	147 mmol/l
K^+	4.7 mmol/l
Urea	14.2 mmol/l
Creatinine	102 µmol/l
Adjusted calcium	3.9 mmol/l

What is the most appropriate initial management?

- A. IV 0.45% saline
- B. IV zoledronic acid
- C. Oral prednisolone
- D. IV pamidronate
- E. IV 0.9% saline

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- ✓ E. IV 0.9% saline

The raised sodium is a function of dehydration and will correct once the patient is adequately rehydrated

Hypercalcaemia: management

The initial management of hypercalcaemia is rehydration with normal saline, typically 3-4 litres/day. Following rehydration bisphosphonates may be used. They typically take 2-3 days to work with maximal effect being seen at 7 days

Other options include:

- calcitonin - quicker effect than bisphosphonates
- steroids in sarcoidosis

There is a limited role for the use of furosemide in hypercalcaemia. It may be useful in patients who cannot tolerate aggressive fluid rehydration

Question 235 of 331

T-Helper cells of the Th1 subset typically secrete:

- A. IFN-beta, IL-4, IL-8
- B. IFN-gamma, IL-2, IL-3
- C. IL-1, IL-6, TNF-alpha
- D. IL-1
- E. IL-4, IL-5, IL-6, IL-10, IL-13

Question 235 of 331

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- E. IL-4, IL-5, IL-6, IL-10, IL-13

T-Helper cells

There are two major subsets of T-Helper cells:

Th1
- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2
- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Question 236 of 331

A 28-year-old female undergoes a renal transplant for focal segmental glomerulosclerosis. Within hours of the operation the patient becomes unwell with features consistent with severe systemic inflammatory response syndrome. The patient is immediately taken back to theatre and the transplanted kidney is removed. What type of immunoglobulins are responsible for the graft rejection?

- A. IgE
- B. IgM
- C. IgG
- D. IgD
- E. IgA

Question 236 of 331

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- B. IgM
- ✓ C. IgG
- D. IgD
- E. IgA

Hyperacute graft rejection is due to pre-existent antibodies to HLA antigens and is therefore IgG mediated

Renal transplant: graft failure

Graft survival
- 1 year = 90%, 10 years = 60% for cadaveric transplants
- 1 year = 95%, 10 years = 70% for living-donor transplants

Post-op problems
- ATN of graft
- vascular thrombosis
- urine leakage
- UTI

Hyperacute acute rejection
- due to antibodies against donor HLA type 1 antigens
- rarely seen due to HLA matching

Causes of acute graft failure (< 6 months)
- acute rejection: give steroids, if resistant use monoclonal antibodies

Causes of chronic graft failure (> 6 months)
- chronic allograft nephropathy
- ureteric obstruction
- recurrence of original renal disease (MCGN > IgA > FSGS)

Question 237 of 331

Which one of the following statements regarding allergy testing is incorrect?

- A. Both irritants and allergens may be tested for using skin patch testing
- B. The radioallergosorbent test determines the level of IgE to a specific allergen
- C. Skin prick testing is easy to perform and inexpensive
- D. Skin prick testing should be read after 48 hours
- E. Skin prick testing normally includes a histamine control

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- E. Skin prick testing normally includes a histamine control

Skin prick testing can be read after 15-20 minutes. Skin patch testing is read after 48 hours

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 238 of 331

Which one of the following statements regarding leptin is incorrect?

- A. Is produced mainly by the hypothalamus
- B. Stimulates the release of melanocyte-stimulating hormone
- C. Obese patients have higher leptin levels
- D. Plays a key role in the regulation of body weight
- E. High levels decrease appetite

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Leptin is secreted by adipose tissue

Obesity: physiology

Leptin

Leptin is thought to play a key role in the regulation of body weight. It is produced by adipose tissue and acts on satiety centres in the hypothalamus and decreases appetite. More adipose tissue (e.g. in obesity) results in high leptin levels.

Leptin stimulates the release of melanocyte-stimulating hormone (MSH) and corticotrophin-releasing hormone (CRH). Low levels of leptin stimulates the release of neuropeptide Y (NPY)

Ghrelin

Where as leptin induces satiety, ghrelin stimulates hunger. It is produced mainly by the fundus of the stomach and the pancreas. Ghrelin levels increase before meals and decrease after meals

Question 239 of 331

Which of the following statements is true regarding autosomal dominant inheritance?

- A. Affected individuals always have affected parents
- B. Only heterozygotes manifest disease
- C. 50% of children will be carriers
- D. Responsible for the majority of enzyme deficiency disorders
- E. The risk remains the same for each successive pregnancy

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Due to non-penetrance affected individuals do not always have affected parents

Autosomal dominant

In autosomal dominant diseases:

- both homozygotes and heterozygotes manifest disease (there is no carrier state)
- both males and females affected
- only affected individuals can pass on disease
- disease is passed on to 50% of children
- normally appears in every generation (although see below)
- risk remains same for each successive pregnancy

Complicating factors:

- non-penetrance: lack of clinical signs and symptoms (normal phenotype) despite abnormal gene. E.g. 40% otosclerosis
- spontaneous mutation: new mutation in one of gametes e.g. 80% of individuals with achondroplasia have unaffected parents

Question 240 of 331

Which one of the following conditions is NOT an autosomal recessive condition?

- A. Haemochromatosis
- B. PKU
- C. Hereditary spherocytosis
- D. Tay-Sach's
- E. Friedreich's ataxia

Question 240 of 331

Which one of the following conditions is NOT an autosomal recessive condition?

- A. Haemochromatosis
- B. PKU
- ✓ C. Hereditary spherocytosis
- D. Tay-Sach's
- E. Friedreich's ataxia

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Hereditary spherocytosis is inherited in an autosomal dominant fashion.

Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's
- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Question 241 of 331

A study is designed to assess the efficacy of a new anti-hypertensive medication. Two groups of patients are randomly assigned, one to take the established drug for 3 months whilst the other takes the new drug for 3 months. Blood pressure is measured before and after the intervention. There is then a period off medication for 1 month. After this period has elapsed the medication that the groups receive is swapped around and again blood pressure is measured before and 3 months later. The difference in blood pressure after the respective medications is calculated for each patient. Which one of the following significance tests is it most appropriate to apply?

- A. Student's unpaired t-test
- B. Student's paired t-test
- C. Pearson's test
- D. Mann-Whitney test
- E. Chi-squared test

Question 241 of 331

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- ✓ B. Student's paired t-test
- C. Pearson's test
- D. Mann-Whitney test
- E. Chi-squared test

This describes a crossover study. As we are comparing parametric data from the same patients (they swapped medication halfway through the study) the Student's paired t-test should be used.

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 242 of 331

What is the typical vital capacity in a male?

- A. 300 ml
- B. 500 ml
- C. 1,500 ml
- D. 2,500 ml
- E. 4,500 ml

Question 242 of 331

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- D. 2,500 ml
- ✓ E. 4,500 ml

Respiratory physiology: lung volumes

Tidal volume (TV)
- volume inspired or expired with each breath at rest
- 500ml in males, 350ml in females

Inspiratory reserve volume (IRV) = 2-3 L
- maximum volume of air that can be inspired at the end of a normal tidal inspiration
- inspiratory capacity = TV + IRV

Expiratory reserve volume (ERV) = 750ml
- maximum volume of air that can be expired at the end of a normal tidal expiration

Residual volume (RV) = 1.2L
- volume of air remaining after maximal expiration
- increases with age
- RV = FRC - ERV

Vital capacity (VC) = 5L
- maximum volume of air that can be expired after a maximal inspiration
- 4,500ml in males, 3,500 mls in females
- decreases with age
- VC = IC + ERV

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

Question 243 of 331

Which one of the following is responsible for the activation of aciclovir?

- A. Guanosine kinase
- B. Protease
- C. Reverse transcriptase
- D. DNA polymerase
- E. Thymidine kinase

Question 243 of 331

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- A. Guanosine kinase
- B. Protease
- C. Reverse transcriptase
- D. DNA polymerase
- ✓ E. Thymidine kinase

Thymidine kinase phosphorylates aciclovir which then inhibits viral DNA polymerase

Antiviral agents

Aciclovir
- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

Ribavirin
- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

Interferons
- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

Amantadine
- used to treat influenza
- inhibits uncoating of virus in cell

Anti-retroviral agent used in HIV

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

Protease inhibitors (PI)
- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz

Question 244 of 331

A study looks at the use of amoxicillin in the treatment of acute sinusitis compared to placebo. The following results are obtained:

	Total number of patients	Number who achieved resolution of symptoms at 7 days
Amoxicillin	100	60
Placebo	75	30

What is the odds ratio a patient achieving resolution of symptoms at 7 days if they take amoxicillin compared to placebo?

- A. 1.5
- B. 0.5
- C. 2.25
- D. 0.6
- E. 1.66

Question 244 of 331

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What is the odds ratio a patient achieving resolution of symptoms at 7 days if they take amoxicillin compared to placebo?

- A. 1.5
- B. 0.5
- ✓ C. 2.25
- D. 0.6
- E. 1.66

The odds of symptoms resolution with amoxicillin = 60 / 40 = 1.5

The odds of symptoms resolution with placebo = 30 / 45 = (2/3)

Therefore the odds ratio = 1.5 / (2/3) = 2.25

Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol = 40 / 20 = 2

The odds of achieving significant pain relief with placebo = 30 / 60 = 0.5

Therefore the odds ratio = 2 / 0.5 = 4

Question 245 of 331

Which one of the following is the most common underlying mechanism causing prolongation of the QT segment?

- A. Opening of calcium channels
- B. Blockage of sodium channels
- C. Opening of sodium channels
- D. Blockage of potassium channels
- E. Opening of potassium channels

Question 245 of 331

Which one of the following is the most common underlying mechanism causing prolongation of the QT segment?

- A. Opening of calcium channels
- B. Blockage of sodium channels
- C. Opening of sodium channels
- ✓ D. Blockage of potassium channels
- E. Opening of potassium channels

In long QT syndrome QT prolongation is due to overload of myocardial cells with positively charged ions during ventricular repolarisation. Around 90-95% of inherited causes are due to defects in potassium channels

Long QT syndrome

Long QT syndrome (LQTS) is associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than 440 ms in males and 450 ms in females.

Congenital
- Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)
- Romano-Ward syndrome (no deafness)

Drugs
- amiodarone
- sotalol
- class 1a antiarrhythmic drugs
- tricyclic antidepressants
- chloroquine
- terfenadine*
- erythromycin

Other causes
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- acute MI
- myocarditis
- hypothermia
- subarachnoid haemorrhage

Management
- beta-blockers**
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 246 of 331

Which one of the following statements is true regarding interferon?

- A. Interferon-beta is produced by leucocytes
- B. Interferon-alpha and interferon-beta bind to the same type of receptor
- C. Interferon-gamma has stronger antiviral action than interferon-alpha
- D. Interferon-alpha has been shown to reduce the frequency of exacerbations in patients with relapsing-remitting multiple sclerosis
- E. Interferon-gamma has a role in chronic hepatitis C

Question 246 of 331

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- E. Interferon-gamma has a role in chronic hepatitis C

Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha
- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

IFN-beta
- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

IFN-gamma
- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

Question 247 of 331

What is the main advantage of non-inferiority trials when testing a new drug?

- A. Prevents ethical dilemmas
- B. Robust results are produced
- C. Useful for conditions where there is no proven drug treatment
- D. Useful for conditions where there is a high placebo response rate
- E. Small sample size is required

Question 247 of 331

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- D. Useful for conditions where there is a high placebo response rate
- ✓ E. Small sample size is required

Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined (-delta to +delta) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e. -delta). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

Question 248 of 331

Which one of the following is least likely to cause hypernatraemia?

- A. IV saline infusion
- B. Hyperosmolar non-ketotic diabetic coma
- C. Digoxin therapy
- D. Diabetes insipidus
- E. Dehydration

Question 248 of 331

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- B. Hyperosmolar non-ketotic diabetic coma
- ✓ C. Digoxin therapy
- D. Diabetes insipidus
- E. Dehydration

Hypernatraemia

Causes of hypernatraemia
- dehydration
- osmotic diuresis e.g. hyperosmolar non-ketotic diabetic coma
- diabetes insipidus
- excess IV saline

Question 249 of 331

Which of the following conditions is NOT inherited in a X-linked recessive fashion:

- A. Myotonic dystrophy
- B. G6PD deficiency
- C. Haemophilia B
- D. Colour blindness
- E. Fabry's disease

Question 249 of 331

Which of the following conditions is NOT inherited in a X-linked recessive fashion:

- ✓ A. Myotonic dystrophy
- B. G6PD deficiency
- C. Haemophilia B
- D. Colour blindness
- E. Fabry's disease

X-linked conditions: Duchenne/Becker, haemophilia, G6PD

X-linked recessive conditions

The following conditions are inherited in a X-linked recessive fashion:

Androgen insensitivity syndrome
Becker muscular dystrophy
Colour blindness
Duchenne muscular dystrophy
Fabry's disease
G6PD deficiency
Haemophilia A,B
Hunter's disease
Lesch-Nyhan syndrome
Nephrogenic diabetes insipidus
Ocular albinism
Retinitis pigmentosa
Wiskott-Aldrich syndrome

The following diseases have varying patterns of inheritance, with the majority being in an X-linked recessive fashion:

Chronic granulomatous disease (in > 70%)

Question 250 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR2?

- A. Haemochromatosis
- B. Type 1 diabetes mellitus
- C. Goodpasture's syndrome
- D. Behcet's disease
- E. Coeliac disease

Question 250 of 331

Which one of the following diseases is most strongly associated with HLA antigen DR2?

- A. Haemochromatosis
- B. Type 1 diabetes mellitus
- ✓ C. Goodpasture's syndrome
- D. Behcet's disease
- E. Coeliac disease

HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

HLA-A3
- haemochromatosis

HLA-B5
- Behcet's disease

HLA-B27
- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DR2
- narcolepsy
- Goodpasture's

HLA-DR3
- coeliac disease
- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4
- type 1 diabetes mellitus*
- rheumatoid arthritis

*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Question 251 of 331

Each one of the following causes of hyponatraemia is associated with a urinary sodium of less than 20 mmol/L, except:

A. Diarrhoea

B. Psychogenic polydipsia

C. Burns

D. Secondary hyperaldosteronism

E. Syndrome of inappropriate ADH

Question 251 of 331

Each one of the following causes of hyponatraemia is associated with a urinary sodium of less than 20 mmol/L, except:

- A. Diarrhoea
- B. Psychogenic polydipsia
- C. Burns
- D. Secondary hyperaldosteronism
- ✓ E. Syndrome of inappropriate ADH

Syndrome of inappropriate ADH is associated with urinary sodium > 20 mmol/l

Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolarity levels aid making a diagnosis

Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)
- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic
- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss
- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)
- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Question 252 of 331

Each one of the following is seen in Wiskott-Aldrich syndrome, except:

- A. Thrombocytopenia
- B. Recurrent chest infections
- C. X-linked recessive inheritance
- D. Mutation in the WASP gene
- E. Psoriasis

Question 252 of 331

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- A. Thrombocytopenia
- B. Recurrent chest infections
- C. X-linked recessive inheritance
- D. Mutation in the WASP gene
- ✓ E. Psoriasis

Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene.

Features
- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia

Question 253 of 331

A 68-year-old man is admitted with haematemesis. A gastroscopy performed as an inpatient shows a carcinoma which is confirmed on biopsy. Who is the most appropriate person to inform the patient of the diagnosis?

- A. The F2 doctor on the ward who has most contact with the patient
- B. The doctor who performed the gastroscopy
- C. His GP following discharge
- D. The consultant in-charge of his care
- E. His next-of-kin after you have told him/her

Question 253 of 331

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- ✓ D. The consultant in-charge of his care
- E. His next-of-kin after you have told him/her

One of the key aims of the entrance exam is to assess a doctors ability to act in a compassionate and empathetic way. Many of you may recall incidences of patients being told about a cancer diagnosis in inappropriate circumstances.

The most appropriate person to inform the patient is the consultant in this scenario. He/she is currently in charge of their care and will be best placed to answer questions about management and prognosis. The F2 doctor will be less able to do this but will at least be known to the patient.

The doctor who performed the gastroscopy is unlikely to know the patient apart from their brief meeting prior to the procedure. Asking the GP to tell the patient is a 'cop-out' on a number of levels. Firstly the patient may feel that the hospital team 'could not be bothered' to tell him themselves. Secondly it results in an unnecessary delay and thirdly the GP may not be best placed to give information on management and prognosis.

Telling the next-of-kin is the worst option as it breaks confidentiality.

Question 254 of 331

Which one of the following statements regarding the use of the p-value in statistical hypothesis testing is correct?

A. The p-value is the probability that the null hypothesis is true

B. 1 - (p-value) is the probability of the alternative hypothesis being true

C. The null hypothesis is rejected if the p-value is smaller than or equal to the significance level

D. The p-value is the probability that a replicating experiment would not yield the same conclusion

E. The p-value is the probability of falsely rejecting the null hypothesis

Question 254 of 331

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- E. The p-value is the probability of falsely rejecting the null hypothesis

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example

- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 255 of 331

Which one of the following processes is responsible for ketone production during diabetic ketoacidosis?

- A. Glycogenolysis
- B. Exchange with hydrogen ions in the collecting ducts
- C. Gluconeogenesis
- D. Decreased plasma bicarbonate levels
- E. Lipolysis

Question 255 of 331

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B. Exchange with hydrogen ions in the collecting ducts

C. Gluconeogenesis

D. Decreased plasma bicarbonate levels

✓ E. Lipolysis

The low-insulin conditions seen in diabetic ketoacidosis stimulate the process of lipolysis and the production of the ketone bodies, beta-hydroxybutyrate and acetoacetate, which can be used as metabolic fuel.

Diabetic ketoacidosis

The most common precipitating factors of diabetic ketoacidosis (DKA) are infection, missed insulin doses and myocardial infarction

American Diabetes Association diagnostic criteria are as follows:

- blood glucose >13.8 mmol/l
- pH < 7.30
- serum bicarbonate <18 mmol/l
- anion gap > 10
- ketonaemia

Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially
- insulin: an intravenous infusion should be started at 6u/hour. Once blood glucose is < 15 mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

Complications of DKA and its treatment

- gastric stasis
- cerebral oedema
- thromboembolism
- acute respiratory distress syndrome
- acute renal failure

Question 256 of 331

Which one of the following statements regarding hypocalcaemia is incorrect?

- A. Most features are a result of neuromuscular excitability
- B. Chronic hypocalcaemia may cause cataracts
- C. Perioral paraesthesia is seen
- D. Chvostek's sign is more sensitive and specific than Trousseau's sign
- E. Prolonged QT interval is seen

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Hypocalcaemia: Trousseau's sign is more sensitive and specific than Chvostek's sign

Hypocalcaemia: features

As extracellular calcium concentrations are important for muscle and nerve function many of the features seen in hypocalcaemia seen a result of neuromuscular excitability

Features
- tetany: muscle twitching and spasm
- perioral paraesthesia
- if chronic: depression, cataracts
- ECG: prolonged QT interval

Trousseau's sign
- carpal spasm if the brachial artery occluded by inflating the blood pressure cuff and maintaining pressure above systolic
- wrist flexion and fingers drawn together
- seen in around 95% of patients with hypocalcaemia and around 1% of normocalcaemic people

Chvostek's sign
- tapping over parotid causes facial muscles to twitch
- seen in around 70% of patients with hypocalcaemia and around 10% of normocalcaemic people

Question 257 of 331

Which one of the following is the most common genetic cause of Prader-Willi syndrome?

- A. Microdeletion of the paternal 15q11-13
- B. Maternal uniparental disomy of chromosome 15
- C. Paternal uniparental disomy of chromosome 15
- D. Microdeletion of the maternal 15q11-13
- E. Trisomy 18

Question 257 of 331

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- E. Trisomy 18

Prader-Willi syndrome

Prader-Willi syndrome is an example of genetic imprinting where the phenotype depends on whether the deletion occurs on a gene inherited from the mother or father:

- Prader-Willi syndrome if gene deleted from father
- Angelman syndrome if gene deleted from mother

Prader-Willi syndrome is associated with the absence of the active Prader-Willi gene on the long arm of chromosome 15. This may be due to:

- microdeletion of paternal 15q11-13 (70% of cases)
- maternal uniparental disomy of chromosome 15

Features

- hypotonia during infancy
- dysmorphic features
- short stature
- hypogonadism and infertility
- learning difficulties
- childhood obesity
- behavioural problems in adolescence

Question 258 of 331

You are a ST1 doctor in general medicine. A 19-year-old female who has type 1 diabetes mellitus is admitted with her fourth episode of diabetic ketoacidosis in the past two months. You suspect she runs her sugars high to keep her weight down. She is generally non-compliant and often self-discharges after 24 hours. What is the most appropriate response?

- A. Take her on a tour of the ward showing her patients with amputated legs or those on dialysis as an incentive to get better control
- B. Have a chat after the ward round about why she thinks her control is so bad
- C. Write a letter to her GP advising him/her of your concerns
- D. Take no action as it is her decision whether she takes her medication or complies with treatment
- E. Tell her she is wasting NHS resources and you do not want to see her turn up at your hospital again

Question 258 of 331

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- E. Tell her she is wasting NHS resources and you do not want to see her turn up at your hospital again

Managing young diabetic patients may be frustrating but needs to be approached in an empathetic manner. Taking time to explore why her control is so bad is the best response in this scenario. The GP should hopefully have a long term relationship with the patient and may be in a position to address these problems.

Taking no action ignores the problem. Trying to scare her by showing her patients with complications is a poor option not least because it fails to respect the privacy of the other patients.

Telling her she is wasting NHS resources is uncaring and unprofessional. Telling her not to turn up at hospital again is indefensible from an ethical and medicolegal perspective.

Question 259 of 331

Which of the following is true regarding endothelin?

- A. It is a potent vasodilator
- B. It is produced mainly by pulmonary tissue
- C. It acts on target cells by stimulating guanylate cyclase
- D. Release is stimulated by nitric oxide
- E. Endothelin antagonists are useful in primary pulmonary hypertension

Question 259 of 331

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Endothelin

Endothelin is a potent, long-acting vasoconstrictor and bronchoconstrictor. It is secreted initially as a prohormone by the vascular endothelium and later converted to ET-1 by the action of endothelin converting enzyme. It acts via interaction with a G-protein linked to phospholipase C leading to calcium release. Endothelin is thought to be important in the pathogenesis of many diseases including primary pulmonary hypertension (endothelin antagonists are now used), cardiac failure, hepatorenal syndrome and Raynaud's

Promotes release
- angiotensin II
- ADH
- hypoxia
- mechanical shearing forces

Inhibits release
- nitric oxide
- prostacyclin

Raised levels in
- MI
- heart failure
- ARF
- asthma
- primary pulmonary hypertension

Question 260 of 331

Which of the following statements is true regarding X-linked recessive inheritance?

- A. A female child of a heterozygous female carrier has a 50% chance of being a carrier
- B. An example is Friedreich's ataxia
- C. 50% of the male offspring of affected males will manifest the disease
- D. An affected child's uncle on the paternal side may also manifest the disease
- E. 50% of the female offspring of affected males will be carriers

Question 260 of 331

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- E. 50% of the female offspring of affected males will be carriers

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 261 of 331

What is the role of troponin in cardiac muscle?

- A. Component of the thick filaments
- B. Acts as a lining of the T tubules
- C. Anchors thick filament to Z-discs
- D. Component of the thin filaments
- E. Anchors thick and thin filaments together

Question 261 of 331

What is the role of troponin in cardiac muscle?

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- C. Anchors thick filament to Z-discs
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- E. Anchors thick and thin filaments together

The other components of thin filaments are actin and tropomyosin. Thick filaments are primarily composed of myosin.

Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superceded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	**Peak value**	**Returns to normal**
Myoglobin	1-2 hours	6-8 hours	1-2 days
CK-MB	2-6 hours	16-20 hours	2-3 days
CK	4-8 hours	16-24 hours	3-4 days
Trop T	4-6 hours	12-24 hours	7-10 days
AST	12-24 hours	36-48 hours	3-4 days
LDH	24-48 hours	72 hours	8-10 days

Question 262 of 331

Each one of the following features is seen in phenylketonuria, except:

- A. Learning difficulties
- B. Seizures
- C. Eczema
- D. Recurrent infections
- E. 'Musty' urine

Question 262 of 331

Each one of the following features is seen in phenylketonuria, except:

- A. Learning difficulties
- B. Seizures
- C. Eczema
- ✓ D. Recurrent infections
- E. 'Musty' urine

Phenylketonuria

Phenylketonuria (PKU) is an autosomal recessive condition caused by a disorder of phenylalanine metabolism. This is due to defect in phenylalanine hydroxylase, an enzyme which converts phenylalanine to tyrosine. High levels of phenylalanine lead to problems such as learning difficulties and seizures. The gene for phenylalanine hydroxylase is located on chromosome 12.

The incidence of PKU is c. 1 in 10,000 live births

Features
- usually presents by 6 months e.g. with developmental delay
- child classically has fair hair and blue eyes
- learning difficulties
- seizures, typically infantile spasms
- eczema
- 'musty' odour to urine and sweat*

Diagnosis
- Guthrie test: the 'heel-prick' test done at 5-9 days of life - also looks for other biochemical disorders such as hypothyroidism
- hyperphenylalaninaemia
- phenylpyruvic acid in urine

Management
- poor evidence base to suggest strict diet prevents learning disabilities
- dietary restrictions are however important during pregnancy as genetically normal fetuses may be affected by high maternal phenylalanine levels

*secondary to phenylacetate, a phenylketone

Question 263 of 331

Which one of the following statements concerning altitude related disorders is true?

- A. Symptoms typically start to develop above 1,500m
- B. Physical fitness protects against altitude related disorders
- C. High altitude pulmonary oedema should be treated with frusemide first-line
- D. Acute mountain sickness is generally a self-limiting condition
- E. Symptoms of acute mountain sickness develop within 4 hours of gaining altitude

Question 263 of 331

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Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

Management of HACE

- descent
- dexamethasone

Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors*
- oxygen if available

*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

Question 264 of 331

Which one of the following significance tests is used to analyse data which is measured and follows a normal distribution?

- A. Chi-squared test
- B. Spearman's rank correlation coefficient
- C. Wilcoxon matched-pairs
- D. Mann-Whitney test
- E. Student's t-test

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- C. Wilcoxon matched-pairs
- D. Mann-Whitney test
- ✓ E. Student's t-test

Student's t-test is used to analyse parametric data. The other tests are used on non-parametric data

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 265 of 331

A 54-year-old woman is admitted to the Medical Admissions Unit following a collapse. Bloods taken on admission show the following:

Magnesium 0.40 mmol/l

Which one of the following factors is most likely to be responsible for this result?

- A. Excessive resuscitation with intravenous saline
- B. Frusemide therapy
- C. Digoxin therapy
- D. Rhabdomyolysis
- E. Hypothermia

Question 265 of 331

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- C. Digoxin therapy
- D. Rhabdomyolysis
- E. Hypothermia

Hypomagnesaemia

Cause of low magnesium
- diuretics
- total parenteral nutrition
- diarrhoea
- alcohol
- hypokalaemia, hypocalcaemia

Features
- paraesthesia
- tetany
- seizures
- arrhythmias
- decreased PTH secretion --> hypocalcaemia
- ECG features similar to those of hypokalaemia
- exacerbates digoxin toxicity

Question 266 of 331

A 33-year-old pregnant woman presents for advice. She is known to have polycystic kidney disease but is currently well. Her father also has polycystic kidneys and is on dialysis . What is the chance her child will also have the disease?

- A. 50% if male
- B. 50%
- C. 25%
- D. 0%
- E. 100%

Question 266 of 331

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- A. 50% if male
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- C. 25%
- D. 0%
- E. 100%

Polycystic kidney disease is usually inherited in an autosomal dominant fashion and hence 50% of her children will be affected, regardless of gender. The autosomal recessive form is rare and usually causes death in childhood.

ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	**ADPKD type 2**
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Question 267 of 331

Which of the following statements is true regarding the standard polymerase chain reaction (PCR)?

- A. Restriction endonuclease enzymes are applied to DNA fragments prior to electrophoresis
- B. PCR use is limited by its relatively low sensitivity
- C. A thermostable DNA polymerase is required
- D. PCR is currently limited to prenatal diagnosis and forensics
- E. A single DNA oligonucleotide primer is necessary

Question 267 of 331

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PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep
- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place
- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR
- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

Question 268 of 331

A study looks at adding a new antiplatelet drug in addition to aspirin to patients who've had a stroke. One hundred and seventy patients are enrolled for the study with 120 receiving the new drug in addition to aspirin and the remainder receiving just aspirin. After 5 years 18 people who received the new drug had a further stroke compared to 10 people who just received aspirin. What is the number needed to treat?

- A. 8
- B. 15
- C. 1.8
- D. 20
- E. 10

Question 268 of 331

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- C. 1.8
- ✓ D. 20
- E. 10

NNT = 1 / (EER - CER), or 1 / Absolute Risk Reduction

Experimental event rate = 18 / 120 = 0.15
Control event rate = 10 / 50 = 0.2

Absolute risk reduction = 0.15 - 0.2 = -0.05
Number needed to treat = 1 / 0.05 = 20

Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by 1/(Absolute risk reduction) and is rounded to the next highest whole number

where

Absolute risk reduction = (Experimental event rate) - (Control event rate)

where

Experimental event rate = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate = (Number who had particular outcome with the control/ (Total number who had the control)

Question 269 of 331

A patient who takes bendroflumethiazide is noted to have a potassium of 3.1 mmol/l. What is the main mechanism causing hypokalaemia in patients taking bendroflumethiazide?

- A. Decreased flow rate in the nephron resulting in a decreased potassium gradient
- B. Increased sodium reaching the collecting ducts
- C. Inhibition of renin-angiotensin-aldosterone system secondary to hypovolaemia
- D. Decreased sodium reaching the distal convoluted tubule
- E. Opening of potassium channel in proximal convoluted tubule

Question 269 of 331

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Bendroflumethiazide - mechanism of hypokalaemia:
- increased sodium reaching the collecting ducts
- activation of the renin-angiotensin-aldosterone

Increased delivery of sodium to the collecting ducts causes the sodium-potassium exchanger to release more potassium into the urine. Another cause is activation of the renin-angiotensin-aldosterone system secondary to hypovolaemia

Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide currently is in hypertension (part of the effect is due to vasodilation)

Common adverse effects
- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects
- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

Question 270 of 331

A new blood test is developed to screen for prostate cancer. Trials have shown it has a sensitivity for detecting clinically significant prostate cancer of 80% but a specificity of 60%. What is the likelihood ratio for a positive test result?

- A. Cannot be calculated
- B. 2
- C. 4
- D. 0.8
- E. 0.2

Question 270 of 331

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Likelihood ratio for a positive test result = sensitivity / (1 - specificity)

Likelihood ratio for a positive test result = sensitivity / (1 - specificity) = 0.8 / (1 - 0.6) = 2

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 271 of 331

Why do patients with chronic kidney disease have a raised phosphate level?

- A. Decreased renal excretion
- B. Increased gut absorption
- C. Hypervitaminosis D
- D. Primary hyperparathyroidism
- E. Decreased 25-alpha hydroxylation of vitamin D

Question 271 of 331

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B. Increased gut absorption

C. Hypervitaminosis D

D. Primary hyperparathyroidism

E. Decreased 25-alpha hydroxylation of vitamin D

Chronic kidney disease: bone disease

Basic problems in chronic kidney disease
- low vitamin D (1-alpha hydroxylation normally occurs in the kidneys)
- high phosphate
- low calcium: due to lack of vitamin D, high phosphate
- secondary hyperparathyroidism: due to low calcium, high phosphate and low vitamin D

Several clinical manifestations may result:

Osteitis fibrosa cystica
- aka hyperparathyroid bone disease

Adynamic
- reduction in cellular activity (both osteoblasts and osteoclasts) in bone
- may be due to over treatment with vitamin D

Osteomalacia
- due to low vitamin D

Osteosclerosis

Osteoporosis

Question 272 of 331

A middle-aged man is diagnosed with nasopharyngeal carcinoma. What type of virus family is associated with this malignancy?

- A. Reovirus
- B. Herpesvirus
- C. Parvovirus
- D. Adenovirus
- E. Hepadnaviridae

Question 272 of 331

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The Epstein-Barr virus is one of the herpes viruses.

Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection
- Burkitt's lymphoma*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also assocaiated with EBV infection.

*EBV is currently thought to be associated with both African and sporadic Burkitt's

Question 273 of 331

A study is performed to find the normal reference range for IgE levels in adults. Assuming IgE levels follow a normal distribution, what percentage of adults will have an IgE level above 2 standard deviations from the mean?

- A. 1.25%
- B. 2.3%
- C. 1.96%
- D. 5%
- E. 0.5%

Question 273 of 331

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- A. 1.25%
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- C. 1.96%
- D. 5%
- E. 0.5%

For normally distributed data 95.4% of values lie within 2 standard deviations of the mean, leaving 4.6% outside this range. Therefore 2.3% of values will be higher and 2.3% will be lower than 2 standard deviations from the mean. This figure is sometimes approximated to 2.5%

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 274 of 331

Which one of the following features is not associated with Turner's syndrome?

- A. Short stature
- B. High-arched palate
- C. Coarctation of the aorta
- D. Webbed neck
- E. Secondary amenorrhoea

Question 274 of 331

Which one of the following features is not associated with Turner's syndrome?

- A. Short stature
- B. High-arched palate
- C. Coarctation of the aorta
- D. Webbed neck
- ✓ E. Secondary amenorrhoea

Primary, not secondary, amenorrhoea is seen in Turner's syndrome

Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 275 of 331

Which one of the following is least associated with homocystinuria?

- A. Recurrent renal stones
- B. Downwards lens dislocation
- C. Deep vein thrombosis
- D. Arachnodactyly
- E. Learning difficulties

Question 275 of 331

Which one of the following is least associated with homocystinuria?

- ✓ A. Recurrent renal stones
- B. Downwards lens dislocation
- C. Deep vein thrombosis
- D. Arachnodactyly
- E. Learning difficulties

Cystinuria not homocystinuria is associated with recurrent renal stones

Homocystinuria

Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathione beta-synthetase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

Features

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria

Treatment is vitamin B6 supplements

Question 276 of 331

A 61-year-old female who has recently emigrated from the Indian subcontinent presents with muscle weakness. Bloods reveal a low serum calcium. A diagnosis of osteomalacia is suspected. Which one of the following, per average serving, provides the best source of vitamin D?

- A. Lentils
- B. Sunflower seeds
- C. Salmon
- D. Cod liver oil
- E. Milk

Question 276 of 331

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- C. Salmon
- ✓ D. Cod liver oil
- E. Milk

Cod liver oil provides around 1,300 IU per 15 ml serving

Vitamin deficiency

The table below summarises vitamin deficiency states

Vitamin	Chemical name	Deficiency state
A	Retinoids	Night-blindness (nyctalopia)
B1	Thiamine	Beriberi • polyneuropathy, Wernicke-Korsakoff syndrome • heart failure
B3	Niacin	Pellagra • dermatitis • diarrhoea • dementia
B6	Pyridoxine	Anaemia, irritability, seizures
B7	Biotin	Dermatitis, seborrhoea
B9	Folic acid	Megaloblastic anaemia, deficiency during pregnancy - neural tube defects
B12	Cyanocobalamin	Megaloblastic anaemia
C	Ascorbic acid	Scurvy • gingivitis • bleeding
D	Ergocalciferol, cholecalciferol	Rickets, osteomalacia
E	Tocopherol, tocotrienol	Mild haemolytic anaemia in newborn infants, ataxia, peripheral neuropathy
K	Naphthoquinone	Haemorrhagic disease of the newborn, bleeding diathesis

Question 277 of 331

Which one of the following genetic conditions is the most prevalent in a Caucasian population?

- A. Wilson's disease
- B. Sickle cell anaemia
- C. Cystic fibrosis
- D. Alpha-1 antitrypsin
- E. Haemochromatosis

Question 277 of 331

Which one of the following genetic conditions is the most prevalent in a Caucasian population?

- A. Wilson's disease
- B. Sickle cell anaemia
- C. Cystic fibrosis
- D. Alpha-1 antitrypsin
- ✓ E. Haemochromatosis

Haemochromatosis is more common than cystic fibrosis

Haemochromatosis is an autosomal recessive disorder with a carrier rate of 1 in 10 and is present in about 1 in 200-400 people. Cystic fibrosis (CF) has a carrier rate of 1 in 25 and is present in about 1 in 2,500 births. CF is often quoted as being the most common lethal inherited condition in Caucasians

Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene
**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 278 of 331

A new biochemical marker has been found which is increased in mothers who are carrying fetuses with Down's syndrome. The new blood test is trialled in 1,000 women over the age of 35 years. Of these women 20 were found to be carrying a fetus with Down's syndrome as assessed using standard measures. The new test was positive in 15 of the 20 cases but was also positive in 30 of the remaining 980 women. What is the positive predictive value of the test?

- A. 0.66
- B. 950/980
- C. 0.33
- D. 0.8
- E. 0.5

Question 278 of 331

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- A. 0.66
- B. 950/980
- ✓ C. 0.33
- D. 0.8
- E. 0.5

A contingency table can be constructed from the above data, as shown below:

	Down's	**Not Down's**
Test positive	15	30
Test negative	5	950

Positive predictive value = TP / (TP + FP) = 15 / (15 + 30) = 0.33

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

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	Disease present	**Disease absent**
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Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 279 of 331

Of the following scenarios, which one would indicate it was inappropriate for the patient to take an airline flight?

- A. A 54-year-old woman who had a laparoscopic cholecystectomy 5 days ago
- B. A 17-year-old flying back to the UK who broke his leg whilst skiing in Canada. Had a plaster cast applied 24 hours ago
- C. A 59-year-old man who had a colonoscopy 2 days ago
- D. A 62-year-old man who had an uncomplicated myocardial infarction 3 weeks ago
- E. A woman who is 27-weeks pregnant with twins

Question 279 of 331

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Following the application of a plaster cast patients should wait 24 hours before short flights (< 2 hours) and 48 hours before longer flights. This is due to the fact that air may be trapped beneath the cast

Fitness to fly

The Civil Aviation Authority (CAA) has issued guidelines on air travel for people with medical conditions; please see the link provided.

Cardiovascular disease
- unstable angina, uncontrolled hypertension, uncontrolled cardiac arrhythmia, decompensated heart failure, severe symptomatic valvular disease: should not fly
- uncomplicated myocardial infarction: may fly after 7-10 days
- complicated myocardial infarction: after 4-6 weeks
- coronary artery bypass graft: after 10-14 days
- percutaneous coronary intervention: after 5 days

Respiratory disease
- pneumonia: should be 'clinically improved with no residual infection'
- pneumothorax: absolute contraindication, the CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air. The British Thoracic Society used to recommend not travelling by air for a period of 6 weeks but this has now been changed to 1 week post check x-ray

Pregnancy
- most airlines do not allow travel after 36 weeks for a single pregnancy and after 32 weeks for a multiple pregnancy
- most airlines require a certificate after 28 weeks confirming that the pregnancy is progressing normally

Surgery
- travel should be avoided for 10 days following abdominal surgery
- laparoscopic surgery: after 24 hours
- colonoscopy: after 24 hours
- following the application of a plaster cast, the majority of airlines restrict flying for 24 hours on flights of less than 2 hours or 48 hours for longer flights

Haematological disorders
- patients with a haemoglobin of greater than 8 g/dl may travel without problems

Question 280 of 331

A 79-year-old complains of lower urinary tract symptoms. Which one of the following statements regarding benign prostatic hyperplasia is incorrect?

- A. Goserelin is licensed for refractory cases
- B. Side-effects of 5 alpha-reductase inhibitors include ejaculation disorders and gynaecomastia
- C. Possible presentations include recurrent urinary tract infection
- D. 5 alpha-reductase inhibitors typically decrease the prostate specific antigen level
- E. More common in black men

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- E. More common in black men

Goserelin (Zoladex) is not used in the management of benign prostatic hyperplasia

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

Risk factors
- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:
- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

Management options
- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin
- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride
- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

Question 281 of 331

Which one of the following best describes the Haldane effect?

- A. Increase in pO2 means CO2 binds less well to Hb
- B. Increasing acidity (or pCO2) means oxygen binds less well to Hb
- C. Decreasing acidity (or pCO2) means oxygen binds less well to Hb
- D. Raised 2,3-DPG enhances oxygen delivery to the tissues
- E. Decrease in pO2 means CO2 binds less well to Hb

Question 281 of 331

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Respiratory physiology

Chloride shift
- CO2 diffuses into RBCs
- CO2 + H20 ---- carbonic anhydrase ---> HCO3- + H+
- H+ combines with Hb
- HCO3- diffuses out of cell,- Cl- replaces it

Bohr effect
- increasing acidity (or pCO2) means O2 binds less well to Hb

Haldane effect
- increase pO2 means CO2 binds less well to Hb

Question 282 of 331

You are a ST1 doctor on a medical ward. It is 5:15pm and you were scheduled to finish your day 15 minutes ago. Today you're particularly keen to leave as it is your wife's birthday and you've arranged a night out. One of the staff nurses bleeps you as Mr Jones, one of your patients, has become drowsy. He was admitted two days ago to your ward with an exacerbation of COPD. What is the most appropriate course of action?

- A. Bleep the on-call doctor yourself and ask him to review
- B. Tell her to try decreasing his oxygen to 24% and see how he is in 30 minutes
- C. Tell the nurse to bleep the on-call doctor
- D. Tell the nurse to bleep the on-call doctor + fill in a clinical incident form as you bleeped after hours
- E. Go and assess the patient yourself

Question 282 of 331

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- D. Tell the nurse to bleep the on-call doctor + fill in a clinical incident form as you bleeped after hours
- ✓ E. Go and assess the patient yourself

This question is mainly about professionalism and 'putting the patient first'.

The most appropriate response is to go and assess the patient yourself. You are most likely to know their history and it is possible that the on-call doctor will be delayed in reaching the ward due to other patients. The next best option is to bleep the on-call doctor yourself. This allows for a proper hand-over, which would not happen if you asked the nurse to bleep the on-call doctor.

Filling in a clinical incident form as you were bleeped after hours is not appropriate.

The worst response would be to ask the nurse to instigate medical treatment without first assessing the patient. This is clearly dangerous.

Question 283 of 331

Where is B-type natriuretic peptide mainly secreted from?

- A. Atrial myocardium
- B. Juxtaglomerular cells
- C. Zona glomerulosa
- D. Ventricular myocardium
- E. Hypothalamus

Question 283 of 331

Where is B-type natriuretic peptide mainly secreted from?

- A. Atrial myocardium
- B. Juxtaglomerular cells
- C. Zona glomerulosa
- ✓ D. Ventricular myocardium
- E. Hypothalamus

B-type natriuretic peptide is mainly secreted by the ventricular myocardium

B-type natriuretic peptide

B-type natriuretic peptide (BNP) hormone produced mainly by the left ventricular myocardium in response to strain

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

Clinical uses of BNP

Diagnosing patients with acute dyspnoea
- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

Prognosis in patients with chronic heart failure
- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure
- effective treatment lowers BNP levels

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 284 of 331

Looser’s zones x-ray are most characteristically associated with which one of the following conditions?

- A. Primary hyperparathyroidism
- B. Hypoparathyroidism
- C. Osteomalacia
- D. Paget's disease
- E. Osteoporosis

Question 284 of 331

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Osteomalacia

Basics
- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

Types
- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis

Features
- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

Investigation
- low Ca2+, PO34-, 25(OH) vitamin D
- raised ALP
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser's zones or pseudofractures)

Treatment
- calcium with vitamin D tablets

Question 285 of 331

Which one of the following statements regarding galactosaemia is incorrect?

- A. Autosomal recessive inheritance
- B. May cause cataracts
- C. Caused by the absence of galactose-1-phosphate uridyl transferase
- D. May cause jaundice
- E. May cause peripheral neuropathy

Question 285 of 331

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- D. May cause jaundice
- ✓ E. May cause peripheral neuropathy

Galactosaemia

Galactosaemia is a rare autosomal recessive condition caused by the absence of galactose-1-phosphate uridyl transferase. This results in intracellular accumulation of galactose-1-phosphate

Features
- jaundice
- failure to thrive
- hepatomegaly
- cataracts
- hypoglycaemia after exposure to galactose
- Fanconi syndrome

Diagnosis
- urine reducing substances

Management is with a galactose free diet

Question 286 of 331

Which one of the following statements regarding vitamin D-resistant rickets is false?

- A. Management includes the use of high-dose vitamin D supplements
- B. Is a X-linked dominant condition
- C. X-ray changes include cupped metaphyses
- D. Failure to thrive may be seen
- E. Decreased urinary phosphate is characteristic

Question 286 of 331

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- D. Failure to thrive may be seen
- ✓ E. Decreased urinary phosphate is characteristic

Vitamin D-resistant rickets

Vitamin D-resistant rickets is a X-linked dominant condition which usually presents in infancy with failure to thrive. It is caused by impaired phosphate reabsorption in the renal tubules

Features
- failure to thrive
- normal serum calcium, low phosphate, elevated alkaline phosphotase
- x-ray changes: cupped metaphyses with widening of the epiphyses

Diagnosis is made by demonstrating increased urinary phosphate

Management
- high-dose vitamin D supplements
- oral phosphate supplements

Question 287 of 331

Which one of the following statements is true regarding monoclonal antibodies?

- A. They are produced by the polymerase chain reaction
- B. Infliximab is useful in chronic lymphocytic leukaemia
- C. A hybridoma is a combination of human spleen cells and mouse B-cells
- D. The constant region of the antibody is human in origin
- E. Alemtuzumab is used in the prevention of ischaemic events in patients undergoing percutaneous coronary interventions

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Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from an human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

Question 288 of 331

A 52-year-old obese lady with type 2 diabetes mellitus is interested in changing her diet. Which one of the following foods has the highest glycaemic index?

- A. Baked potato
- B. Apple
- C. Peanut
- D. Digestive biscuit
- E. Brown rice

Question 288 of 331

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- E. Brown rice

Whilst white rice has a glycaemic index of 87 brown rice has a much lower value of 58

Glycaemic index

The glycaemic index (GI) describes the capacity of a food to raise blood glucose compared glucose in normal glucose-tolerant individuals. Foods with a high GI may be associated with an increased risk of obesity and the post-prandial hyperglycaemia associated with such foods may also increase the risk of type 2 diabetes mellitus

High GI	White rice (87), baked potato (85), white bread (70)
Medium GI	Couscous (65), boiled new potato (62), digestive biscuit (59), brown rice (58)
Low GI	Fruit and vegetables, peanuts

The glycaemic index is shown in brackets. Glucose, by definition, would have a glycaemic index of 100

Question 289 of 331

Patients with deficiencies of which one of the following complement protein(s) are predisposed to immune complex diseases?

- A. C1-INH
- B. C1q, C1rs, C2, C4
- C. C5-9
- D. C3
- E. C3bBb

Question 289 of 331

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- C. C5-9
- D. C3
- E. C3bBb

Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency
- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 290 of 331

Which one of the following is not a risk factor for the development of pre-eclampsia?

- A. Previous history of pre-eclampsia
- B. Body mass index of 34 kg/m^2
- C. Age of 42 years
- D. Multiple pregnancy
- E. Multiparity

Question 290 of 331

Which one of the following is not a risk factor for the development of pre-eclampsia?

- A. Previous history of pre-eclampsia
- B. Body mass index of 34 kg/m^2
- C. Age of 42 years
- D. Multiple pregnancy
- ✓ E. Multiparity

No previous pregnancies is a risk factor for pre-eclampsia. Questions on maternal health during pregnancy are now common in the MRCP

Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m^2
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count < 100 * 10^6/l, abnormal liver enzymes or HELLP syndrome

Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral methyldopa is often used first-line with oral labetalol, nifedipine and hydralazine also being used
- for severe hypertension IV labetalol and IV hydralazine are used in addition to the above
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Question 291 of 331

A study compares the sensitivity of two tests for colorectal cancer. The first test has a sensitivity of 85% whilst the second test has a sensitivity of 91%. What type of significance test should be used for comparing the two results?

- A. Wilcoxon matched-pairs
- B. Mann-Whitney test
- C. Student's t-test
- D. Chi-squared test
- E. Pearson's test

Question 291 of 331

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As percentages are being compared the chi-squared test should be used

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 292 of 331

Which one of the following types of immunoglobulins are responsible for haemolytic blood transfusion reactions?

- A. IgD
- B. IgE
- C. IgM
- D. IgA
- E. IgG

Question 292 of 331

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Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

IgG	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
IgA	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
IgM	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
IgD	1%	Monomer	Involved in activation of B cells
IgE	0.1%	Monomer	Involved in allergic reactions

Question 293 of 331

Which of the following physiological effects would be expected following administration of atropine?

- A. Bradycardia + mydriasis
- B. Tachycardia + miosis
- C. Bradycardia + salivation
- D. Bradycardia + miosis
- E. Tachycardia + mydriasis

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Atropine

Atropine is an antagonist of the muscarinic acetylcholine receptor

Uses
- resuscitation
- treatment of organophosphate poisoning

Physiological effects
- tachycardia
- mydriasis

Question 294 of 331

A nurse who is known to have an allergy to latex develops a widespread urticarial rash and facial oedema shortly after eating lunch. Which food is she most likely to have consumed?

- A. Orange
- B. Apple
- C. Grapes
- D. Pear
- E. Banana

Question 294 of 331

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- A. Orange
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- C. Grapes
- D. Pear
- ✓ E. Banana

The nurse is likely to suffer from latex-fruit syndrome.

Latex allergy

Sensitivity to latex may cause a number of problems:

- type I hypersensitivity (anaphylaxis)
- type IV hypersensitivity (allergic contact dermatitis)
- irritant contact dermatitis

Latex allergy is more common in children with myelomeningocele spina bifida.

Latex-fruit syndrome

It is recognised that many people who are allergic to latex are also allergic to fruits, particularly banana, pineapple, avocado, chestnut, kiwi fruit, mango, passionfruit and strawberry.

Question 295 of 331

A study looks at whether a new oral treatment for patients with heart failure can prevent hospital admissions. When reviewing the data how should it be decided if the test was statistically significant?

- A. p-value < 2 standard deviates from mean
- B. p-value < (1 - type II error)
- C. p-value < significance level
- D. p-value < power
- E. p-value < 0.05

Question 295 of 331

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The significance level of a test is defined as the probability of rejecting the null hypothesis when the null hypothesis is actually true (a Type I error). It is often represented by the Greek symbol alpha.

A study is only statistically significant if the p-value reaches the significance level set before the study is started. Popular levels of significance are 5% (0.05), 1% (0.01) and 0.1% (0.001).

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example

- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 296 of 331

A 68-year-old woman presents with lethargy and generalised aches. As part of a blood screen the following results are obtained:

Calcium 2.83 mmol/l

Albumin 42 g/l

ESR 26 mm/hr

What is the most likely cause of these blood results?

- A. Multiple myeloma
- B. Sarcoidosis
- C. Normal
- D. Breast cancer metastases
- E. Primary hyperparathyroidism

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This question tests whether you have an understanding of the incidence of common disorders. All of the above may cause hypercalcaemia but cancer and primary hyperparathyroidism are the most common causes in this age group. A normal ESR (given her age) points towards a diagnosis of primary hyperparathyroidism.

Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, Ca2+ containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

*other causes of granulomas may lead to hypercalcaemia e.g. tuberculosis and histoplasmosis

**usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 297 of 331

Which one of the following techniques would be most suitable to detect and quantify a viral protein?

- A. Polymerase chain reaction
- B. Northern blotting
- C. Western blotting
- D. Southern blotting
- E. Eastern blotting

Question 297 of 331

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Molecular biology techniques
- SNOW (**S**outh - **NO**rth - **W**est)
- DROP (**D**NA - **R**NA - **P**rotein)

Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Question 298 of 331

Which one of the following immunoglobulins is involved in the activation of B-cells?

- A. IgD
- B. IgM
- C. IgE
- D. IgG
- E. IgA

Question 298 of 331

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IgD is involved in the activation of B-cells

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The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

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Question 299 of 331

Which one of the following statements is true regarding cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA)?

A. Targeted against myeloperoxidase

B. Associated with Wegener's granulomatosis

C. Can be used to monitor activity in autoimmune haemolytic anaemia

D. Is more commonly seen in ulcerative colitis than perinuclear ANCA

E. Positive in > 90% of hepatitis C associated vasculitis

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- D. Is more commonly seen in ulcerative colitis than perinuclear ANCA
- E. Positive in > 90% of hepatitis C associated vasculitis

cANCA = Wegener's; pANCA = Churg-Strauss + others

ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:
- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

cANCA
- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

pANCA
- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)
- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

Question 300 of 331

The average weight loss of a patient following a new type of bariatric surgery is 18 kg. The standard deviation of weight loss is 3kg. Assuming the weight loss is normally distributed, what percentage of patients will loss between 9 and 27 kg?

- A. 97.4%
- B. 95%
- C. 95.4%
- D. 68.3%
- E. 99.7%

Question 300 of 331

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- B. 95%
- C. 95.4%
- D. 68.3%
- ✓ E. 99.7%

99.7% of values of a normally distributed variable lie within 3 standard deviations of the mean.

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 301 of 331

Which cell organelle is involved in the synthesis of lipids?

- A. Golgi apparatus
- B. Smooth endoplasmic reticulum
- C. Ribosome
- D. Rough endoplasmic reticulum
- E. Nucleolus

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- D. Rough endoplasmic reticulum
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Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	**Main function**
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Energy production. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide

Question 302 of 331

Where is somatostatin secreted from?

- A. D cells in the pancreas
- B. I cells in upper small intestine
- C. K cells in upper small intestine
- D. S cells in upper small intestine
- E. G cells in stomach

Question 302 of 331

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- B. I cells in upper small intestine
- C. K cells in upper small intestine
- D. S cells in upper small intestine
- E. G cells in stomach

D cells are also found in the stomach and intestine

Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
Gastrin	G cells in antrum of the stomach	Distension of stomach, extrinsic nerves Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
CCK	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
Secretin	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
VIP	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion
Somatostatin	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Question 303 of 331

Pellagra is caused by a deficiency in:

- A. Vitamin B12
- B. Thiamine
- C. Nicotinic acid
- D. Vitamin B2
- E. Vitamin B6

Question 303 of 331

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- ✓ C. Nicotinic acid
- D. Vitamin B2
- E. Vitamin B6

Pellagra

Pellagra is a caused by nicotinic acid (niacin) deficiency. The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin)

Features

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

Question 304 of 331

A 25-year-old woman presents with a symmetrical arthropathy affecting her hands. On examination she has synovitis of the 2nd and 2rd metacarpophalangeal joints. What type of HLA allele is most associated with this condition?

- A. HLA DR3
- B. HLA A3
- C. HLA DR4
- D. HLA DR2
- E. HLA B27

Question 304 of 331

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- A. HLA DR3
- B. HLA A3
- ✓ C. HLA DR4
- D. HLA DR2
- E. HLA B27

Rheumatoid arthritis - HLA DR4

This patient has rheumatoid arthritis.

HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

HLA-A3
- haemochromatosis

HLA-B5
- Behcet's disease

HLA-B27
- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DR2
- narcolepsy
- Goodpasture's

HLA-DR3
- coeliac disease
- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4
- type 1 diabetes mellitus*
- rheumatoid arthritis

*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Question 305 of 331

Which foramen does the oculomotor nerve go through?

- A. Superior orbital fissure
- B. Foramen ovale
- C. Foramen rotundum
- D. Optic canal
- E. Inferior orbital fissure

Question 305 of 331

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Foramina of the skull

Questions asking about foramina of the skull have come up in the exam in previous years. Below is a brief summary of the major foramina, please see the Wikipedia link for a full list.

Foramen	Bone	Vessels	Nerves
Optic canal	Sphenoid	Ophthalmic artery	Optic nerve (II)
Superior orbital fissure	Sphenoid	Superior ophthalmic vein Inferior ophthalmic vein	Oculomotor nerve (III) Trochlear nerve (IV) lacrimal, frontal and nasociliary branches of ophthalmic nerve (V1) Abducent nerve (VI)
Inferior orbital fissure	Sphenoid and maxilla	Inferior ophthalmic veins Infraorbital artery Infraorbital vein	Zygomatic nerve and infraorbital nerve of maxillary nerve (V2) Orbital branches of pterygopalatine ganglion
Foramen rotundum	Sphenoid	-	Maxillary nerve (V2)
Foramen ovale	Sphenoid	Accessory meningeal artery	Mandibular nerve (V3)
Jugular foramen	Occipital and temporal	Posterior meningeal artery Ascending pharyngeal artery Inferior petrosal sinus Sigmoid sinus Internal jugular vein	Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI)

Question 306 of 331

A 23-year-old man is admitted with sepsis. Blood cultures are reported as follows:
Neisseria gonorrhoeae

Which of the following complement proteins is the patient most likely to deficient in?

- A. C1q, C1rs, C2, C4
- B. C3a + C5a
- C. C5-9
- D. C4
- E. C2

Question 306 of 331

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- ✓ C. C5-9
- D. C4
- E. C2

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection and other Gram negative diplococcal infections

Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency
- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 307 of 331

Which one of the following is in direct anatomical contact with the right kidney?

- A. Gallbladder
- B. Liver
- C. Stomach
- D. Distal part of small intestine
- E. Duodenum

Question 307 of 331

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Renal anatomy

The tables below show the anatomical relations of the kidneys:

Right kidney

Direct contact	Layer of peritoneum in-between
Right suprarenal gland Duodenum Colon	Liver Distal part of small intestine

Left kidney

Direct contact	Layer of peritoneum in-between
Left suprarenal gland Pancreas Colon	Stomach Spleen Distal part of small intestine

Question 308 of 331

A small study looks at the weight of patients diagnosed with type 2 diabetes mellitus. Overall 64 patients were reviewed. The average weight was 81 kg, with a standard deviation of 12 kg. What is the standard error of the mean?

- A. Square root (64 / 12)
- B. Square root (81 / 12)
- C. 12 / 9
- D. 9 / 12
- E. 1.5

Question 308 of 331

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- C. 12 / 9
- D. 9 / 12
- ✓ E. 1.5

Standard error of the mean = standard deviation / square root (number of patients)

The standard error of the mean is calculated by the standard deviation / square root (number of patients)= 12 / square root (64) = 12 / 8 = 1.5

Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- SEM = SD / square root (n)
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation i.e. the 95% confidence interval = mean - (1.96 *SEM) to the mean + (1.96 * SEM)

Question 309 of 331

Which one of the following is most commonly secreted by T-helper cells subset 2 (Th2 cells) ?

- A. Interleukin 2
- B. Tumour necrosis factor
- C. Interferon gamma
- D. Interleukin 4
- E. Interleukin 3

Question 309 of 331

Which one of the following is most commonly secreted by T-helper cells subset 2 (Th2 cells) ?

- A. Interleukin 2
- B. Tumour necrosis factor
- C. Interferon gamma
- ✓ D. Interleukin 4
- E. Interleukin 3

T-Helper cells

There are two major subsets of T-Helper cells:

Th1
- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2
- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Question 310 of 331

Which one of the following features is least associated with zinc deficiency?

- A. Acrodermatitis
- B. Alopecia
- C. Short stature
- D. Perioral dermatitis
- E. Gingivitis

Question 310 of 331

Which one of the following features is least associated with zinc deficiency?

- A. Acrodermatitis
- B. Alopecia
- C. Short stature
- D. Perioral dermatitis
- ✓ E. Gingivitis

Gingivitis is more commonly seen in vitamin C deficiency

Zinc deficiency

Features
- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Question 311 of 331

Which layer of the epidermis is immediately next to the dermis?

- A. Stratum granulosum
- B. Stratum lucidum
- C. Stratum corneum
- D. Stratum germinativum
- E. Stratum spinosum

Question 311 of 331

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- C. Stratum corneum
- ✓ D. Stratum germinativum
- E. Stratum spinosum

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

Epidermis

The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina

It may be divided in to five layers:

Layer	Description
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

Question 312 of 331

A 62-year-old man is admitted to resus with a low GCS. Blood gases taken on admission show the following:

pH 7.23

pCO2 2.2 kPa

pO2 13.8 kPa

IV access is obtained and bloods are taken. He is given supportive care with oxygen and fluids. Renal function results show:

Na^+	143 mmol/l
K^+	4.2 mmol/l
Chloride	109 mmol/l
Bicarbonate	12 mmol/l
Urea	2.1 mmol/l
Creatinine	79 µmol/l
Glucose	7.1 mmol/l

Which one of the following diagnoses would be most consistent with these results?

- A. Massive pulmonary embolism
- B. Methanol poisoning
- C. Paraquat poisoning
- D. Diabetic ketoacidosis
- E. Addisonian crisis

Question 312 of 331

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- C. Paraquat poisoning
- D. Diabetic ketoacidosis
- E. Addisonian crisis

This patient has a raised anion gap metabolic acidosis which may be caused by methanol poisoning. Massive pulmonary embolism is unlikely given the pO2 as is diabetic ketoacidosis given the blood glucose.

Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by: $(Na^+ + K^+) - (Cl^- + HCO_3^-)$. If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap (= hyperchloraemic metabolic acidosis)

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Raised anion gap

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:

- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Question 313 of 331

Which one of the following syndromes is associated with an increased risk of Crohn's disease?

- A. Turner's syndrome
- B. Down's syndrome
- C. Fragile X syndrome
- D. Patau syndrome
- E. Edward's syndrome

Question 313 of 331

Which one of the following syndromes is associated with an increased risk of Crohn's disease?

- ✓ A. Turner's syndrome
- B. Down's syndrome
- C. Fragile X syndrome
- D. Patau syndrome
- E. Edward's syndrome

Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Question 314 of 331

A study is performed to assess the correlation between age and systolic blood pressure. Which one of the following statements regarding the calculation of the correlation coefficient, r, is incorrect?

- A. A value of r greater than 0 implies a positive correlation between age and systolic blood pressure
- B. If r = 0 then there is no correlation between systolic blood pressure and age
- C. r may lie anywhere between -1 and 1
- D. May be used to predict systolic blood pressure for a given age
- E. Do not provide evidence of cause and effect

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- ✓ D. May be used to predict systolic blood pressure for a given age
- E. Do not provide evidence of cause and effect

Linear regression is needed to predict systolic blood pressure in this scenario

Correlation and linear regression

Two measurements, or variables, may be plotted on a scatter plot. For example, age may be marked along the x axis and systolic blood pressure along the y axis

Correlation

The correlation coefficient (sometimes referred to as Pearson's product-moment coefficient) indicates how closely the points lie to a line drawn through the plotted data. It is denoted by the value r which may lie anywhere between -1 and 1.

For example

- r = 1 - strong positive correlation (e.g. systolic blood pressure always increases with age)
- r = 0 - no correlation (e.g. there is no correlation between systolic blood pressure and age)
- r = - 1 - strong negative correlation (e.g. systolic blood pressure always decreases with age)

Whilst correlation coefficients give information about how one variable may increase or decrease as another variable increases they do not give information about how much the variable will change. They also do not provide information on cause and effect

Linear regression

In contrast to the correlation coefficient, linear regression may be used to predict how much one variable changes when a second variable is changed. A regression equation may be formed, y = a + bx, where

- y = the variable being calculated
- a = the intercept value, when x = 0
- b = the slope of the line or regression coefficient. Simply put, how much y changes for a given change in x
- x = the second variable

Question 315 of 331

A study is performed comparing two chemotherapy regimes for patients with small cell lung cancer. The end point of the study is survival time. Which one of the following types statistical measures is it most appropriate to compare survival time with?

- A. Odds ratio
- B. Pearson's product-moment coefficient
- C. Relative risk
- D. Hazard ratio
- E. Absolute risk reduction

Question 315 of 331

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- B. Pearson's product-moment coefficient
- C. Relative risk
- ✓ D. Hazard ratio
- E. Absolute risk reduction

Hazard ratio

The hazard ratio (HR) is similar to relative risk but is used when risk is not constant to time. It is typically used when analysing survival over time

Question 316 of 331

A couple present for genetic counselling. The male partner has haemophilia whilst the female partner has been screened and shown to be a carrier of the gene causing haemophilia. What is the chance that a child would have haemophilia?

- A. 25% if male child, 0% if female child
- B. 50%
- C. 100% if male child, 0% if female child
- D. 50% if male child, 0% if female child
- E. 25%

Question 316 of 331

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- ✓ B. 50%
- C. 100% if male child, 0% if female child
- D. 50% if male child, 0% if female child
- E. 25%

This question asks about the unusual situation of an affected male having children with a heterozygous (carrier) female. In this situation 50% of all children will be affected

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 317 of 331

A new adjuvant treatment for women with breast cancer is investigated. The study looks at the recurrence rate after 5 years. The following data is obtained:

	Number of patients	**Number who had a recurrence within a 5 year period**
New drug	200	40
Placebo	400	100

What is the relative risk reduction?

- A. 50%
- B. 20%
- C. 4
- D. 0.8
- E. 5%

Question 317 of 331

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What is the relative risk reduction?

- A. 50%
- ✓ B. 20%
- C. 4
- D. 0.8
- E. 5%

Relative risk reduction = (EER - CER) / CER

Experimental event rate, EER = 40 / 200 = 0.2
Control event rate, CER = 100 / 400 = 0.25
Relative risk reduction = (EER - CER) / CER = (0.2 - 0.25) / 0.25 = -0.2 or a 20% reduction

Relative risk

Relative risk (RR) is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER)

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate, EER = 60 / 100 = 0.6
Control event rate, CER = 20 / 80 = 0.25
Therefore the relative risk = EER / CER = 0.6 / 0.25 = 2.4

If the risk ratio is > 1 then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is < 1 then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

Relative risk reduction (RRR) or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate
Using the above data, RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140%

Question 318 of 331

In terms of the cell cycle, which one of the following phases determine the length of the cell cycle:

- A. M
- B. M0
- C. G1
- D. S
- E. G2

Question 318 of 331

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- A. M
- B. M0
- ✓ C. G1
- D. S
- E. G2

Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

Question 319 of 331

A 45-year-old man who is known to have Marfan's syndrome presents with lower back pain. This has been present for a few months now and is associated with headaches, leg pain and intemittent episodes of urinary incontinence. What is the most likely diagnosis?

- A. Depression
- B. Spinal stenosis
- C. Leaking aortic abdominal aneurysm
- D. Multiple sclerosis
- E. Dural ectasia

Question 319 of 331

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- C. Leaking aortic abdominal aneurysm
- D. Multiple sclerosis
- ✓ E. Dural ectasia

Dural ectasia affects around 60% of patients with Marfan's syndrome. It may cause lower back pain associated with neurological problems such as bladder and bowel dysfunction.

Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 patients.

Features

- tall stature with arm span to height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Question 320 of 331

You are caring for a local cardiology consultant's father who has been admitted following a myocardial infarction. He bleeps you from the switchboard and asks how his father is doing. You recognise his voice on the phone. What is the most appropriate response?

- A. Decline to give any details over the phone but offer to meet the consultant face-to-face for a chat
- B. As a matter of professional courtesy ask for his advice on post-myocardial infarction care
- C. Ask permission from his father then give relevant details
- D. Give full details include the troponin I value and offer to fax the ECG
- E. Say he is 'doing fine'

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- ✓ C. Ask permission from his father then give relevant details
- D. Give full details include the troponin I value and offer to fax the ECG
- E. Say he is 'doing fine'

The main nub of this question relates to confidentiality. You cannot give details over the phone to anyone, even his son, without the patient's express permission. Whilst it may be presumed that this is what the patient would want it is impossible to be sure of the family dynamics.

If the patient has given permission and you are sure you are speaking to the son then giving relevant details is the best option. Asking the consultant to come in as an option but may not be necessary if the previous conditions are met. Saying he is 'doing fine' is unlikely to satisfy a consultant cardiologist.

Giving details without first getting permission from the patient is breaking confidentiality, however well intentioned. Involving a relative in the management of a patient is inappropriate and the worst option.

Question 321 of 331

Potential complications of Paget's disease include each of the following except:

- A. Deafness
- B. Cerebral calcification
- C. Skull thickening
- D. Bone sarcoma
- E. Fractures

Question 321 of 331

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- A. Deafness
- ✓ B. Cerebral calcification
- C. Skull thickening
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- E. Fractures

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors
- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic
- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's
- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications
- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 322 of 331

Which of the following is not true regarding B-type natriuretic peptide?

- A. Secreted mainly by the ventricles
- B. Acts as a diuretic
- C. Acts as a vasoconstrictor
- D. Levels rise in left ventricular failure
- E. Reduces sympathetic tone

Question 322 of 331

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- E. Reduces sympathetic tone

BNP - actions:
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

B-type natriuretic peptide

B-type natriuretic peptide (BNP) hormone produced mainly by the left ventricular myocardium in response to strain

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP
- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

Clinical uses of BNP

Diagnosing patients with acute dyspnoea
- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

Prognosis in patients with chronic heart failure
- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure
- effective treatment lowers BNP levels

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 323 of 331

A 16-year-old male is reviewed in the endocrinology clinic due to lack of pubertal development. On examination his testes are undescended and there is only scanty pubic hair. What is the most likely diagnosis?

- A. Down's syndrome
- B. Kallman's syndrome
- C. Dubin-Johnson syndrome
- D. Turner's syndrome
- E. Klinefelter's syndrome

Question 323 of 331

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- C. Dubin-Johnson syndrome
- D. Turner's syndrome
- E. Klinefelter's syndrome

Cryptorchidism is more suggestive of Kallman's than Klinefelter's syndrome

Kallman's syndrome

Kallman's syndrome is a recognised cause of delayed puberty secondary to hypogonadotrophic hypogonadism. It is usually inherited as an X-linked recessive trait. Kallman's syndrome is thought to be caused by failure of GnRH-secreting neurons to migrate to the hypothalamus.

The clue given in many questions is lack of smell (anosmia) in a boy with delayed puberty

Features

- 'delayed puberty'
- hypogonadism, cryptorchidism
- anosmia
- sex hormone levels are low
- LH, FSH levels are inappropriately low/normal
- patients are typically of normal or above average height

Cleft lip/palate and visual/hearing defects are also seen in some patients

Question 324 of 331

You are a ST1 doctor in medicine doing a nightshift. An elderly patient with colorectal cancer has been admitted to the Emergency Department with suspected bowel obstruction. The Emergency Department F2 doctor has tried to refer the patient to the surgeons but was told that as no surgical intervention is likely the patient should be admitted to the medics. The F2 doctor therefore phones yourself and asks you to accept the patient. What is the most appropriate response?

- A. Accept the patient and ask the staff to transfer her to the medical assessment unit
- B. Simply refuse in order to avoid the patient being admitted under an inappropriate specialty
- C. Tell the surgical registrar that you will contact the on-call surgical consultant if he refuses to accept the patient
- D. Go down to the emergency department and review the patient
- E. Phone the surgical team yourself to discuss the matter

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- ✓ D. Go down to the emergency department and review the patient
- E. Phone the surgical team yourself to discuss the matter

Scenarios similar to this occur on an almost daily basis for admitting medical teams. The priority in all of this has to be the patient. It may be the case if the patient is end-stage then medical admission is more appropriate. If they are Duke's A and awaiting an operation then clearly they are surgical. Until you review the patient yourself you will not have all the facts and this is therefore the best option.

Discussing the matter with the surgical team will help to clarify their opinion about the patient and is the next best option. Accepting the patient without review risks placing a patient with an acute surgical problem on a medical ward. This may delay or compromise care.

Getting into an argument with the surgical registrar is not constructive and is a poor choice, as is simply refusing to see the patient as this indicates a disregard for the patient.

Question 325 of 331

The adrenergic receptor is an example of a:

- A. Intracellular receptor
- B. Tyrosine kinase receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Ligand-gated ion channel

Question 325 of 331

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- A. Intracellular receptor
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- C. Guanylate cyclase receptor
- ✓ D. G protein-coupled receptor
- E. Ligand-gated ion channel

Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel
- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 326 of 331

Which one of the following conditions is NOT an autosomal dominant condition?

- A. Retinoblastoma
- B. Tuberose sclerosis
- C. Achondroplasia
- D. Myotonic dystrophy
- E. Albinism

Question 326 of 331

Which one of the following conditions is NOT an autosomal dominant condition?

- A. Retinoblastoma
- B. Tuberose sclerosis
- C. Achondroplasia
- D. Myotonic dystrophy
- ✓ E. Albinism

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease*

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 327 of 331

What is the correct formula to calculate the negative predictive value of a screening test? TP = true positive; FP = false positive; TN = true negative; FN = false negative

- A. TN / (TN + FN)
- B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. Sensitivity / (1 - specificity)
- E. TP / (TP + FN)

Question 327 of 331

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TP = true positive; FP = false positive; TN = true negative; FN = false negative

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- B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. Sensitivity / (1 - specificity)
- E. TP / (TP + FN)

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 328 of 331

Which of the following is most likely to cause hypokalaemia associated with alkalosis?

- A. Acetazolamide
- B. Partially treated diabetic ketoacidosis
- C. Diarrhoea
- D. Cushing's syndrome
- E. Renal tubular acidosis

Question 328 of 331

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Hypokalaemia and acid-base balance

Potassium and hydrogen can be thought of as competitors. Hyperkalaemia tends to be associated with acidosis because as potassium levels rise fewer hydrogen ions can enter the cells

Hypokalaemia with alkalosis
- vomiting
- diuretics
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)

Hypokalaemia with acidosis
- diarrhoea
- renal tubular acidosis
- acetazolamide
- partially treated diabetic ketoacidosis

Question 329 of 331

Which one of the following causes of primary immunodeficiency is due to a defect in B-cell function?

- A. Di George syndrome
- B. Chediak-Higashi syndrome
- C. Common variable immunodeficiency
- D. Chronic granulomatous disease
- E. Wiskott-Aldrich syndrome

Question 329 of 331

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- ✓ C. Common variable immunodeficiency
- D. Chronic granulomatous disease
- E. Wiskott-Aldrich syndrome

Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders
- DiGeorge syndrome

Combined B- and T-cell disorders
- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Question 330 of 331

Which one of the following pathophysiological changes is most responsible for emphysema?

- A. Mucosal oedema and mucus plugging
- B. Destruction of alveolar walls secondary to proteinases
- C. Airway hypersensitivity
- D. Smooth muscle contraction
- E. Hypertrophy of mucous secreting glands

Question 330 of 331

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Proteinases such as elastase cause irreversible damage to the supporting connective tissue of the alveolar septa. Smoking accelerates this process.

COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

Other causes
- cadmium (used in smelting)
- coal
- cotton
- cement
- grain

Question 331 of 331

Which one of the following defines the standard error of the mean?

- A. Square root (Standard deviation / number of patients)
- B. Number of patients / square root (mean)
- C. Number of patients / square root (standard deviation)
- D. Standard deviation / square root (number of patients)
- E. Standard deviation / square root (mean)

Question 331 of 331

Which of the following conditions is not caused by a trinucleotide repeat expansion?

- A. Fragile X syndrome
- B. Huntington's
- C. Ataxia telangiectasia
- D. Myotonic dystrophy
- E. Friedreich's ataxia

Question 1 of 116

A 56-year-old man with metastatic prostate cancer comes for review. He is known to have spinal metastases but until now has not had any significant problems with pain control. Unfortunately he is now getting regular back pain despite taking paracetamol 1g qds. Neurological examination is unremarkable. What is the most appropriate next step?

- A. Switch to co-codamol 30/500
- B. Refer for radiotherapy
- C. Add oral bisphosphonate
- D. Add diclofenac
- E. Add dexamethasone

Question 1 of 116

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- A. Switch to co-codamol 30/500
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- C. Add oral bisphosphonate
- D. Add diclofenac
- E. Add dexamethasone

Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Bone pain often responds well to NSAIDs. Both radiotherapy and bisphosphonates have a role in managing bony pain but these are not first-line treatments

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 2 of 116

A 4-year-old boy is admitted after developing a haemarthrosis in his right knee whilst playing in the garden. The following blood results are obtained:

Platelets	220 * 10^9/l
PT	12 secs
APTT	78 secs
Factor VIIIc activity	Normal

What is the most likely diagnosis?

- A. Antithrombin III deficiency
- B. Von Willebrand's disease
- C. Antiphospholipid syndrome
- D. Haemophilia A
- E. Haemophilia B

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- D. Haemophilia A
- E. Haemophilia B

A grossly elevated APTT may be caused by heparin therapy, haemophilia or antiphospholipid syndrome. A normal factor VIIIc activity points to a diagnosis of haemophilia B (lack of factor IX). Antiphospholipid syndrome is a prothrombotic condition

Haemophilia

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

Features
- haemoarthroses, haematomas
- prolonged bleeding after surgery or trauma

Blood tests
- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

Question 3 of 116

Which one of the following cytotoxic agents acts by inhibiting dihydrofolate reductase and thymidylate synthesis?

- A. Methotrexate
- B. Vincristine
- C. Bleomycin
- D. Cyclophosphamide
- E. Doxorubicin

Question 3 of 116

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	**Mechanism of action**	**Adverse effects**
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 4 of 116

A 52-year-old man with a history of anaemia and abdominal discomfort is diagnosed as having chronic myeloid leukaemia. What is the mechanism of action of imatinib?

- A. EGF receptor antagonist
- B. Tyrosine kinase inhibitor
- C. Anti-CD52 monoclonal antibody
- D. Anti-CD23 monoclonal antibody
- E. p53 inhibitor

Question 4 of 116

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- D. Anti-CD23 monoclonal antibody
- E. p53 inhibitor

Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor

Imatinib is an inhibitor of the tyrosine kinase associated with the BCR-ABL defect

Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)
- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management
- hydroxyurea
- interferon-alpha
- imatinib
- allogenic bone marrow transplant

Imatinib
- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Question 5 of 116

A 12-year-old boy is noted to bleed excessively during an elective dental extraction. Following the procedure, examination reveals petechial skin haemorrhages. Blood results show:

Hb	12.3 g/dl
Plt	255 * 10^9/l
WBC	7.9 * 10^9/l
PT	13.3 secs
APTT	39 secs
Factor VIII activity	87%

What is the most likely diagnosis?

- A. Disseminated intravascular coagulation
- B. Idiopathic thrombocytopenic purpura
- C. Von Willebrand's disease
- D. Haemophilia A
- E. Haemophilia B

Question 5 of 116

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- D. Haemophilia A
- E. Haemophilia B

The combination of a petechial skin rash combined with a slightly elevated APTT and reduced factor VIII activity make Von Willebrand's disease the most likely diagnosis

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 6 of 116

A 52-year-old woman with a history of hypothyroidism presents with lethargy and a sore tongue. Blood tests are reported as follows:

Hb 10.7 g/dl

MCV 121 fl

Plt 177 * 10^9/l

WBC 5.4 * 10^9/l

Further tests are ordered:

Vitamin B12 64 ng/l (200-900 ng/l)

Folic acid 7.2 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- A. 1 mg of IM hydroxocobalamin once every 3 months
- B. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- C. 1 mg of IM hydroxocobalamin once every 2 months + folic acid 5mg od
- D. Give folic acid 5mg od one week then recheck bloods
- E. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months + folic acid 5mg od

Question 6 of 116

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- D. Give folic acid 5mg od one week then recheck bloods
- E. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months + folic acid 5mg od

If the patient was deficient in folic acid it would important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord.

Vitamin B12 deficiency

Vitamin B12 is mainly used in the body for red blood cell development and also maintenance of the nervous system. It is absorbed after binding to intrinsic factor (secreted from parietal cells in the stomach) and is actively absorbed in the terminal ileum. A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Causes of vitamin B12 deficiency

- pernicious anaemia
- post gastrectomy
- poor diet
- disorders of terminal ileum (site of absorption): Crohn's, blind-loop etc

Features of vitamin B12 deficiency

- macrocytic anaemia
- sore tongue and mouth
- neurological symptoms: e.g. Ataxia
- neuropsychiatric symptoms: e.g. Mood disturbances

Management

- if no neurological involvement 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- if a patient is also deficient in folic acid then it is important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

Question 7 of 116

A 72-year-old women is found to have a marked lymphocytosis associated with smudge cells on the blood film. A diagnosis of chronic lymphocytic leukaemia is suspected. Which one of the following is the investigation of choice?

- A. Immunophenotyping
- B. Bone marrow aspiration
- C. Protein electrophoresis
- D. White cell scan
- E. Bone marrow trephine

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- C. Protein electrophoresis
- D. White cell scan
- E. Bone marrow trephine

CLL - immunophenotyping is investigation of choice

Immunophenotyping will demonstrate the cells to be B-cells (CD19 positive). CD5 and CD23 are also characteristically positive in chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 8 of 116

A 50-year-old man with a history of ulcerative colitis comes for review. Six years ago he had an ileostomy formed which has been functioning well until now. Unfortunately he is currently suffering significant pain around the stoma site. On examination a deep erythematous ulcer is noted with a ragged edge. The surrounding skin is erythematous and swollen. What is the most likely diagnosis?

- A. Munchausen's syndrome
- B. Irritant contact dermatitis
- C. Pyoderma gangrenosum
- D. Dermatitis artefacta
- E. Stomal granuloma

Question 8 of 116

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- B. Irritant contact dermatitis
- C. Pyoderma gangrenosum
- D. Dermatitis artefacta
- E. Stomal granuloma

Pyoderma gangrenosum is associated with inflammatory bowel disease and may be seen around the stoma site. Treatment is usually with immunosuppressants as surgery may worsen the problem

A differential diagnosis would be malignancy and hence lesions should be referred for specialist opinion to evaluate the need for a biopsy. Irritant contact dermatitis is common but would not be expected to cause such a deep ulcer.

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic systems e.g. fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 9 of 116

Which one of the following may be used to monitor patients with colorectal cancer?

- A. CA-125
- B. Carcinoembryonic antigen
- C. Alpha-fetoprotein
- D. CA 19-9
- E. CA 15-3

Question 9 of 116

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- A. CA-125
- B. Carcinoembryonic antigen
- C. Alpha-fetoprotein
- D. CA 19-9
- E. CA 15-3

Carcinoembryonic antigen may be used to monitor for recurrence in patients post-operatively or to assess response to treatment in patients with metastatic disease

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Question 10 of 116

A 33-year-old male patient with a history of recurrent nose bleeds, iron-deficiency anaemia and dyspnoea is found to have a pulmonary AV malformation on pulmonary angiography. What is the likely underlying diagnosis?

- A. Haemophilia A
- B. Hereditary haemorrhagic telangiectasia
- C. Mantle cell lymphoma
- D. Wegener's granulomatosis
- E. Down's syndrome

Question 10 of 116

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- C. Mantle cell lymphoma
- D. Wegener's granulomatosis
- E. Down's syndrome

Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history

Features

- epistaxis
- telangiectasia develop is skin, mucous membranes and internal organs
- associated with pulmonary AV malformations and other AV malformations in 10%
- may present as iron-deficiency anaemia secondary to bleeding in the GI tract or nasal mucosa

Question 11 of 116

Which one of the following is least likely to cause a warm autoimmune haemolytic anaemia?

- A. Mycoplasma infection
- B. Methyldopa
- C. Chronic lymphocytic leukaemia
- D. Lymphoma
- E. Systemic lupus erythematous

Question 11 of 116

Which one of the following is least likely to cause a warm autoimmune haemolytic anaemia?

- A. Mycoplasma infection
- B. Methyldopa
- C. Chronic lymphocytic leukaemia
- D. Lymphoma
- E. Systemic lupus erythematous

Mycoplasma infection causes a cold autoimmune haemolytic anaemia. Systemic lupus erythematous can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia (AIHA) may be divided in to 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

Warm AIHA

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyldopa

Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Question 12 of 116

Which one of the following is a marker of a bad prognosis in acute lymphoblastic leukaemia?

- A. Pre-B phenotype
- B. Presentation in childhood
- C. Initial white cell count of 18 * 10^9/l
- D. Female sex
- E. Philadelphia chromosome positive

Question 12 of 116

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- C. Initial white cell count of 18 * 10^9/l
- D. Female sex
- E. Philadelphia chromosome positive

Philadelphia translocation, t(9;22) - good prognosis in CML, poor prognosis in AML + ALL

Acute lymphoblastic leukaemia: prognostic features

Good prognostic factors
- FAB L1 type
- common ALL
- pre-B phenotype
- low initial WBC

Poor prognostic factors
- FAB L3 type
- T or B cell surface markers
- Philadelphia translocation, t(9;22)
- age < 2 years or > 10 years
- male sex
- CNS involvement
- high initial WBC (e.g. > 100 * 10^9/l)
- non-Caucasian

Question 13 of 116

A 42-year-old female is noted to have a Hb of 17.8 g/dL. Which one of the following is least likely to be the cause?

- A. Polycythaemia rubra vera
- B. Chronic obstructive pulmonary disease
- C. Hypernephroma
- D. Haemochromatosis
- E. Dehydration

Question 13 of 116

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- B. Chronic obstructive pulmonary disease
- C. Hypernephroma
- D. Haemochromatosis
- E. Dehydration

Haemochromatosis is not associated with polycythaemia. Blood tests typically reveal a raised ferritin and iron, associated with a transferrin saturation of greater than 60% and a low total iron binding capacity

Polycythaemia

Polycythaemia may be relative, primary (polycythaemia rubra vera) or secondary

Relative causes
- dehydration
- stress: Gaisbock syndrome

Primary
- polycythaemia rubra vera

Secondary causes
- COPD
- altitude
- obstructive sleep apnoea
- excessive erythropoietin: cerebellar haemangioma, hypernephroma, hepatoma, uterine fibroids*

To differentiate between true (primary or secondary) polycythaemia and relative polycythaemia red cell mass studies are sometimes used. In true polycythaemia the total red cell mass in males > 35 ml/kg and in women > 32 ml/kg

*uterine fibroids may cause menorrhagia which in turn leads to blood loss - polycythaemia is rarely a clinical problem

Question 14 of 116

A 49-year-old female is admitted to hospital due to shortness of breath and pleuritic chest pain. She also complains of a marked decrease in appetite for the past 4 months. An admission chest x-ray shows a right-sided pleural effusion. An underlying malignancy is suspected and a series of tumour markers are requested:

CA 19-9 55 u/ml (< 40)

CA 125 654 u/ml (< 30)

CA 15-3 9 u/ml (<40)

What is the most likely underlying diagnosis?

- A. Ovarian fibroma
- B. Small cell lung cancer
- C. Pancreatic carcinoma
- D. Hepatocellular cancer
- E. Breast carcinoma

Question 14 of 116

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- C. Pancreatic carcinoma
- D. Hepatocellular cancer
- E. Breast carcinoma

This patient has Meig's syndrome - an ovarian fibroma associated with a pleural effusion and ascites

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 15 of 116

A 21-year-old man comes for review. He recently had an abdominal ultrasound for episodic right upper quadrant pain which demonstrated gallstones. A full blood count was also ordered which was reported as follows:

Hb 9.8 g/dl

MCV 91 fl

Plt 177 * 10^9/l

WBC 5.3 * 10^9/l

The patient also mentions that his father had a splenectomy at the age of 30 years. Which one of the following tests is most likely to be diagnostic?

- A. Ham's test
- B. PAS staining of erythrocytes
- C. Glucose-6-phoshate dehydrogenase levels
- D. Osmotic fragility test
- E. Direct Coombs' test

Question 15 of 116

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- C. Glucose-6-phoshate dehydrogenase levels
- D. Osmotic fragility test
- E. Direct Coombs' test

This patient has hereditary spherocytosis as evidenced by the normocytic anaemia, gallstones and family history.

Hereditary spherocytosis

Basics
- most common hereditary haemolytic anaemia in northern Europeans
- autosomal dominant defect of RBC cytoskeleton
- biconcave disc --> spherocyte
- red cell survival reduced, destroyed by spleen

Presentation
- e.g. failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

Diagnosis
- osmotic fragility test

Management
- folate replacement
- splenectomy

Question 16 of 116

Which one of the following is not a feature of paroxysmal nocturnal haemoglobinuria?

- A. Haemolytic anaemia
- B. Positive Ham test
- C. Haemoglobinuria
- D. Aplastic anaemia
- E. Haemarthrosis

Question 16 of 116

Which one of the following is not a feature of paroxysmal nocturnal haemoglobinuria?

- A. Haemolytic anaemia
- B. Positive Ham test
- C. Haemoglobinuria
- D. Aplastic anaemia
- E. Haemarthrosis

Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology
- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features
- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopaenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis
- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management
- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation

Question 17 of 116

A 22-year-old man with sickle cell anaemia presents with vomiting, abdominal pain and a rash. Blood results are as follows:

Hb	4.6 g/dl
Reticulocytes	3%

Infection with a parvovirus is suspected. What is the likely diagnosis?

- A. Thrombotic crisis
- B. Sequestration crisis
- C. Transformation to myelodysplasia
- D. Haemolytic crisis
- E. Aplastic crisis

Question 17 of 116

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- A. Thrombotic crisis
- B. Sequestration crisis
- C. Transformation to myelodysplasia
- D. Haemolytic crisis
- E. Aplastic crisis

The sudden fall in haemoglobin without an appropriate reticulocytosis (3% is just above the normal range) is typical of an aplastic crisis, usually secondary to parvovirus infection

Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:
- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

Thrombotic crises
- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain

Sequestration crises
- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO2 - the most common cause of death after childhood

Aplastic crises
- caused by infection with parvovirus
- sudden fall in haemoglobin

Haemolytic crises
- rare
- fall in haemoglobin due an increased rate of haemolysis

Question 18 of 116

Which one of the following factors is most associated with an increased risk of developing bladder cancer?

- A. Strongyloides stercoralis infection
- B. Beryllium salt exposure
- C. Aniline dye exposure
- D. Aflatoxin exposure
- E. Long term phenytoin use

Question 18 of 116

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- C. Aniline dye exposure
- D. Aflatoxin exposure
- E. Long term phenytoin use

Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

Question 19 of 116

A 34-year-old man who is HIV positive is starting treatment for Burkitt's lymphoma. His chemotherapy regime includes cyclophosphamide, vincristine, methotrexate and prednisolone. Around 24 hours after starting chemotherapy he becomes confused and complains of muscle cramps in his legs. Which one of the following is most likely to have occurred?

- A. Prednisolone-induced psychosis
- B. Hypercalcaemia
- C. Methotrexate pneumonitis leading to hypoxia
- D. Haemorrhagic cystitis leading to acute renal failure
- E. Tumour lysis syndrome

Question 19 of 116

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- E. Tumour lysis syndrome

Burkitt's lymphoma is a common cause of tumour lysis syndrome

Burkitt's lymphoma

Burkitt's lymphoma is a high-grade B-cell neoplasm. There are two major forms:

- endemic (African) form: typically involves maxilla or mandible
- sporadic form: abdominal (e.g. ileo-caecal) tumours are the most common form. More common in patients with HIV

Burkitt's lymphoma is associated with the c-myc gene translocation, usually t(8:14). The Epstein-Barr virus (EBV) is strongly implicated in the development of the African form but the link to sporadic Burkitt's is less clear

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Complications of tumour lysis syndrome include:

- hyperkalaemia
- hyperphosphataemia
- hypocalcaemia
- hyperuricaemia
- acute renal failure

Question 20 of 116

A 67-year-old man with a 10-year history of gastro-oesophageal reflux disease is investigated for dysphagia. An endoscopy shows an obstructive lesion highly suspicious of oesophageal cancer. What is the biopsy most likely to show?

- A. Squamous cell carcinoma
- B. Normal squamous epithelium
- C. Adenocarcinoma
- D. Leiomyoma
- E. Metaplastic columnar epithelium

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- A. Squamous cell carcinoma
- B. Normal squamous epithelium
- C. Adenocarcinoma
- D. Leiomyoma
- E. Metaplastic columnar epithelium

Oesophageal cancer
- squamous cell carcinoma is more common overall
- adenocarcinoma is more common in patients with GORD or Barrett's

Metaplastic columnar epithelium would be seen with Barrett's but this is not consistent with the obstructive lesion seen on endoscopy.

Oesophageal cancer

Oesophageal cancer is most commonly due to a squamous carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is the most common type of cancer to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

Risk factors
- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

Question 21 of 116

Which one of the following viruses is associated with nasopharyngeal carcinoma?

- A. Adenovirus
- B. Rhinovirus
- C. Herpes simplex virus
- D. Epstein-Barr virus
- E. Picornavirus

Question 21 of 116

Which one of the following viruses is associated with nasopharyngeal carcinoma?

- A. Adenovirus
- B. Rhinovirus
- C. Herpes simplex virus
- D. Epstein-Barr virus
- E. Picornavirus

EBV: associated malignancies:
- Burkitt's lymphoma
- Hodgkin's lymphoma
- nasopharyngeal carcinoma

Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection
- Burkitt's lymphoma*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also assocaiated with EBV infection.

*EBV is currently thought to be associated with both African and sporadic Burkitt's

Question 22 of 116

Which one of the following features is least recognised in thrombotic thrombocytopenic purpura?

- A. Fever
- B. Microangiopathic haemolytic anaemia
- C. Renal failure
- D. Thrombocytopenia
- E. Livedo reticularis

Question 22 of 116

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- A. Fever
- B. Microangiopathic haemolytic anaemia
- C. Renal failure
- D. Thrombocytopenia
- E. Livedo reticularis

Livedo reticularis is not commonly seen in thrombotic thrombocytopenic purpura. It occurs more commonly in conditions such as antiphospholipid syndrome and cholesterol embolism

Thrombotic thrombocytopenic purpura

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia
- renal failure

Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV

Question 23 of 116

Which one of the following would most suggest a leukaemoid reaction rather than chronic myeloid leukaemia?

- A. Raised packed cell volume
- B. Right shift of neutrophils
- C. A low leucocyte alkaline phosphatase score
- D. Dohle bodies in the white cells
- E. Positive osmotic fragility test

Question 23 of 116

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E. Positive osmotic fragility test

Leukaemoid reaction

The leukaemoid reaction describes the presence of immature cells such as myeloblasts, promyelocytes and nucleated red cells in the peripheral blood. This may be due to infiltration of the bone marrow causing the immature cells to be 'pushed out' or sudden demand for new cells

Causes
- severe infection
- severe haemolysis
- massive haemorrhage
- metastatic cancer with bone marrow infiltration

A relatively common clinical problem is differentiating chronic myeloid leukaemia from a leukaemoid reaction. The following differences may help:

Leukaemoid reaction
- high leucocyte alkaline phosphatase score
- toxic granulation (Dohle bodies) in the white cells
- 'left shift' of neutrophils i.e. three or less segments of the nucleus

Chronic myeloid leukaemia
- low leucocyte alkaline phosphatase score

Question 24 of 116

A 49-year-old women is referred to the haematology clinic with easy bruising and recurrent epistaxis. She is otherwise well. Blood tests reveal the following:

Hb 12.9 g/dl

Platelets 19 * 10^9/l

WCC 6.6 * 10^9/l

The patient refuses consent for a bone marrow examination. What is the most appropriate initial management?

- A. Platelet transfusion
- B. Oral prednisolone
- C. No treatment
- D. ABVD chemotherapy
- E. Splenectomy

Question 24 of 116

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- E. Splenectomy

ITP - give oral prednisolone

The likely diagnosis in this patient is idiopathic thrombocytopenic purpura. The first line treatment in such patients is high-dose prednisolone. Bone marrow examination would demonstrate increased megakaryocytes

ITP: investigation and management

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

Investigations

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

Management

- oral prednisolone (80% of patients respond)
- splenectomy if platelets < 30 after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide

Question 25 of 116

A 65-year-old woman is reviewed. She is on the waiting list for a varicose vein operation but during the preoperative assessment was noted to have a raised lymphocyte count. She reports feeling well currently and clinical examination is normal. Her bloods were as follows:

Hb 11.8 g/dl

Plt 184 * 10^9/l

WBC 21.2 * 10^9/l

There are no previous bloods to compare these results with. Following referral to haematology a diagnosis of chronic lymphocytic leukaemia was made. What is the most appropriate management?

- A. No treatment + cancel operation
- B. No treatment + go ahead with operation
- C. Chlorambucil + cancel operation
- D. Fludarabine + go ahead with operation but with quinolone prophylaxis
- E. Alemtuzumab + cancel operation

Question 25 of 116

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- E. Alemtuzumab + cancel operation

There is no indication for treating this patient at the current time or not going ahead with surgery

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 26 of 116

A patient with a history of recurrent thromboembolic events develops a deep vein thrombosis despite full anticoagulation with heparin. Which one of the following causes of thrombophilia is associated with resistance to heparin?

- A. Protein S deficiency
- B. Antithrombin III deficiency
- C. Protein C deficiency
- D. Lupus anticoagulant
- E. Activated protein C resistance

Question 26 of 116

A patient with a history of recurrent thromboembolic events develops a deep vein thrombosis despite full anticoagulation with heparin. Which one of the following causes of thrombophilia is associated with resistance to heparin?

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Heparin works by binding to antithrombin III, enhancing its anticoagulant effect by inhibiting the formation of thrombin and other clotting factors. Patients with antithrombin III deficiency may therefore by resistant to heparin treatment

Antithrombin III deficiency

Antithrombin III deficiency is an inherited cause of thrombophilia occurring in approximately 1:2,000 of the population. Inheritance is autosomal dominant

Antithrombin III inhibits several clotting factors, primarily thrombin, factor X and factor IX. It mediates the effects of heparin

Antithrombin III deficiency comprises a heterogeneous group of disorders, with some patients having a deficiency of normal antithrombin III whilst others produce abnormal antithrombin III

Features
- recurrent venous thromboses
- arterial thromboses do occur but is uncommon

Management
- thromboembolic events are treated with lifelong warfarinisation
- heparinisation during pregnancy*
- antithrombin III concentrates (often using during surgery or childbirth)

*as patients with antithrombin III deficiency have a degree of resistance to heparin anti-Xa levels should be monitored carefully to ensure adequate anticoagulation

Question 27 of 116

Which of the following is most associated with thymomas?

- A. Myelodysplasia
- B. Thrombocytopenia
- C. Acute myeloid leukaemia
- D. Acute lymphoblastic leukaemia
- E. Red cell aplasia

Question 27 of 116

Which of the following is most associated with thymomas?

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- D. Acute lymphoblastic leukaemia
- E. Red cell aplasia

Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with
- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death
- compression of airway
- cardiac tamponade

Question 28 of 116

A 24-year-old nulliparous female with a history of recurrent deep vein thrombosis presents with shortness of breath. The full blood count and clotting screen reveals the following results:

Hb 12.4 g/dl

Plt 137

WBC 7.5 * 10^9/l

PT 14 secs

APTT 46 secs

What is the most likely underlying diagnosis?

- A. Third generation oral contraceptive pill use
- B. Protein C deficiency
- C. Antithrombin III deficiency
- D. Antiphospholipid syndrome
- E. Activated protein C resistance

Question 28 of 116

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Antiphospholipid syndrome: (paradoxically) prolonged APTT + low platelets

The combination of a prolonged APTT and thrombocytopenia make antiphospholipid syndrome the most likely diagnosis

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 29 of 116

A 72-year-old man is admitted with a deep vein thrombosis. He is normally fit and well but has recently lost weight. Blood tests reveal the following:

IgG 889 mg/dl (range 600-1300 mg/dl)

IgM 1674 mg/dl (range 50-330 mg/dl)

IgA 131 mg/dl (range 60-300 mg/dl)

What is the most likely diagnosis?

- A. Monoclonal gammopathy of undetermined significance
- B. Acute promyelocytic leukaemia
- C. Waldenstrom's macroglobulinaemia
- D. Antiphospholipid syndrome
- E. Multiple myeloma

Question 29 of 116

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IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is more likely than monoclonal gammopathy of undetermined significance given the weight loss and deep vein thrombosis (evidence of hyperviscosity).

IgG and IgA and the most common type of immunoglobulins produced in myeloma.

Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Question 30 of 116

Each one of the following may cause eosinophilia, except:

- A. Allergic bronchopulmonary aspergillosis
- B. Extrinsic allergic alveolitis
- C. Churg-Strauss syndrome
- D. Psoriasis
- E. Toxocara infection

Question 30 of 116

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- B. Extrinsic allergic alveolitis
- C. Churg-Strauss syndrome
- D. Psoriasis
- E. Toxocara infection

Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes
- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Loffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes
- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes
- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

Question 31 of 116

A 73-year-old woman presents with lethargy for the past two weeks. Clinical examination is unremarkable. Her past medical history includes polymyalgia rheumatica and ischaemic heart disease. Screening blood tests are ordered and the full blood count is reported as follows:

Hb 12.9 g/dl

Plt 158 * 10^9/l

WBC 19.0 * 10^9/l

Neuts 4.2 * 10^9/l

Lymphs 14.1 * 10^9/l

What is the most likely diagnosis?

- A. Lymphoma
- B. Nicorandil-related lymphocytosis
- C. Transient viral illness
- D. Chronic lymphocytic leukaemia
- E. Secondary to steroid use

Question 31 of 116

A 73-year-old woman presents with lethargy for the past two weeks. Clinical examination is unremarkable. Her past medical history includes polymyalgia rheumatica and ischaemic heart disease. Screening blood tests are ordered and the full blood count is reported as follows:

Hb 12.9 g/dl

Plt 158 * 10^9/l

WBC 19.0 * 10^9/l

Neuts 4.2 * 10^9/l

Lymphs 14.1 * 10^9/l

What is the most likely diagnosis?

- A. Lymphoma
- B. Nicorandil-related lymphocytosis
- C. Transient viral illness
- D. Chronic lymphocytic leukaemia
- E. Secondary to steroid use

Such a lymphocytosis is an elderly patient is very likely to be caused by chronic lymphocytic leukaemia. Steroids tend to cause a neutrophilia. It would be unusual for a viral illness to cause such a marked lymphocytosis in an elderly person.

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 32 of 116

A 67-year-old man is diagnosed with myelofibrosis. What is the most common presenting symptom of myelofibrosis?

- A. Lethargy
- B. Anorexia and weight loss
- C. Night sweats
- D. Easy bruising
- E. Splenomegaly

Question 32 of 116

A 67-year-old man is diagnosed with myelofibrosis. What is the most common presenting symptom of myelofibrosis?

- A. Lethargy
- B. Anorexia and weight loss
- C. Night sweats
- D. Easy bruising
- E. Splenomegaly

Myelofibrosis - most common presenting symptom - lethargy

Whilst all the above may be seen in myelofibrosis lethargy is the most common

Myelofibrosis

Overview
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features
- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings
- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)

Question 33 of 116

Which one of the following translocations is associated with acute promyelocytic leukaemia?

- A. t(15;17)
- B. t(9;17)
- C. t(9;22)
- D. t(15;22)
- E. t(17;22)

Question 33 of 116

Which one of the following translocations is associated with acute promyelocytic leukaemia?

- A. t(15;17)
- B. t(9;17)
- C. t(9;22)
- D. t(15;22)
- E. t(17;22)

Acute promyelocytic leukaemia - t(15;17)

Acute promyelocytic leukaemia

You are not normally expected to be able to differentiate the different subtypes of acute myeloid leukaemia (AML) for the MRCP. An exception to this is acute promyelocytic leukaemia (APML, the M3 subtype of AML). The importance of identifying APML lies in both the presentation (classically disseminated intravascular coagulation) and management

APML is associated with the t(15;17) translocation which causes fusion of the PML and RAR-alpha genes.

Features

- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Question 34 of 116

A 51-year-old female is referred to the haematology clinic with a haemoglobin of 19.2 g/dl. She is a non-smoker. Her oxygen saturations on room air are 98% and she is noted to have mass in the left upper quadrant. What is the most useful test to establish whether she has polycythaemia rubra vera?

- A. Bone marrow aspiration
- B. Blood film
- C. Red cell mass
- D. Transferrin saturation
- E. JAK2 mutation screen

Question 34 of 116

A 51-year-old female is referred to the haematology clinic with a haemoglobin of 19.2 g/dl. She is a non-smoker. Her oxygen saturations on room air are 98% and she is noted to have mass in the left upper quadrant. What is the most useful test to establish whether she has polycythaemia rubra vera?

- A. Bone marrow aspiration
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- D. Transferrin saturation
- E. JAK2 mutation screen

Polycythaemia rubra vera - JAK2 mutation

The discovery of the JAK2 mutation has made red cell mass a second-line investigation for patients with suspected JAK2-negative polycythaemia rubra vera

Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

Features
- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed
- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:
- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphotase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count >450 * 10^9/l)
B2	Neutrophil leucocytosis (neutrophil count > 10 * 10^9/l in non-smokers; > 12.5*10^9/l in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Question 35 of 116

Which one of the following malignancies may be associated with HTLV-1?

- A. Adult T-cell leukaemia
- B. Colorectal cancer
- C. Burkitt's lymphoma
- D. Medullary thyroid cancer
- E. Breast cancer

Question 35 of 116

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- A. Adult T-cell leukaemia
- B. Colorectal cancer
- C. Burkitt's lymphoma
- D. Medullary thyroid cancer
- E. Breast cancer

Haematological malignancies: infections

Viruses
- EBV: Hodgkin's and Burkitt's lymphoma, nasopharyngeal carcinoma
- HTLV-1: Adult T-cell leukaemia/lymphoma
- HIV-1: High-grade B-cell lymphoma

Bacteria
- *Helicobacter pylori*: gastric lymphoma (MALT)

Protozoa
- malaria: Burkitt's lymphoma

Question 36 of 116

Which one of the following ethnic groups have an increased incidence of prostate cancer?

- A. Afro-Caribbean
- B. Ashkenazi Jews
- C. Chinese
- D. Indian subcontinent
- E. White

Question 36 of 116

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- D. Indian subcontinent
- E. White

Prostate cancer: features

Prostate cancer is the second most common cancer in adult males in the UK and is the most common malignant condition in men over 65 years.

Risk factors
- increasing age
- Afro-Caribbean ethnicity

Features
- bladder outlet obstruction: hesitancy, urinary retention
- haematuria, haematospermia
- pain: back, perineal or testicular
- digital rectal examination: asymmetrical, hard, nodular enlargement with loss of median sulcus

Question 37 of 116

A 71-year-old woman who is known to have multiple myeloma is admitted with confusion. Blood tests show the following:

Corrected calcium 2.91 mmol/l

Which one of the following is the most significant cause of the raised calcium level?

- A. Adverse effects of standard treatment
- B. Increased osteoclastic activation
- C. Impaired renal function
- D. Increased renal tubular calcium reabsorption
- E. Elevated PTH-rP levels

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Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 38 of 116

What is the mechanism of action of DDAVP in von Willebrand's disease?

- A. Prevents renal excretion of von Willebrand's factor
- B. Promotes breakdown of large multimers
- C. Induces release of von Willebrand's factor from endothelial cells
- D. Inhibits breakdown of von Willebrand's factor
- E. Acts as substitute carrier molecule for factor VIII

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Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 39 of 116

A 62-year-old man presents with lethargy. A full blood count is taken and is reported as follows:

Hb 10.2 g/dl

Platelets 330 * 10^9/l

WBC 15.2 * 10^9/l

Film Leucoerythroblastic picture. Tear-drop poikilocytes seen

What is the most likely diagnosis?

- A. Aplastic anaemia
- B. Chronic lymphocytic leukaemia
- C. Myelofibrosis
- D. Chronic myeloid leukaemia
- E. Post-splenectomy

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- E. Post-splenectomy

Tear-drop poikilocytes = myelofibrosis

Thrombocytopenia and leucopenia are seen in progressive disease

Blood films: typical pictures

Hyposplenism e.g. post-splenectomy
- target cells
- Howell-Jolly bodies
- Cabot's rings
- siderotic granules
- acanthocytes
- schizocytes

Iron-deficiency anaemia
- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

Myelofibrosis
- 'tear-drop' poikilocytes

Intravascular haemolysis
- schistocytes

Megaloblastic anaemia
- hypersegmented neutrophils

Question 40 of 116

What is the mechanism of action of cisplatin?

- A. Stabilises DNA-topoisomerase II complex
- B. Causes cross-linking in DNA
- C. Inhibits ribonucleotide reductase
- D. Inhibits purine synthesis
- E. Inhibits formation of microtubules

Question 40 of 116

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 41 of 116

Which of the following is a cause of extravascular haemolysis?

- A. Hereditary spherocytosis
- B. G6PD deficiency
- C. Disseminated intravascular coagulation
- D. Mismatched blood transfusion
- E. Haemolytic uraemic syndrome

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Haemolytic anaemias: by site

In intravascular haemolysis free haemoglobin is released which binds to haptoglobin. As haptoglobin becomes saturated haemoglobin binds to albumin forming methaemalbumin (detected by Schumm's test). Free haemoglobin is excreted in the urine as haemoglobinuria, haemosiderinuria

Intravascular haemolysis: causes

- mismatched blood transfusion
- G6PD deficiency
- red cell fragmentation: heart valves, TTP, DIC, HUS
- paroxysmal nocturnal haemoglobinuria
- cold autoimmune haemolytic anaemia

Extravascular haemolysis: causes

- haemoglobinopathies: sickle cell, thalassaemia
- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

Question 42 of 116

Which one of the following features is least recognised in myeloma?

- A. Bone pain
- B. Amyloidosis
- C. Lethargy
- D. Night sweats
- E. Pathological fractures

Question 42 of 116

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Night sweats are a feature of non-Hodgkin's lymphoma

Myeloma: features

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Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 43 of 116

A 31-year-old woman who is 25-weeks pregnant is brought to the Emergency Department by her husband. Over the past two days she has become increasingly confused. Her temperature is 37.8ºC and blood pressure is 104/62 mmHg. Blood tests show:

Hb	8.3 g/dl
Platelets	88 * 10^9/l
WBC	15.1 * 10^9/l
Blood film	Fragmented red blood cells
Sodium	139 mmol/l
Potassium	5.2 mmol/l
Urea	19.4 mmol/l
Creatinine	296 µmol/l

What is the most appropriate treatment?

- A. Rituximab
- B. Intravenous immunoglobulin
- C. Methylprednisolone
- D. Ceftriaxone + vancomycin
- E. Plasma exchange

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TTP - plasma exchange is first-line

This patient has thrombotic thrombocytopenic purpura, a condition associated with pregnancy

Thrombotic thrombocytopenic purpura: management

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine

Question 44 of 116

A 26-year-old man with a history of hereditary haemorrhagic telangiectasia is planning to start a family. What is the mode of inheritance?

- A. Autosomal dominant with incomplete penetrance
- B. Autosomal codominant
- C. Autosomal recessive with incomplete penetrance
- D. Autosomal dominant
- E. Autosomal recessive

Question 44 of 116

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Hereditary haemorrhagic telangiectasia - autosomal dominant

Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history

Features

- epistaxis
- telangiectasia develop is skin, mucous membranes and internal organs
- associated with pulmonary AV malformations and other AV malformations in 10%
- may present as iron-deficiency anaemia secondary to bleeding in the GI tract or nasal mucosa

Question 45 of 116

Which of the following is a cause of intravascular haemolysis?

- A. Hereditary spherocytosis
- B. Sickle cell anaemia
- C. Paroxysmal nocturnal haemoglobinuria
- D. Haemolytic disease of the newborn
- E. Warm autoimmune haemolytic anaemia

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- red cell fragmentation: heart valves, TTP, DIC, HUS
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Extravascular haemolysis: causes

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- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

Question 46 of 116

A 64-year-old man is reviewed in the haematology clinic. Which one of the following features would suggest that a diagnosis monoclonal gammopathy of undetermined significance is more likely than myeloma?

- A. Bone pain
- B. IgG paraprotein band = 18g/l
- C. Creatinine = 160 µmol/l
- D. Raised beta-2 microglobulin
- E. Lytic lesions on x-ray

Question 46 of 116

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- C. Creatinine = 160 µmol/l
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- E. Lytic lesions on x-ray

Paraproteinaemia is seen in both myeloma and monoclonal gammopathy of undetermined significance (MGUS) - at this level a diagnosis of MGUS is more likely. The other features indicate myeloma

MGUS

Monoclonal gammopathy of undetermined significance (MGUS, also known as benign paraproteinaemia and monoclonal gammopathy) is a common condition that causes a paraproteinaemia and is often mistaken for myeloma. Differentiating features are listed below. Around 10% of patients eventually develop myeloma at 5 years, with 50% at 15 years

Features

- usually asymptomatic
- no bone pain or increased risk of infections
- around 10-30% of patients have a demyelinating neuropathy

Differentiating features from myeloma

- normal immune function
- normal beta-2 microglobulin levels
- lower level of paraproteinaemia than myeloma (e.g. < 30g/l IgG, or < 20g/l IgA)
- stable level of paraproteinaemia
- no clinical features of myeloma (e.g. lytic lesions on x-rays or renal disease)

Question 47 of 116

A 54-year-old female is receiving a course of chemotherapy for breast cancer. She is experiencing troublesome vomiting which has not been helped by domperidone. What is the most appropriate next management step?

- A. Add an antihistamine
- B. Add a 5HT2 antagonist
- C. Add a phenothiazine
- D. Add a dopamine receptor antagonist
- E. Add a 5HT3 antagonist

Question 47 of 116

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- C. Add a phenothiazine
- D. Add a dopamine receptor antagonist
- E. Add a 5HT3 antagonist

Chemotherapy side-effects: nausea and vomiting

Nausea and vomiting are common side-effects of chemotherapy. Risk factors for the development of symptoms include:

- anxiety
- age less than 50 years old
- concurrent use of opioids
- the type of chemotherapy used

For patients at low-risk of symptoms then drugs such as metoclopramide may be used first-line. For high-risk patients then 5HT3 receptor antagonists such as ondansetron are often effective, especially if combined with dexamethasone

Question 48 of 116

Which of the following is a good prognostic factor in chronic lymphocytic leukaemia?

- A. Female sex
- B. Lymphocyte doubling time < 12 months
- C. CD38 expression positive
- D. Age > 70 years
- E. Raised LDH

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Chronic lymphocytic leukaemia: prognostic factors

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive

Question 49 of 116

What is the most common complication seen in patients with polycythaemia rubra vera?

- A. Chronic myeloid leukaemia
- B. Osteosarcoma
- C. Myelodysplasia
- D. Myelofibrosis
- E. Acute myeloid leukaemia

Question 49 of 116

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- D. Myelofibrosis
- E. Acute myeloid leukaemia

Polycythaemia rubra vera - around 30% progress to myelofibrosis

Whilst a significant percentage of patients (around 5-15%) develop an acute leukaemia, myelofibrosis is a more common transformation

Polycythaemia rubra vera: management

Polycythaemia rubra vera is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets.. It has peak incidence in the sixth decade, with typical features including hyperviscosity, pruritus and splenomegaly

Management

- venesection - first line treatment
- hydroxyurea -slight increased risk of secondary leukaemia
- phosphorus-32 therapy

Prognosis

- thrombotic events are a significant cause of morbidity and mortality
- 30% of patients progress to myelofibrosis
- 5-15% of patients progress to acute leukaemia

Question 50 of 116

Which one of the following is the most common type of Hodgkin's lymphoma?

- A. Lymphocyte predominant
- B. Nodular sclerosing
- C. Lymphocyte depleted
- D. Mixed cellularity
- E. Hairy cell

Question 50 of 116

Which one of the following is the most common type of Hodgkin's lymphoma?

- A. Lymphocyte predominant
- B. Nodular sclerosing
- C. Lymphocyte depleted
- D. Mixed cellularity
- E. Hairy cell

Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Histological classification
- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis
- weight loss > 10% in last 6 months
- fever > 38ºC
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:
- age = 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/µl or < 8%
- male
- albumin < 40 g/l
- white blood count = 15,000/µl

Question 51 of 116

A 45-year-old man known to have haemochromatosis attends for blood test to assess when he next needs venesection. Of the options given, which one of the following blood tests should be used to assess the adequacy of venesection?

- A. Ferritin
- B. Serum iron
- C. Haemoglobin
- D. Total iron binding capacity
- E. Haematocrit

Question 51 of 116

A 45-year-old man known to have haemochromatosis attends for blood test to assess when he next needs venesection. Of the options given, which one of the following blood tests should be used to assess the adequacy of venesection?

- A. Ferritin
- B. Serum iron
- C. Haemoglobin
- D. Total iron binding capacity
- E. Haematocrit

The British Committee for Standards in Haematology recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:

- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

Diagnostic tests

- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection

- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 52 of 116

A man is investigated for anaemia. A blood film is ordered and reported as follows:
Ring sideroblasts

Which one of the following is least likely to give this picture?

- A. Anti-tuberculosis medication
- B. Alcohol
- C. Pyridoxine
- D. Lead
- E. Myelodysplasia

Question 52 of 116

A man is investigated for anaemia. A blood film is ordered and reported as follows:
Ring sideroblasts

Which one of the following is least likely to give this picture?

- A. Anti-tuberculosis medication
- B. Alcohol
- C. Pyridoxine
- D. Lead
- E. Myelodysplasia

Pyridoxine is actually a treatment for sideroblastic anaemia. Rarely pyridoxine deficiency may be the cause

Sideroblastic anaemia

Sideroblastic anaemia is a condition where red cells fail to completely form haem, whose biosynthesis takes place partly in the mitochondrion. This leads to deposits of iron in the mitochondria that form a ring around the nucleus called a ring sideroblast. It may be congenital or acquired

Congenital cause: delta-aminolevulinate synthase-2 deficiency

Acquired causes
- myelodysplasia
- alcohol
- lead
- anti-TB medications

Investigations
- hypochromic microcytic anaemia (more so in congenital)
- bone marrow: sideroblasts and increased iron stores

Management
- supportive
- treat any underlying cause
- pyridoxine may help

Question 53 of 116

In idiopathic thrombocytopenic purpura what are the autoantibodies most commonly directed at?

- A. Platelet activating factor
- B. Glycoprotein IIb/IIIa complex
- C. ATP receptor
- D. Anti-thrombin III receptor
- E. ADP receptor

Question 53 of 116

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- E. ADP receptor

ITP

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex.

ITP can be divided into acute and chronic forms:

Acute ITP
- more commonly seen in children
- equal sex incidence
- may follow an infection or vaccination
- usually runs a self-limiting course over 1-2 weeks

Chronic ITP
- more common in young/middle-aged women
- tends to run a relapsing-remitting course

Evan's syndrome
- ITP in association with autoimmune haemolytic anaemia (AIHA)

Question 54 of 116

Burkitt's lymphoma is associated with a mutation in which one of the following genes?

- A. Cyclin D1 gene
- B. PML gene
- C. BCR-ABL gene
- D. RAR-alpha gene
- E. MYC gene

Question 54 of 116

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- A. Cyclin D1 gene
- B. PML gene
- C. BCR-ABL gene
- D. RAR-alpha gene
- E. MYC gene

Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome
- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)
- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)
- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)
- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

Question 55 of 116

Regarding the Ann-Arbor classification of Hodgkin's lymphoma, which one of the following would be staged as IIIB?

- A. Nodes on both sides of diaphragm with pruritus
- B. Two or more lymph nodes on the same side of the diaphragm with pruritus
- C. Nodes on both sides of diaphragm with night sweats
- D. Two or more lymph nodes on the same side of the diaphragm with night sweats
- E. Two or more lymph nodes on the same side of the diaphragm with no systemic symptoms

Question 55 of 116

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- D. Two or more lymph nodes on the same side of the diaphragm with night sweats
- E. Two or more lymph nodes on the same side of the diaphragm with no systemic symptoms

Hodgkin's lymphoma: staging

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Ann-Arbor staging of Hodgkin's lymphoma

- I: single lymph node
- II: 2 or more lymph nodes/regions on same side of diaphragm
- III: nodes on both sides of diaphragm
- IV: spread beyond lymph nodes

Each stage may be subdivided into A or B

- A = no systemic symptoms other than pruritus
- B = weight loss > 10% in last 6 months, fever > 38c, night sweats (poor prognosis)

Question 56 of 116

Which one of the following is not an indication for treatment in chronic lymphocytic leukaemia?

- A. Massive splenomegaly
- B. Platelet count of 77 * 10^9/l
- C. Night sweats
- D. Lymphocyte count of 65 * 10^9/l
- E. Extreme fatigue

Question 56 of 116

Which one of the following is not an indication for treatment in chronic lymphocytic leukaemia?

- A. Massive splenomegaly
- B. Platelet count of 77 * 10^9/l
- C. Night sweats
- D. Lymphocyte count of 65 * 10^9/l
- E. Extreme fatigue

The absolute lymphocyte count is not an indication for treatment, rather than the rate of increase (see guidelines below)

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 57 of 116

Each one of the following is associated with iron-deficiency anaemia, except:

- A. Atrophic glossitis
- B. Onycholysis
- C. Post-cricoid webs
- D. Koilonychia
- E. Angular stomatitis

Question 57 of 116

Each one of the following is associated with iron-deficiency anaemia, except:

- A. Atrophic glossitis
- B. Onycholysis
- C. Post-cricoid webs
- D. Koilonychia
- E. Angular stomatitis

Iron deficiency anaemia

Features
- koilonychia
- atrophic glossitis
- post-cricoid webs
- angular stomatitis

Blood film
- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

Question 58 of 116

A 35-year-old female who is 34 weeks pregnant presents with a swollen, painful right calf. A deep vein thrombosis is confirmed on Doppler scan. What is the preferred anticoagulant?

- A. Clopidogrel
- B. Aspirin
- C. Intravenous heparin
- D. Warfarin
- E. Subcutaneous low molecular weight heparin

Question 58 of 116

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- A. Clopidogrel
- B. Aspirin
- C. Intravenous heparin
- D. Warfarin
- E. Subcutaneous low molecular weight heparin

Although teratogenic effects of warfarin are greater in the first trimester most clinicians would use low molecular weight heparin in this situation. Another factor to consider is the risk of peripartum haemorrhage and potential problems reversing the effects of warfarin if this occurred

Pregnancy: DVT/PE

Overview
- pregnancy is a hypercoagulable state
- majority occur in last trimester

Pathophysiology
- increase in factors VII, VIII, X and fibrinogen
- decrease in protein S
- uterus presses on IVC causing venous stasis in legs

Management
- warfarin contraindicated
- S/C low-molecular weight heparin preferred to IV heparin (less bleeding and thrombocytopenia)

Question 59 of 116

What is the most common inherited bleeding disorder?

- A. Haemophilia A
- B. Activated protein C resistance
- C. Haemophilia B
- D. Antithrombin III deficiency
- E. von Willebrand's disease

Question 59 of 116

What is the most common inherited bleeding disorder?

- A. Haemophilia A
- B. Activated protein C resistance
- C. Haemophilia B
- D. Antithrombin III deficiency
- E. von Willebrand's disease

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 60 of 116

A 31-year-old man is referred to the acute medical unit with a painful swollen left leg. The patient reports that he has the 'Factor V Leiden mutation'. Which one of the following best describes the pathophysiology of his condition?

- A. Protein S deficiency
- B. Activated protein C excess
- C. Antithrombin deficiency
- D. Resistance to action of protein C
- E. Activated protein C deficiency

Question 60 of 116

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- B. Activated protein C excess
- C. Antithrombin deficiency
- D. Resistance to action of protein C
- E. Activated protein C deficiency

Factor V Leiden mutation results in activated protein C resistance

Activated protein C resistance

Activated protein C resistance is the most common inherited thrombophilia. It is due to a mutation in the Factor V Leiden gene. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Question 61 of 116

A 52-year-old is found to have chronic myeloid leukaemia following investigation for splenomegaly. Which one of the following best describes the function of the BCR-ABL fusion protein?

- A. Epidermal growth factor receptor
- B. Phospholipase C
- C. CD52 co-receptor
- D. Tyrosine kinase
- E. Fibroblast growth factor receptor

Question 61 of 116

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- B. Phospholipase C
- C. CD52 co-receptor
- D. Tyrosine kinase
- E. Fibroblast growth factor receptor

Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)
- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management
- hydroxyurea
- interferon-alpha
- imatinib
- allogenic bone marrow transplant

Imatinib
- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Question 62 of 116

A 73-year-old man is prescribed cetuximab after being diagnosed with metastatic colorectal cancer. What target is this monoclonal antibody directed against?

- A. Vascular endothelial growth factor receptor
- B. Angiopoietin-2 receptors
- C. CD20 protein complex
- D. Epidermal growth factor receptor
- E. Fibroblast growth factor receptor

Question 62 of 116

A 73-year-old man is prescribed cetuximab after being diagnosed with metastatic colorectal cancer. What target is this monoclonal antibody directed against?

- A. Vascular endothelial growth factor receptor
- B. Angiopoietin-2 receptors
- C. CD20 protein complex
- D. Epidermal growth factor receptor
- E. Fibroblast growth factor receptor

Cetuximab - monoclonal antibody against the epidermal growth factor receptor

Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from an human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

Question 63 of 116

A 18-year-old man who is known to have hereditary spherocytosis is admitted to hospital with lethargy. Admission bloods show the following:

Hb 4.7 g/dl

Retics 0.3%

What is the most likely explanation for these findings?

- A. Haemolytic crisis
- B. Recent ciprofloxacin therapy
- C. Parvovirus infection
- D. Sequestration crises
- E. Angiodysplastic bowel lesions

Question 63 of 116

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What is the most likely explanation for these findings?

- A. Haemolytic crisis
- B. Recent ciprofloxacin therapy
- C. Parvovirus infection
- D. Sequestration crises
- E. Angiodysplastic bowel lesions

This man has had an aplastic crisis secondary to parvovirus infection.

Hereditary spherocytosis

Basics
- most common hereditary haemolytic anaemia in northern Europeans
- autosomal dominant defect of RBC cytoskeleton
- biconcave disc --> spherocyte
- red cell survival reduced, destroyed by spleen

Presentation
- e.g. failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

Diagnosis
- osmotic fragility test

Management
- folate replacement
- splenectomy

Question 64 of 116

A 62-year-old man is called for review after a positive faecal occult blood test done as part of the national screening programme. During counselling for colonoscopy he asks what percentage of patients with a positive faecal occult blood test have colorectal cancer. What is the most accurate answer?

- A. 0.5 - 2%
- B. 5 - 15%
- C. 20 - 30%
- D. 30 - 50%
- E. 55 - 75%

Question 64 of 116

A 62-year-old man is called for review after a positive faecal occult blood test done as part of the national screening programme. During counselling for colonoscopy he asks what percentage of patients with a positive faecal occult blood test have colorectal cancer. What is the most accurate answer?

- A. 0.5 - 2%
- B. 5 - 15%
- C. 20 - 30%
- D. 30 - 50%
- E. 55 - 75%

Colorectal cancer screening - PPV of FOB = 5 - 15%

There is also a 30-45% chance of having an adenoma with a positive faecal occult blood test

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cance

Question 65 of 116

A 27-year-old male is receiving cyclophosphamide as part of his chemotherapy for non-Hodgkin' lymphoma. What is the most appropriate management to reduce the likelihood of haemorrhagic cystitis?

- A. Hydration + tranexamic acid
- B. Hydration + twice-daily bladder washouts
- C. Hydration + prophylactic antibiotics
- D. Hydration + twice-daily bladder washouts + prophylactic antibiotics
- E. Hydration + mesna

Question 65 of 116

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- C. Hydration + prophylactic antibiotics
- D. Hydration + twice-daily bladder washouts + prophylactic antibiotics
- E. Hydration + mesna

Cyclophosphamide - haemorrhagic cystitis - prevent with mesna

Cyclophosphamide may be converted to urotoxic metabolites such as acrolein. Mesna binds to these metabolites through its sulfhydryl-moieties and reduces the incidence of haemorrhagic cystitis

Cyclophosphamide

Cyclophosphamide is an alkylating agent used in the management of cancer and autoimmune conditions. It works by causing cross-linking of DNA

Adverse effects

- haemorrhagic cystitis: incidence reduced by the use of hydration and mesna
- myelosuppression
- transitional cell carcinoma

Question 66 of 116

A 35-year-old woman presents with menorrhagia and a persistent sore throat. A full blood count shows her to be pancytopenic. Which one of the following medications is most likely to account for this finding?

- A. Trimethoprim
- B. Rifampicin
- C. Olanzapine
- D. Montelukast
- E. Clomifene

Question 66 of 116

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- A. Trimethoprim
- B. Rifampicin
- C. Olanzapine
- D. Montelukast
- E. Clomifene

Drug-induced pancytopaenia

Drug causes of pancytopaenia

- cytotoxics
- antibiotics: trimethoprim, chloramphenicol
- anti-rheumatoid: gold, penicillamine
- carbimazole*
- anti-epileptics: carbamazepine
- sulphonylureas: tolbutamide

*causes both agranulocytosis and pancytopaenia

Question 67 of 116

A 74-year-old woman with a past history of chronic lymphocytic leukaemia presents with lethargy. The following blood results are obtained:

Hb	7.9 g/dl
Plt	158 * 10^9/l
WCC	24.0 * 10^9/l

Blood film: normochromic, normocytic anaemia

What complication has most likely occurred?

- A. Paroxysmal nocturnal haemoglobinuria
- B. Microangiopathic haemolytic anaemia
- C. Sideroblastic anaemia
- D. Warm autoimmune haemolytic anaemia
- E. Cold autoimmune haemolytic anaemia

Question 67 of 116

A 74-year-old woman with a past history of chronic lymphocytic leukaemia presents with lethargy. The following blood results are obtained:

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Plt	158 * 10^9/l
WCC	24.0 * 10^9/l

Blood film: normochromic, normocytic anaemia

What complication has most likely occurred?

- A. Paroxysmal nocturnal haemoglobinuria
- B. Microangiopathic haemolytic anaemia
- C. Sideroblastic anaemia
- D. Warm autoimmune haemolytic anaemia
- E. Cold autoimmune haemolytic anaemia

Warm autoimmune haemolytic anaemia occurs in around 10-15% of patients with chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 68 of 116

A 54-year-old woman presents to the Emergency Department with a five day history of back pain. Her past medical history includes breast cancer and osteoarthritis. The back pain is located in the lower thoracic region and is made worse by coughing and sneezing. There has been no change in bowel habit or urinary symptoms. On examination there is diffuse tenderness in the lower thoracic region. Peri-anal sensation is normal and lower limb reflexes are brisk. Which one of the following is the most appropriate management plan?

- A. Organise outpatient MRI
- B. Oral paracetamol + urgent MRI
- C. Oral paracetamol + urgent thoracic/lumbar spine x-ray
- D. Oral dexamethasone + urgent thoracic/lumbar spine x-ray
- E. Oral dexamethasone + urgent MRI

Question 68 of 116

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- C. Oral paracetamol + urgent thoracic/lumbar spine x-ray
- D. Oral dexamethasone + urgent thoracic/lumbar spine x-ray
- E. Oral dexamethasone + urgent MRI

This woman has spinal cord compression until proven otherwise and should have urgent assessment.

Recent NICE guidelines suggest contacting the local metastatic spinal cord compression coordinator in this situation. This should hopefully prevent delays in treatment by ensuring the patient is admitted to the most appropriate place

Spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. It is more common in patients with lung, breast and prostate cancer

Features

- back pain: may be worse on lying down and coughing
- neurological signs depend on the level of the lesion. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

Management

- high-dose oral dexamethasone
- urgent oncological assessment for consideration of radiotherapy or surgery

Question 69 of 116

What is the most useful marker of prognosis in myeloma?

- A. Calcium level
- B. Urine Bence-Jones protein levels
- C. Alkaline phosphotase
- D. ESR
- E. B2-microglobulin

Question 69 of 116

What is the most useful marker of prognosis in myeloma?

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- D. ESR
- E. B2-microglobulin

Myeloma: prognosis

B2-microglobulin is a useful marker of prognosis - raised levels imply poor prognosis. Low levels of albumin are also associated with a poor prognosis

International prognostic index

Stage	Criteria	Median survival (months)
I	B2 microglobulin < 3.5 mg/l Albumin > 35 g/l	62
II	Not I or III	45
III	B2 microglobulin > 5.5 mg/l	29

Question 70 of 116

A 61-year-old presents for review. She has been having atypical lower back pain for the past two months. An x-ray of her lumbar spine reported raised the possibility of spinal metastases but there is no current evidence of a primary tumour. A series of tumour markers were sent. Which one of the following is most associated with raised levels of CA 15-3?

- A. Pancreatic cancer
- B. Colorectal cancer
- C. Breast cancer
- D. Ovarian cancer
- E. Hepatocellular carcinoma

Question 70 of 116

A 61-year-old presents for review. She has been having atypical lower back pain for the past two months. An x-ray of her lumbar spine reported raised the possibility of spinal metastases but there is no current evidence of a primary tumour. A series of tumour markers were sent. Which one of the following is most associated with raised levels of CA 15-3?

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- D. Ovarian cancer
- E. Hepatocellular carcinoma

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 71 of 116

A woman is prescribed docetaxel as part of her chemotherapy for breast cancer. What is the mechanism of action of docetaxel?

- A. Inhibits RNA synthesis
- B. Stabilizes DNA-topoisomerase II complex
- C. Prevents microtubule disassembly
- D. Inhibits formation of microtubules
- E. Causes cross-linking in DNA

Question 71 of 116

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- D. Inhibits formation of microtubules
- E. Causes cross-linking in DNA

Taxanes (e.g. Docetaxel) prevent microtubule disassembly

Like other taxanes the principal mechanism of action is the prevention of microtubule disassembly.

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 72 of 116

Which one of the following haematological malignancies is most commonly associated with the t(11;14) translocation?

- A. Acute promyelocytic leukaemia
- B. Burkitt's lymphoma
- C. Acute lymphoblastic leukaemia
- D. Mantle cell lymphoma
- E. Chronic myeloid leukaemia

Question 72 of 116

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- D. Mantle cell lymphoma
- E. Chronic myeloid leukaemia

Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome
- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)
- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)
- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)
- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

Question 73 of 116

A 30-year-old man enquires about screening for haemochromatosis as his brother was diagnosed with the condition 2 years ago. The patient is currently well with no features suggestive of haemochromatosis. What is the most appropriate investigation?

- A. Serum total iron-binding capacity
- B. HFE gene analysis
- C. Serum transferrin saturation
- D. Serum ferritin
- E. Serum iron

Question 73 of 116

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- B. HFE gene analysis
- C. Serum transferrin saturation
- D. Serum ferritin
- E. Serum iron

Screening for haemochromatosis
- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

Serum transferrin saturation is currently the preferred investigation for population screening. However, the patient has a sibling with haemochromatosis and therefore HFE gene analysis is the most suitable investigation. In clinical practice this would be combined with iron studies as well

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:
- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive
Diagnostic tests
- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis
- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection
- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 74 of 116

A patient presents as she has a strong family history of cancer. Which one of the following cancers is least likely to be inherited?

- A. Colorectal cancer
- B. Breast cancer
- C. Gastric cancer
- D. Endometrial cancer
- E. Ovarian cancer

Question 74 of 116

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- E. Ovarian cancer

Between 5 and 10% of all breast cancers are thought to be hereditary. Mutation in the BRCA1 and BRCA2 genes also increase the risk of ovarian cancer. For colorectal cancer around 5% of cases are caused by hereditary non-polyposis colorectal carcinoma (HNPCC) and 1% are due to familial adenomatous polyposis. Women who have HNPCC also have a markedly increased risk for developing endometrial cancer - around 5% of endometrial cancers occur in women with this risk factor.

Cancer in the UK

The most common causes of cancer in the UK are as follows*

- 1. Breast
- 2. Lung
- 3. Colorectal
- 4. Prostate
- 5. Bladder
- 6. Non-Hodgkin's lymphoma
- 7. Melanoma
- 8. Stomach
- 9. Oesophagus
- 10. Pancreas

The most common causes of death from cancer in the UK are as follows:

- 1. Lung
- 2. Colorectal
- 3. Breast
- 4. Prostate
- 5. Oesophagus
- 6. Stomach
- 7. Bladder
- 8. Non-Hodgkin's lymphoma
- 9. Ovarian
- 10. Leukaemia

*excludes non-melanoma skin cancer

Question 75 of 116

Which one of the following is least associated with small cell lung cancer?

- A. Bad prognosis
- B. Cushing's syndrome
- C. PTH-related peptide secretion
- D. Hyponatraemia
- E. Lambert-Eaton syndrome

Question 75 of 116

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- B. Cushing's syndrome
- C. PTH-related peptide secretion
- D. Hyponatraemia
- E. Lambert-Eaton syndrome

Paraneoplastic features of lung cancer
- squamous cell: PTHrp, clubbing, HPOA
- small cell: ADH, ACTH, Lambert-Eaton syndrome

PTH-related peptide secretion is seen in squamous cell lung cancer

Lung cancer: small cell

Features
- usually central
- arise from APUD* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome
- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

Management
- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- radiotherapy: only used for debulking
- chemotherapy: good response to combination chemotherapy, may extend life by approximately 4 months

*an acronym for
- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

Question 76 of 116

Which one of the following is least associated with thrombocytopenia?

- A. Heparin therapy
- B. Rheumatoid arthritis
- C. Infectious mononucleosis
- D. Liver disease
- E. Pregnancy

Question 76 of 116

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Rheumatoid arthritis, unlike systemic lupus erythematous, is generally associated with a thrombocytosis. In some cases of Felty's syndrome thrombocytopaenia may be seen secondary to hypersplenism. This however represents a small percentage of patients with rheumatoid arthritis

Thrombocytopenia

Causes of severe thrombocytopenia

- ITP
- DIC
- TTP
- haematological malignancy

Causes of moderate thrombocytopenia

- heparin induced thrombocytopenia (HIT)
- drug-induced (e.g. quinine, diuretics, sulphonamides, aspirin, thiazides)
- alcohol
- liver disease
- hypersplenism
- viral infection (EBV, HIV, hepatitis)
- pregnancy
- SLE/antiphospholipid syndrome
- vitamin B12 deficiency

Question 77 of 116

Which one of the following is least associated with eosinophilia?

- A. Churg-Strauss syndrome
- B. Nematode infection
- C. Histoplasmosis
- D. Allergic bronchopulmonary aspergillosis
- E. Asthma

Question 77 of 116

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- D. Allergic bronchopulmonary aspergillosis
- E. Asthma

Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes
- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Loffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes
- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes
- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

Question 78 of 116

Which one of the following therapeutic options is least recognised in the treatment of aplastic anaemia?

- A. Interferon-alpha
- B. Stem cell transplantation
- C. Anti-lymphocyte globulin
- D. Anti-thymocyte globulin
- E. Platelet transfusion

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- D. Anti-thymocyte globulin
- E. Platelet transfusion

Aplastic anaemia: management

Supportive
- blood products
- prevention and treatment of infection

Anti-thymocyte globulin (ATG) and anti-lymphocyte globulin (ALG)
- prepared in animals (e.g. rabbits or horses) by injecting human lymphocytes
- is highly allergenic and may cause serum sickness (fever, rash, arthralgia), therefore steroid cover usually given
- immunosuppression using agents such as ciclosporin may also be given

Stem cell transplantation
- allogeneic transplants have a success rate of up to 80%

Question 79 of 116

Which one of the following is least recognised as a treatment modality in idiopathic thrombocytopenic purpura?

- A. Plasma exchange
- B. Splenectomy
- C. IV immunoglobulin
- D. Cyclophosphamide
- E. Oral prednisolone

Question 79 of 116

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- C. IV immunoglobulin
- D. Cyclophosphamide
- E. Oral prednisolone

ITP: investigation and management

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

Investigations

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

Management

- oral prednisolone (80% of patients respond)
- splenectomy if platelets < 30 after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide

Question 80 of 116

Which of the following factors is associated with a good prognosis in acute myeloid leukaemia?

- A. Translocation between chromosome 9 and 14
- B. Translocation between chromosome 15 and 17
- C. 25% blast following first course of chemotherapy
- D. Deletion of chromosome 5
- E. Deletion of chromosome 7

Question 80 of 116

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- D. Deletion of chromosome 5
- E. Deletion of chromosome 7

Acute myeloid leukaemia - good prognosis: t(15;17)

A translocation between chromosome 15 and 17 is seen in acute promyelocytic leukaemia, which is known to carry a good prognosis

Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features
- > 60 years
- > 20% blasts after first course of chemo
- cytogenics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3
- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)
- MO - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

Question 81 of 116

A 72-year-old man is diagnosed with prostate cancer and goserelin (Zoladex) is prescribed. Which one of the following is it most important to co-prescribe for the first two weeks of treatment?

- A. Tamoxifen
- B. Lansoprazole
- C. Allopurinol
- D. Cyproterone acetate
- E. Tamsulosin

Question 81 of 116

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- C. Allopurinol
- D. Cyproterone acetate
- E. Tamsulosin

Anti-androgen treatment such as cyproterone acetate should be co-prescribed when starting gonadorelin analogues due to the risk of tumour flare. This phenomenon is secondary to initial stimulation of luteinising hormone release by the pituitary gland resulting in increased testosterone levels.

Prostate cancer: management

Localised prostate cancer (T1/T2)
Treatment depends on life expectancy and patient choice. Options include:

- conservative: active monitoring & watchful waiting
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Localised advanced prostate cancer (T3/T4)
Options include:

- hormonal therapy: see below
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Metastatic prostate cancer disease - hormonal therapy
Synthetic GnRH agonist

- e.g. Goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen

- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Orchidectomy

Question 82 of 116

A 43-year-old woman is about to start treatment with trastuzumab for metastatic breast cancer. What is the most important investigation to perform prior to initiating treatment?

- A. Pulmonary function tests
- B. Echo
- C. Liver function tests
- D. Chest x-ray
- E. Glucose tolerance test

Question 82 of 116

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- B. Echo
- C. Liver function tests
- D. Chest x-ray
- E. Glucose tolerance test

Trastuzumab (Herceptin) - cardiac toxicity is common

Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Question 83 of 116

Each one of the following is associated with hyposplenism, except:

- A. Sickle-cell anaemia
- B. Liver cirrhosis
- C. Systemic lupus erythematous
- D. Coeliac disease
- E. Splenectomy

Question 83 of 116

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- D. Coeliac disease
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Hyposplenism

Causes
- splenectomy
- sickle-cell
- coeliac disease, dermatitis herpetiformis
- Graves' disease
- systemic lupus erythematosus
- amyloid

Features
- Howell-Jolly bodies
- siderocytes

Question 84 of 116

Which one of the following is least associated with hepatocellular carcinoma?

- A. Hepatitis C
- B. Primary biliary cirrhosis
- C. Aflatoxin
- D. Wilson's disease
- E. Haemochromatosis

Question 84 of 116

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Hepatocellular carcinoma

Risk factors
- hepatitis B and C
- cirrhosis*: alcohol, haemochromatosis, primary biliary cirrhosis
- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda

*Wilson's disease is an exception

Question 85 of 116

Which one of the following haematological disorders is most associated with gingival hyperplasia?

- A. Chronic lymphocytic leukaemia
- B. Myelofibrosis
- C. Polycythaemia rubra vera
- D. Haemophilia A
- E. Acute myeloid leukaemia

Question 85 of 116

Which one of the following haematological disorders is most associated with gingival hyperplasia?

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- C. Polycythaemia rubra vera
- D. Haemophilia A
- E. Acute myeloid leukaemia

Gingival hyperplasia: phenytoin, ciclosporin, calcium channel blockers and AML

Gingival hyperplasia

Drug causes of gingival hyperplasia
- phenytoin
- ciclosporin
- calcium channel blockers (especially nifedipine)

Other causes of gingival hyperplasia include
- acute myeloid leukaemia (myelomonocytic and monocytic types)

Question 86 of 116

Which electrolyte disturbance is cisplatin most associated with?

- A. Hypocalcaemia
- B. Hyponatraemia
- C. Hypomagnesaemia
- D. Hypokalaemia
- E. Hypercalcaemia

Question 86 of 116

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- B. Hyponatraemia
- C. Hypomagnesaemia
- D. Hypokalaemia
- E. Hypercalcaemia

Cisplatin is associated with hypomagnesaemia

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 87 of 116

A 54-year-old woman who has had a hysterectomy presents for advice about hormone replacement therapy. Which one of the following would result from the use of a combined oestrogen-progestogen preparation compared to an oestrogen-only preparation?

- A. Decreased risk of venous thromboembolism
- B. Increased risk of a stroke
- C. Increased risk of breast cancer
- D. Increased risk of endometrial cancer
- E. Better control of symptoms

Question 87 of 116

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- D. Increased risk of endometrial cancer
- E. Better control of symptoms

HRT: adding a progestogen increases the risk of breast cancer

This is the rationale behind giving women who've had a hysterectomy oestrogen-only treatment

Hormone replacement therapy: adverse effects

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen (combined with a progestogen in women with a uterus) to help alleviate menopausal symptoms.

Side-effects
- nausea
- breast tenderness
- fluid retention and weight gain

Potential complications
- increased risk of breast cancer: increased by the addition of a progestogen
- increased risk of endometrial cancer: reduced by the addition of a progestogen but not eliminated completely. The BNF states that the additional risk is eliminated if a progestogen is given continuously
- increased risk of venous thromboembolism: increased by the addition of a progestogen

Breast cancer
- in the Women's Health Initiative (WHI) study there was a relative risk of 1.26 at 5 years of developing breast cancer
- the increased risk relates to duration of use
- breast cancer incidence is higher in women using combined preparations compared to oestrogen-only preparations
- the risk of breast cancer begins to decline when HRT is stopped and by 5 years it reaches the same level as in women who have never taken HRT

Question 88 of 116

Of the following options, which one is the best diagnostic test for paroxysmal nocturnal haemoglobinuria?

- A. Osmotic fragility test
- B. FMC-7 staining
- C. PAS staining of erythrocytes
- D. Flow cytometry for CD59 and CD55
- E. Immunophenotyping for CD19 and CD20

Question 88 of 116

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- C. PAS staining of erythrocytes
- D. Flow cytometry for CD59 and CD55
- E. Immunophenotyping for CD19 and CD20

Flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology
- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features
- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopaenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis
- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management
- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation

Question 89 of 116

A 66-year-old woman is referred by her GP with anaemia. She has been feeling generally unwell for the past 3 weeks. Bloods on admission show:

Hb 8.7 g/dl

MCV 87 fl

Plt 198 * 10^9/l

WBC 5.3 * 10^9/l

Further tests were then ordered:

Reticulocytes	5.2%l
Direct antiglobulin test	Positive, C3d only
Film	Marked red cell agglutination at room temperature

Which one of the following is the most likely underlying cause?

- A. Non-Hodgkin's lymphoma
- B. Mycoplasma pneumonia
- C. Chronic myeloid leukaemia
- D. Acute myeloid leukaemia subtype M3
- E. Cytomegalovirus infection

Question 89 of 116

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- E. Cytomegalovirus infection

The blood results suggest warm autoimmune haemolytic anaemia (AIHA) which may be caused by non-Hodgkin's lymphoma. Mycoplasma pneumonia is associated with cold AIHA. The other three listed conditions are not commonly associated with AIHA.

Autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia (AIHA) may be divided in to 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

Warm AIHA

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyldopa

Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Question 90 of 116

Which one of the following is least associated with thymomas?

- A. Syndrome inappropriate ADH
- B. Myasthenia gravis
- C. Red cell aplasia
- D. Dermatomyositis
- E. Motor neurone disease

Question 90 of 116

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- D. Dermatomyositis
- E. Motor neurone disease

Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with
- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death
- compression of airway
- cardiac tamponade

Question 91 of 116

Which one of the following is not a risk factor for the development of bladder cancer?

- A. Occupational exposure to aniline dyes
- B. Cyclophosphamide
- C. Strongyloides infection
- D. Smoking
- E. Occupational history involving rubber manufacture

Question 91 of 116

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- B. Cyclophosphamide
- C. Strongyloides infection
- D. Smoking
- E. Occupational history involving rubber manufacture

Schistosomiasis rather than Strongyloides infection is associated with an increased risk of bladder cancer

Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

Question 92 of 116

Which one of the following is the most common inherited thrombophilia?

- A. Protein S deficiency
- B. Antithrombin III deficiency
- C. Protein C deficiency
- D. Activated protein C resistance
- E. Von Willebrand's disease

Question 92 of 116

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- C. Protein C deficiency
- D. Activated protein C resistance
- E. Von Willebrand's disease

Activated protein C resistance (Factor V Leiden) is the most common inherited thrombophilia

Activated protein C resistance is due a point mutation in the Factor V gene, encoding for the Leiden allele. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Von Willebrand's disease is the most common inherited bleeding disorder

Thrombophilia: causes

Inherited
- activated protein C resistance (factor V Leiden)
- antithrombin III deficiency
- protein C deficiency
- protein S deficiency

Acquired
- antiphospholipid syndrome
- the Pill

Question 93 of 116

A 67-year-old man is investigated for dyspepsia. A gastroscopy reveals a suspicious lesion which is biopsied. Which one of the following findings on biopsy would be most consistent with a diagnosis of gastric adenocarcinoma?

- A. Columnar metaplasia
- B. Histiocytic infiltration
- C. Paneth cell metaplasia
- D. Giant cell granulomas
- E. Signet ring cells

Question 93 of 116

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- C. Paneth cell metaplasia
- D. Giant cell granulomas
- E. Signet ring cells

Gastric adenocarcinoma - signet ring cells

Gastric cancer

Epidemiology
- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Columbia than the West
- more common in males, 2:1

Associations
- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

Investigation
- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Question 94 of 116

A 48-year-old female who has just completed a course of chemotherapy complains of difficulty using her hands associated with 'pins and needles'. She has also experienced urinary hesitancy. Which cytotoxic drug is most likely to be responsible?

- A. Doxorubicin
- B. Cyclophosphamide
- C. Methotrexate
- D. Vincristine
- E. Bleomycin

Question 94 of 116

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- D. Vincristine
- E. Bleomycin

Vincristine is associated with peripheral neuropathy. Urinary hesitancy may develop secondary to bladder atony.

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 95 of 116

A 28-year-old man is investigated for cervical lymphadenopathy. A biopsy shows nodular sclerosing Hodgkin's lymphoma. Which one of the following factors is associated with a poor prognosis?

- A. History of Epstein Barr virus infection
- B. Mediastinal involvement
- C. Female sex
- D. Night sweats
- E. Lymphocytes 20% of total white blood cells

Question 95 of 116

A 28-year-old man is investigated for cervical lymphadenopathy. A biopsy shows nodular sclerosing Hodgkin's lymphoma. Which one of the following factors is associated with a poor prognosis?

- A. History of Epstein Barr virus infection
- B. Mediastinal involvement
- C. Female sex
- D. Night sweats
- E. Lymphocytes 20% of total white blood cells

Night sweats are a 'B' symptom and imply a poor prognosis

Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Histological classification

- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis

- weight loss > 10% in last 6 months
- fever > 38ºC
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:

- age = 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/µl or < 8%
- male
- albumin < 40 g/l
- white blood count = 15,000/µl

Question 96 of 116

A 24-year-old man is diagnosed with a deep vein thrombosis of his right leg. He is initially treated with low-molecular weight heparin but is switched after three days to warfarin. He then develops necrotic skin lesions on his lower limbs and forearms. Which one of the following conditions is characteristically associated with this complication?

- A. Protein S deficiency
- B. Antiphospholipid syndrome
- C. Antithrombin III deficiency
- D. Activated protein C resistance
- E. Protein C deficiency

Question 96 of 116

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- C. Antithrombin III deficiency
- D. Activated protein C resistance
- E. Protein C deficiency

Protein C deficiency

Protein C deficiency is an autosomal codominant condition which causes an increased risk of thrombosis

Features

- venous thromboembolism
- skin necrosis following the commencement of warfarin: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

Question 97 of 116

A 71-year-old woman with no significant past medical history is investigated for lymphocytosis. She has recently lost 7kg in weight and complains of lethargy. The following blood results are obtained:

Hb	9.8 g/dl
Plt	104 * 10^9/l
WBC	70.3 * 10^9/l
Blood film:	Lymphocytosis. Smudge cells seen

Four months previously her white cell count was 30.5 * 10^9/l. What is the most appropriate management?

- A. Imatinib
- B. Cyclophosphamide
- C. No treatment, monitor full blood count
- D. Chlorambucil
- E. Rituximab

Question 97 of 116

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- D. Chlorambucil
- E. Rituximab

CLL - treatment - chlorambucil

This patient has chronic lymphocytic leukaemia. The lymphocyte doubling time is less than 6 months, the patient has some evidence of marrow failure and also has systemic symptoms. She should therefore be treated and of the options given chlorambucil is the most appropriate treatment. As with many haematological cancers such patients are often entered into randomised trials

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 98 of 116

A 17-year-old man is investigated after he bled excessively following a tooth extraction. The following results are obtained:

Plt 173 * 10^9/l

PT 12.9 secs

APTT 84 secs

Which clotting factor is he most likely to be deficient in?

- A. Factor VI
- B. Factor VII
- C. Factor VIII
- D. Factor IX
- E. Factor X

Question 98 of 116

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Plt 173 * 10^9/l

PT 12.9 secs

APTT 84 secs

Which clotting factor is he most likely to be deficient in?

- A. Factor VI
- B. Factor VII
- C. Factor VIII
- D. Factor IX
- E. Factor X

This man is most likely to have haemophilia A, which accounts for 90% of cases of haemophilia.

Haemophilia

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

Features
- haemoarthroses, haematomas
- prolonged bleeding after surgery or trauma

Blood tests
- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

Question 99 of 116

A 25-year-old woman with primary antiphospholipid syndrome is reviewed. She has just had a booking ultrasound which confirms a viable pregnancy. This is her first pregnancy and she is otherwise fit and well. Which one of the following is the recommend treatment?

- A. Aspirin + prednisolone
- B. Low-molecular weight heparin
- C. Prednisolone + low-molecular weight heparin
- D. Aspirin + low-molecular weight heparin
- E. Aspirin

Question 99 of 116

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- B. Low-molecular weight heparin
- C. Prednisolone + low-molecular weight heparin
- D. Aspirin + low-molecular weight heparin
- E. Aspirin

Antiphospholipid syndrome in pregnancy: aspirin + LMWH

Antiphospholipid syndrome: pregnancy

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

Question 100 of 116

What is the lifetime risk of developing colorectal cancer in the United Kingdom?

- A. 1%
- B. 2%
- C. 5%
- D. 10%
- E. 15%

Question 100 of 116

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- B. 2%
- C. 5%
- D. 10%
- E. 15%

Colorectal cancer is the third most common cancer in the UK, with approximately 30,000 new cases in England and Wales per year

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Question 101 of 116

A 34-year-old man is reviewed four years after having an orchidectomy for a testicular teratoma. What are the most useful follow-up investigation(s) to detecf disease recurrence?

- A. CRP + beta-HCG
- B. Testosterone + beta-HCG
- C. ESR + alpha-fetoprotein
- D. Alpha-fetoprotein + beta-HCG
- E. LDH + ESR

Question 101 of 116

A 34-year-old man is reviewed four years after having an orchidectomy for a testicular teratoma. What are the most useful follow-up investigation(s) to detecf disease recurrence?

- A. CRP + beta-HCG
- B. Testosterone + beta-HCG
- C. ESR + alpha-fetoprotein
- D. Alpha-fetoprotein + beta-HCG
- E. LDH + ESR

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 102 of 116

A 34-year-old man who is known to have type 1 von Willebrand's disease asks for advice. He is due to have a tooth extracted at the dentist next week. Which one of the following is the most appropriate management to reduce the risk of bleeding?

- A. Mefanamic acid
- B. Vitamin K
- C. Desmopressin
- D. Factor VIII concentrate
- E. Factor VII concentrate

Question 102 of 116

A 34-year-old man who is known to have type 1 von Willebrand's disease asks for advice. He is due to have a tooth extracted at the dentist next week. Which one of the following is the most appropriate management to reduce the risk of bleeding?

- A. Mefanamic acid
- B. Vitamin K
- C. Desmopressin
- D. Factor VIII concentrate
- E. Factor VII concentrate

Blood products such as factor VIII concentrate should be avoided when possible to minimise the risk of transfusion acquired viral illnesses.

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types

- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 103 of 116

A 67-year-old woman is diagnosed with multiple myeloma. Which one of the following complications is she most likely to develop as a result of her primary diagnosis?

- A. Renal failure
- B. Venous thromboembolism
- C. Hypercalcaemia
- D. Carpal tunnel syndrome
- E. Pathological fracture

Question 103 of 116

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- A. Renal failure
- B. Venous thromboembolism
- C. Hypercalcaemia
- D. Carpal tunnel syndrome
- E. Pathological fracture

This is a difficult question as all of the above may be seen with myeloma. However, up to 60% of patients will develop a pathological fracture.

Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 104 of 116

Patients with Sjogren's syndrome are at an increased risk of which one of the following malignancies?

- A. Myeloma
- B. Oesophageal cancer
- C. Intraocular melanoma
- D. Squamous cell skin cancer
- E. Non-Hodgkin's lymphoma

Question 104 of 116

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- B. Oesophageal cancer
- C. Intraocular melanoma
- D. Squamous cell skin cancer
- E. Non-Hodgkin's lymphoma

Patients with Sjogren's syndrome have an increased risk of lymphoid malignancies

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features
- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation
- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management
- artificial saliva and tears
- pilocarpine may stimulate saliva production

Question 105 of 116

A 48-year-old man is diagnosed with acute myeloid leukaemia and cytogenics are performed. Which one of the following is associated most with a poor prognosis?

- A. Deletions of chromosome 5
- B. Translocation between chromosome 15 and 17
- C. Deletions of chromosome 15
- D. Translocation between chromosome 9 and 14
- E. Deletions of chromosome 8

Question 105 of 116

A 48-year-old man is diagnosed with acute myeloid leukaemia and cytogenics are performed. Which one of the following is associated most with a poor prognosis?

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- B. Translocation between chromosome 15 and 17
- C. Deletions of chromosome 15
- D. Translocation between chromosome 9 and 14
- E. Deletions of chromosome 8

Acute myeloid leukaemia - poor prognosis: deletion of chromosome 5 or 7

Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features
- > 60 years
- > 20% blasts after first course of chemo
- cytogenics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3
- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)
- MO - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

Question 106 of 116

A 77-year-old man with a history of chronic lymphocytic leukaemia is admitted to the Acute Medical Unit with pneumonia. This is his fourth admission for pneumonia in the past six months. Which one of the following factors is most likely to be responsible?

- A. Hypersplenism
- B. Decreased lymphocyte survival
- C. Hypogammaglobulinaemia
- D. Transformation to high-grade lymphoma
- E. Immature lymphocytes

Question 106 of 116

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- C. Hypogammaglobulinaemia
- D. Transformation to high-grade lymphoma
- E. Immature lymphocytes

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 107 of 116

A patient with metastatic cancer asks to be switched from MST 90 mg bd to fentanyl patches. What is the equivalent number of patches which should be applied?

- A. Half a fentanyl '25' patch
- B. One fentanyl '25' patch
- C. One fentanyl '50' patch
- D. One fentanyl '75' patch
- E. One fentanyl '100' patch

Question 107 of 116

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- D. One fentanyl '75' patch
- E. One fentanyl '100' patch

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 108 of 116

Which one of the following is associated with a high leucocyte alkaline phosphatase score?

- A. Myelofibrosis
- B. Pernicious anaemia
- C. Infectious mononucleosis
- D. Paroxysmal nocturnal haemoglobinuria
- E. Chronic myeloid leukaemia

Question 108 of 116

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Leucocyte alkaline phosphatase

Raised in
- myelofibrosis
- leukaemoid reactions
- polycythaemia rubra vera
- infections
- steroids, Cushing's syndrome
- pregnancy, oral contraceptive pill

Low in
- chronic myeloid leukaemia
- pernicious anaemia
- paroxysmal nocturnal haemoglobinuria
- infectious mononucleosis

uestion 109 of 116

Which one of the following features is least associated with Waldenstrom's macroglobulinaemia?

- A. Cryoglobulinaemia
- B. Bone pain
- C. Retinal vein thrombosis
- D. Hepatosplenomegaly
- E. Monoclonal IgM paraproteinaemia

Question 109 of 116

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- D. Hepatosplenomegaly
- E. Monoclonal IgM paraproteinaemia

Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Question 110 of 116

A 17-year-old male is diagnosed with alpha-thalassaemia. What chromosome is the alpha-globulin genes located on?

- A. Chromosome 4
- B. Chromosome 8
- C. Chromosome 12
- D. Chromosome 16
- E. Chromosome 20

Question 110 of 116

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- C. Chromosome 12
- D. Chromosome 16
- E. Chromosome 20

Alpha-thalassaemia

Alpha-thalassaemia is due to a deficiency of alpha chains in haemoglobin

Overview
- 2 separate alpha-globulin genes are located on each chromosome 16

Clinical severity depends on the number of alpha chains present

If 1 or 2 alpha chains are absent then the blood picture would be hypochromic and microcytic, but the Hb level would be typically normal

Loss of 3 alpha chains results in a hypochromic microcytic anaemia with splenomegaly. This is known as Hb H disease

If all 4 alpha chains absent (i.e. homozygote) then death in utero (hydrops fetalis, Bart's hydrops)

Question 111 of 116

A 71-year-old woman with metastatic breast cancer comes to surgery with her husband. She is known to have spinal metastases but her back pain is not controlled with a combination of paracetamol, diclofenac and MST 30mg bd. Her husband reports she is using 10mg of oral morphine solution around 6-7 times a day for breakthrough pain. The palliative care team at the hospice tried using a bisphosphonate but this unfortunately resulted in persistent myalgia and arthralgia. What is the most appropriate next step?

- A. Switch to oxycodone
- B. Increase MST
- C. Increase MST + add dexamethasone
- D. Increase MST + suggest course of complimentary therapies
- E. Increase MST + refer for radiotherapy

Question 111 of 116

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Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Palliative care prescribing: pain

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- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
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Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

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From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 112 of 116

Interferon alpha is a recognised treatment for which one of the following haematological disorders?

- A. Acute lymphoblastic leukaemia
- B. Myelofibrosis
- C. Burkitt's lymphoma
- D. Hairy cell leukaemia
- E. Acute myeloid leukaemia

Question 112 of 116

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- C. Burkitt's lymphoma
- D. Hairy cell leukaemia
- E. Acute myeloid leukaemia

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha is produced by leucocytes and has an antiviral action. It has been shown to be useful in the management of hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer and hairy cell leukaemia

Hairy cell leukaemia

Hairy cell leukaemia is a rare malignant proliferation disorder of B cells. It is more common in males (4:1)

Features

- pancytopenia
- splenomegaly
- skin vasculitis in 1/3 patients
- 'dry tap' despite bone marrow hypercellularity
- tartrate resistant acid phosphotase (TRAP) stain positive

Management

- chemotherapy is first-line: cladribine, pentostatin
- immunotherapy is second-line: rituximab, interferon-alpha

Question 113 of 116

A 72-year-old woman is admitted with confusion and pallor. Her daughter reports that she has been getting more confused are tired for the past three months. Blood tests are reported as follows:

Hb 8.9 g/dl

MCV 125 fl

Plt 148 * 10^9/l

WBC 4.4 * 10^9/l

In light of the macrocytic anaemia some further tests are ordered:

Intrinsic factor antibodies	Negative
Vitamin B12	94 ng/l (200-900 ng/l)
Folic acid	1.1 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- A. Oral folic acid + blood transfusion
- B. Oral folic acid + start Intramuscular vitamin B12 when folic acid levels are normal
- C. Intramuscular vitamin B12 + start oral folic acid when vitamin B12 levels are normal
- D. Blood transfusion
- E. Oral prednisolone

Question 113 of 116

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- D. Blood transfusion
- E. Oral prednisolone

It is important in a patient who is also deficient in both vitamin B12 and folic acid to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

Macrocytic anaemia

Macrocytic anaemia can be divided into causes associated with a megaloblastic bone marrow and those with a normoblastic bone marrow

Megaloblastic causes	Normoblastic causes
• vitamin B12 deficiency • folate deficiency • cytotoxics e.g. hydroxyurea	• alcohol • liver disease • hypothyroidism • pregnancy • reticulocytosis e.g. haemolysis • aplastic anaemia • myelodysplasia • drugs: cytotoxics

Question 114 of 116

A 4-year-old girl with sickle cell anaemia presents with abdominal pain. On examination she is noted to have splenomegaly and is clinically anaemic. What is the most likely diagnosis?

- A. Liver cirrhosis
- B. Parvovirus infection
- C. Sequestration crisis
- D. *Salmonella* infection
- E. Thrombotic crisis

Question 114 of 116

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Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:
- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

Thrombotic crises
- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain

Sequestration crises
- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO2 - the most common cause of death after childhood

Aplastic crises
- caused by infection with parvovirus
- sudden fall in haemoglobin

Haemolytic crises
- rare
- fall in haemoglobin due an increased rate of haemolysis

Question 115 of 116

A women who is about to commence trastuzumab treatment for breast cancer has an echocardiogram. Which class of chemotherapeutic agent would predispose her to developing cardiac dysfunction?

- A. Vinca alkaloids
- B. Platinium-based compounds
- C. Anthracyclines
- D. Taxanes
- E. Topoisomerase inhibitors

Question 115 of 116

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Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Question 116 of 116

Each one of the following is associated with polycythaemia rubra vera, except:

- A. Splenomegaly
- B. Hyperviscosity
- C. Raised ESR
- D. Hypertension
- E. Pruritus

Question 116 of 116

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B. Hyperviscosity

C. Raised ESR

D. Hypertension

E. Pruritus

Polycythaemia rubra vera is associated with a low ESR

Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

Features

- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphotase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count >450 * 10^9/l)
B2	Neutrophil leucocytosis (neutrophil count > 10 * 10^9/l in non-smokers; > 12.5*10^9/l in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Question 1 of 117

A 30-year-old female in her third trimester of pregnancy mentions during an antenatal appointment that she has noticed an itchy rash around her umbilicus. This is her second pregnancy and she had no similar problems in her first pregnancy. Examination reveals blistering lesions in the peri-umbilical region and on her arms. What is the likely diagnosis?

- A. Seborrhoeic dermatitis
- B. Pompholyx
- C. Polymorphic eruption of pregnancy
- D. Lichen planus
- E. Pemphigoid gestationis

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- E. Pemphigoid gestationis

Polymorphic eruption of pregnancy is not associated with blistering

Pemphigoid gestationis is the correct answer. Polymorphic eruption of pregnancy is not associated with blistering

Skin disorders associated with pregnancy

Polymorphic eruption of pregnancy
- pruritic condition associated with last trimester
- lesions often first appear in abdominal striae
- management depends on severity: emollients, mild potency topical steroids and oral steroids may be used

Pemphigoid gestationis
- pruritic blistering lesions
- often develop in peri-umbilical region, later spreading to the trunk, back, buttocks and arms
- usually presents 2nd or 3rd trimester and is rarely seen in the first pregnancy
- oral corticosteroids are usually required

Question 2 of 117

A 62-year-old female is referred to dermatology due to a lesion over her shin. It initially started as a small red papule which later became a deep, red, necrotic ulcers with a violaceous border. What is the likely diagnosis?

- A. Necrobiosis lipoidica diabeticorum
- B. Syphilis
- C. Erythema nodosum
- D. Pretibial myxoedema
- E. Pyoderma gangrenosum

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- E. Pyoderma gangrenosum

This is a classic description of pyoderma gangrenosum

Shin lesions

The differential diagnosis of shin lesions includes the following conditions:
- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum
- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema
- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum
- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 3 of 117

A 19-year-old student presents with a three day history of a 1 cm golden, crusted lesion on the border of her lower lip. What is the most suitable management?

- A. Oral co-amoxiclav
- B. Oral penicillin
- C. Oral flucloxacillin
- D. Oral flucloxacillin + penicillin
- E. Topical fusidic acid

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Impetigo - topical fusidic acid --> oral flucloxacillin / topical retapamulin

This history is typical of impetigo. As the lesion is small and localised topical fusidic acid is recommended

Impetigo: management

Limited, localised disease
- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease
- oral flucloxacillin
- oral erythromycin if penicillin allergic

Question 4 of 117

A 22-year-old woman presents due to hypopigmented skin lesions on her chest and back. She has recently returned from the south of France and has tanned skin. On examination the lesions are slightly scaly. What is the most likely diagnosis?

- A. Tinea corporis
- B. Pityriasis versicolor
- C. Porphyria cutanea tarda
- D. Lyme disease
- E. Psoriasis

Question 4 of 117

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- D. Lyme disease
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Pityriasis versicolor

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by Malassezia furfur (formerly termed Pityrosporum ovale)

Features
- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

Predisposing factors
- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

Management
- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

Question 5 of 117

A 28-year-old man presents with multiple protuberant lesions around the anus which have been present for about 6 weeks. He reports it is painful when he passes a stool although there is no change in bowel habit. What is the most likely diagnosis?

- A. Haemorrhoids
- B. Anal cancer
- C. Genital warts
- D. Anal skin tags
- E. Crohn's disease

Question 5 of 117

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Ambiguous questions such as this are common in the MRCP. Whilst a case could be made for any of the answers the most likely cause from the above list, in a 28-year-old male, is genital warts

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 6 of 117

A 74-year-old lady with a history of hypothyroidism presents in January with a rash down the right side of her body. On examination an erythematous rash with patches of hyperpigmentation and telangiectasia is found. What is the likely diagnosis?

- A. Erythema marginatum
- B. Herpes zoster
- C. Pretibial myxoedema
- D. Erythema ab igne
- E. Xanthomata

Question 6 of 117

A 74-year-old lady with a history of hypothyroidism presents in January with a rash down the right side of her body. On examination an erythematous rash with patches of hyperpigmentation and telangiectasia is found. What is the likely diagnosis?

- A. Erythema marginatum
- B. Herpes zoster
- C. Pretibial myxoedema
- D. Erythema ab igne
- E. Xanthomata

This is a classic presentation of erythema ab igne. Despite the name, pretibial myxoedema is associated with hyperthyroidism rather than hypothyroidism.

Hypothyroidism can make patients feel cold and hence more likely to sit next a heater / fire.

Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

Question 7 of 117

A 39-year-old female has a pigmented mole removed from her leg which histology shows to be a malignant melanoma. What is the single most important prognostic marker?

- A. Number of episodes of sunburn before the age of 18 years
- B. Age of patient
- C. Diameter of melanoma
- D. Depth of melanoma
- E. Mutation in the MC1R gene

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Melanoma: the invasion depth of the tumour is the single most important prognostic factor

Malignant melanoma: prognostic factors

The invasion depth of a tumour (Breslow depth) is the single most important factor in determining prognosis of patients with malignant melanoma

Breslow Thickness	Approximate 5 year survival
< 1 mm	95-100%
1 - 2 mm	80-96%
2.1 - 4 mm	60-75%
> 4 mm	50%

Question 8 of 117

A 67-year-old man with a history of Parkinson's disease presents due to the development of an itchy, red rash on his neck, behind his ears and around the nasolabial folds. He had a similar flare up last winter but did not seek medical attention. What is the most likely diagnosis?

- A. Levodopa associated dermatitis
- B. Seborrhoeic dermatitis
- C. Flexural psoriasis
- D. Acne rosacea
- E. Fixed drug reaction to ropinirole

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- E. Fixed drug reaction to ropinirole

Seborrhoeic dermatitis is more common in patients with Parkinson's disease

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short perio

Question 9 of 117

A 62-year-old female is referred due to a long-standing ulcer above the right medial malleolus. Ankle-brachial pressure index readings are as follows:

Right 0.95

Left 0.95

To date it has been managed by the District Nurse with standard dressings. What is the most appropriate management to maximize the likelihood of the ulcer healing?

- A. Compression bandaging
- B. Intermittent pneumatic compression
- C. Hydrocolloid dressings
- D. Refer to vascular surgeon
- E. Topical flucloxacillin

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Management of venous ulceration - compression bandaging

The ankle-brachial pressure index readings indicate a reasonable arterial supply and suggest the ulcers are venous in nature.

Venous ulceration

Venous ulceration is typically seen above the medial malleolus

Investigations

- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

Management

- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

Question 10 of 117

A 43-year-old man comes for review. A few months ago he developed redness around his nose and cheeks. This is worse after drinking alcohol. He is concerned as one of his work colleagues asked him if he had a drink problem despite him drinking 14 units per week. On examination he has erythema as described above with some pustules on the nose and telangiectasia on the cheeks. What is the most likely diagnosis?

- A. Mitral stenosis
- B. Seborrhoeic dermatitis
- C. Alcohol-related skin changes
- D. Acne rosacea
- E. Systemic lupus erythematosus

Question 10 of 117

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- B. Seborrhoeic dermatitis
- C. Alcohol-related skin changes
- D. Acne rosacea
- E. Systemic lupus erythematosus

This is a typical history of acne rosacea

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 11 of 117

A 25-year-old man presents with a widespread rash over his body. The torso and limbs are covered with multiple erythematous lesions less than 1 cm in diameter which in parts are covered by a fine scale. You note that two weeks earlier he was seen with to a sore throat when it was noted that he had exudative tonsillitis. Other than a history of asthma he is normally fit and well. What is the most likely diagnosis?

- A. Pityriasis Rosea
- B. Pityriasis versicolor
- C. Syphilis
- D. Discoid eczema
- E. Guttate psoriasis

Question 11 of 117

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- D. Discoid eczema
- E. Guttate psoriasis

Psoriasis: guttate

Guttate psoriasis is more common in children and adolescents. It may be precipitated by a streptococcal infection 2-4 weeks prior to the lesions appearing

Features
- tear drop papules on the trunk and limbs

Management
- most cases resolve spontaneously within 2-3 months
- there is no firm evidence to support the use of antibiotics to eradicate streptococcal infection
- topical agents as per psoriasis
- UVB phototherapy
- tonsillectomy may be necessary with recurrent episodes

Question 12 of 117

A 64-year-old patient is referred to dermatology outpatients due to a rash. A diagnosis necrolytic migratory erythema of is made. What is the most likely underlying diagnosis?

- A. Gastrinoma
- B. Lung cancer
- C. Glucagonoma
- D. Pancreatic cancer
- E. Lymphoma

Question 12 of 117

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- E. Lymphoma

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 13 of 117

A 54-year-old man presents with a brown velvety rash on the back of his neck around his axilla. A clinical diagnosis of acanthosis nigricans is made. Which one of the following conditions is most associated with this kind of rash?

- A. Hypothyroidism
- B. Psoriasis
- C. Tuberculosis
- D. Ulcerative colitis
- E. Acute pancreatitis

Question 13 of 117

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- C. Tuberculosis
- D. Ulcerative colitis
- E. Acute pancreatitis

Acanthosis nigricans

Describes symmetrical, brown, velvety plaques that are often found on the neck, axilla and groin

Causes

- internal malignancy (esp. gastrointestinal)
- insulin-resistant diabetes mellitus
- obesity
- acromegaly
- Cushing's disease
- hypothyroidism
- polycystic ovarian syndrome
- familial
- Prader-Willi syndrome
- drugs: oral contraceptive pill, nicotinic acid

Question 14 of 117

A 34-year-old man presents for the removal of a mole. Where on the body are keloid scars most likely to form?

- A. Sternum
- B. Lower back
- C. Abdomen
- D. Flexor surfaces of limbs
- E. Scalp

Question 14 of 117

A 34-year-old man presents for the removal of a mole. Where on the body are keloid scars most likely to form?

- A. Sternum
- B. Lower back
- C. Abdomen
- D. Flexor surfaces of limbs
- E. Scalp

Keloid scars are most common on the sternum

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 15 of 117

A 67-year-old man who is a retired builder presents following the development of a number of red, scaly lesions on his left temple. These were initially small and flat but are now erythematous and rough to touch. What is the most likely diagnosis?

- A. Pityriasis versicolor
- B. Seborrhoeic keratosis
- C. Polymorphous light eruption
- D. Actinic keratoses
- E. Malignant melanoma

Question 15 of 117

A 67-year-old man who is a retired builder presents following the development of a number of red, scaly lesions on his left temple. These were initially small and flat but are now erythematous and rough to touch. What is the most likely diagnosis?

- A. Pityriasis versicolor
- B. Seborrhoeic keratosis
- C. Polymorphous light eruption
- D. Actinic keratoses
- E. Malignant melanoma

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 16 of 117

A 34-year-old man presents to dermatology clinic with an itchy rash on his palms. He has also noticed the rash around the site of a recent scar on his forearm. Examination reveals papules with a white-lace pattern on the surface. Some isolated white streaks are also noted on the mucous membranes of the mouth. What is the diagnosis?

- A. Lichen planus
- B. Scabies
- C. Lichen sclerosus
- D. Morphea
- E. Pityriasis rosea

Question 16 of 117

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- D. Morphea
- E. Pityriasis rosea

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

This is a typical history of lichen planus.

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 17 of 117

A 55-year-old female is referred to dermatology due to a lesions over both shins. On examination symmetrical erythematous lesions are found with an orange peel texture. What is the likely diagnosis?

- A. Pretibial myxoedema
- B. Pyoderma gangrenosum
- C. Necrobiosis lipoidica diabeticorum
- D. Erythema nodosum
- E. Syphilis

Question 17 of 117

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- E. Syphilis

Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 18 of 117

Which of the following skin conditions is not associated with diabetes mellitus?

- A. Necrobiosis lipoidica
- B. Sweet's syndrome
- C. Granuloma annulare
- D. Vitiligo
- E. Lipoatrophy

Question 18 of 117

Which of the following skin conditions is not associated with diabetes mellitus?

- A. Necrobiosis lipoidica
- B. Sweet's syndrome
- C. Granuloma annulare
- D. Vitiligo
- E. Lipoatrophy

Sweet's syndrome is also known as acute febrile neutrophilic dermatosis has a strong association with acute myeloid leukaemia. It is not associated with diabetes mellitus

Skin disorders associated with diabetes

Note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is often not included in a differential of potential causes

Necrobiosis lipoidica
- shiny, painless areas of yellow/red/brown skin typically on the shin
- often associated with surrounding telangiectasia

Infection
- candidiasis
- staphylococcal

Neuropathic ulcers

Vitiligo

Lipoatrophy

Granuloma annulare*
- papular lesions that are often slightly hyperpigmented and depressed centrally

*it is not clear from recent studies if there is actually a significant association between diabetes mellitus and granuloma annulare, but it is often listed in major textbooks

Question 19 of 117

A 38-year-old woman with a history of rheumatoid arthritis and epilepsy presents with generalised increased hair growth over her trunk and arms. Which one of the following drugs is associated with hypertrichosis?

- A. Sodium valproate
- B. Prednisolone
- C. Phenytoin
- D. Ciclosporin
- E. Methotrexate

Question 19 of 117

A 38-year-old woman with a history of rheumatoid arthritis and epilepsy presents with generalised increased hair growth over her trunk and arms. Which one of the following drugs is associated with hypertrichosis?

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- B. Prednisolone
- C. Phenytoin
- D. Ciclosporin
- E. Methotrexate

Phenytoin is associated with hirsuitism rather than hypertrichosis

Hirsuitism and hypertrichosis

Hirsuitism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Causes of hirsuitism

- polycystic ovarian syndrome
- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

Causes of hypertrichosis

- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa

Question 20 of 117

A 23-year-old man presents with a three day history of general malaise and low-grade temperature. Yesterday he developed extensive painful ulceration of his mouth and gums. On examination his temperature is 37.4ºC, pulse 84 / min and there is submandibular lymphadenopathy. What is the most likely diagnosis?

- A. Epstein Barr virus
- B. Lichen planus
- C. HIV seroconversion illness
- D. Herpes simplex virus infection
- E. Oral *Candida*

Question 20 of 117

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- C. HIV seroconversion illness
- D. Herpes simplex virus infection
- E. Oral *Candida*

This man has gingivostomatitis, a characteristic feature of primary herpes simplex virus infection

Herpes simplex virus

There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

Features

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

Question 21 of 117

A 54-year-old man is referred to the dermatology outpatient department due to a facial rash which has persisted for the past 12 months. On examination there is a symmetrical rash consisting of extensive pustules and papules which affects his nose, cheeks and forehead. What is the most appropriate treatment?

- A. Ciprofloxacin
- B. Isotretinoin
- C. Oxytetracycline
- D. Hydroxychloroquine
- E. Prednisolone

Question 21 of 117

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- B. Isotretinoin
- C. Oxytetracycline
- D. Hydroxychloroquine
- E. Prednisolone

As there is extensive involvement oral oxytetracycline should probably be used rather than topical metronidazole

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 22 of 117

A 31-year-old woman develops with painful, purple lesions on her shins. Which one of the following medications is most likely to be responsible?

- A. Montelukast
- B. Lansoprazole
- C. Combined oral contraceptive pill
- D. Sodium valproate
- E. Carbimazole

Question 22 of 117

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- E. Carbimazole

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 23 of 117

Which one of the following conditions is most strongly associated with erythema multiforme?

- A. Crohn's disease
- B. Tuberculosis
- C. Sarcoidosis
- D. Herpes simplex virus
- E. Streptococcal infections

Question 23 of 117

Which one of the following conditions is most strongly associated with erythema multiforme?

- A. Crohn's disease
- B. Tuberculosis
- C. Sarcoidosis
- D. Herpes simplex virus
- E. Streptococcal infections

This is difficult as both herpes simplex and streptococcal infections are known causes of erythema multiforme (EM). However, studies suggest that HSV is the trigger in over 50% of cases. Streptococcal infections and sarcoidosis are more strongly associated with erythema nodosum

Erythema multiforme

Erythema multiforme
- target lesions (typically worse on peripheries e.g. palms and soles)
- severe = Stevens-Johnson syndrome (blistering and mucosal involvement)

Causes
- viruses: herpes simplex virus, Orf
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

Question 24 of 117

An 18-year-old female is reviewed in the dermatology clinic complaining of scalp hair loss. Which one of the following conditions is least likely to be responsible?

- A. Porphyria cutanea tarda
- B. Discoid lupus
- C. Tinea capitis
- D. Alopecia areata
- E. Telogen effluvium

Question 24 of 117

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- B. Discoid lupus
- C. Tinea capitis
- D. Alopecia areata
- E. Telogen effluvium

Porphyria cutanea tarda is a recognised cause of hypertrichosis

Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

Scarring alopecia
- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis*

Non-scarring alopecia
- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

*scarring would develop in untreated tinea capitis if a kerion develops

Question 25 of 117

Which of the following conditions is most associated with onycholysis?

- A. Bullous pemphigoid
- B. Raynaud's disease
- C. Osteogenesis imperfecta
- D. Oesophageal cancer
- E. Scabies

Question 25 of 117

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- C. Osteogenesis imperfecta
- D. Oesophageal cancer
- E. Scabies

Raynaud's disease causes onycholysis, as can any cause of impaired circulation

Onycholysis

Onycholysis describes the separation of the nail plate from the nail bed

Causes

- idiopathic
- trauma e.g. excessive manicuring
- infection: especially fungal
- skin disease: psoriasis, dermatitis
- impaired peripheral circulation e.g. Raynaud's
- systemic disease: hyper- and hypothyroidism

Question 26 of 117

A 85-year-old lady presents to dermatology clinic complaining of itchy white plaques affecting her vulva. There is no history of vaginal discharge or bleeding. A similar plaque is also seen on her inner thigh. What is the likely diagnosis?

- A. *Candida*
- B. Lichen planus
- C. Lichen sclerosus
- D. Herpes simplex
- E. Seborrhoeic dermatitis

Question 26 of 117

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- A. *Candida*
- B. Lichen planus
- C. Lichen sclerosus
- D. Herpes simplex
- E. Seborrhoeic dermatitis

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

The correct answer is lichen sclerosus. *Candida* may cause pruritus and white plaques but lesions would not also be seen on her inner thigh

Lichen sclerosus

Lichen sclerosus was previously termed lichen sclerosus et atrophicus. It is an inflammatory condition which usually affects the genitalia and is more common in elderly females. Lichen sclerosus leads to atrophy of the epidermis with white plaques forming

Features
- itch is prominent

A biopsy is often performed to exclude other diagnoses

Management
- topical steroids and emollients
- increased risk of vulval cancer

Question 27 of 117

A 43-year-old man is admitted to the Emergency Department with a rash and feeling generally unwell. He is known to have epilepsy and his medication was recently changed to phenytoin three weeks ago. Around one week ago he started to develop mouth ulcers associated with malaise and a cough. Two days ago he started to develop a widespread red rash which has now coalesced to form large fluid-filled blisters, covering around 30% of his body area. The lesions separate when slight pressure is applied. On examination his temperature is 38.3ºC and pulse 126 / min. Blood results show:

Na^+	144 mmol/l
K^+	4.2 mmol/l
Bicarbonate	19 mmol/l
Urea	13.4 mmol/l
Creatinine	121 µmol/l

What is the most likely diagnosis?

- A. Phenytoin-induced neutropaenia
- B. Drug-induced lupus
- C. Kawasaki disease
- D. Toxic epidermal necrolysis
- E. Staphylococcal Scalded Skin syndrome

Question 27 of 117

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- B. Drug-induced lupus
- C. Kawasaki disease
- D. Toxic epidermal necrolysis
- E. Staphylococcal Scalded Skin syndrome

Toxic epidermal necrolysis

Toxic epidermal necrolysis (TEN) is a potentially life-threatening skin disorder that is most commonly seen secondary to a drug reaction. In this condition the skin develops a scalded appearance over an extensive area. Some authors consider TEN to be the severe end of a spectrum of skin disorders which includes erythema multiforme and Stevens-Johnson syndrome

Features
- systemically unwell e.g. pyrexia, tachycardic
- positive Nikolsky's sign: the epidermis separates with mild lateral pressure

Drugs known to induce TEN
- phenytoin
- sulphonamides
- allopurinol
- penicillins
- carbamazepine
- NSAIDs

Management
- stop precipitating factor
- supportive care, often in intensive care unit
- intravenous immunoglobulin has been shown to be effective and is now commonly used first-line
- other treatment options include: immunosuppressive agents (ciclosporin and cyclophosphamide), plasmapheresis

Question 28 of 117

Which one of the following complications is most associated with psoralen + ultraviolet A light (PUVA) therapy?

- A. Squamous cell cancer
- B. Osteoporosis
- C. Basal cell cancer
- D. Dermoid cysts
- E. Malignant melanoma

Question 28 of 117

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The most significant complication of PUVA therapy for psoriasis is squamous cell skin cancer.

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 29 of 117

Which one of the following conditions is least likely to be associated with pyoderma gangrenosum?

- A. Ulcerative colitis
- B. Syphilis
- C. Lymphoma
- D. IgA monoclonal gammopathy
- E. Rheumatoid arthritis

Question 29 of 117

Which one of the following conditions is least likely to be associated with pyoderma gangrenosum?

- A. Ulcerative colitis
- B. Syphilis
- C. Lymphoma
- D. IgA monoclonal gammopathy
- E. Rheumatoid arthritis

Syphilis is not commonly associated with pyoderma gangrenosum

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 30 of 117

A 26-year-old newly qualified nurse presents as she has developed a bilateral erythematous rash on both hands. She has recently emigrated from the Philippines and has no past medical history of note. A diagnosis of contact dermatitis is suspected. What is the most suitable to test to identify the underlying cause?

- A. Radioallergosorbent test (RAST)
- B. Latex IgM levels
- C. Skin prick test
- D. Urinary porphyrins
- E. Skin patch test

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- B. Latex IgM levels
- C. Skin prick test
- D. Urinary porphyrins
- E. Skin patch test

The skin patch test is useful in this situation as it may also identify for irritants, not just allergens

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 31 of 117

A 36-year-old woman is reviewed. She presented 4 weeks ago with itchy dry skin on her arms and was diagnosed as having atopic eczema. She was prescribed hydrocortisone 1% cream with an emollient. Unfortunately there has been no improvement in her symptoms. What is the next step in management, alongside continued regular use of an emollient?

- A. Betamethasone valerate 0.1%
- B. Clobetasone butyrate 0.05%
- C. Clobetasol propionate 0.05%
- D. Topical tetracycline
- E. Regular wet wraps

Question 31 of 117

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- C. Clobetasol propionate 0.05%
- D. Topical tetracycline
- E. Regular wet wraps

Topical steroids
- moderate: Clobetasone butyrate 0.05%
- potent: Betamethasone valerate 0.1%
- very potent: Clobetasol propionate 0.05%

Clobetasone butyrate 0.05% is a moderately potent topical steroid and would be the most suitable next step in management. It is important to note the potency difference between two very similar sounding steroids - Clobetasone butyrate 0.05% (moderate) and Clobetasol propionate 0.05% (very potent)

Eczema: topical steroids

Use weakest steroid cream which controls patients symptoms

The table below shows topical steroids by potency

Mild	Moderate	Potent	Very potent
Hydrocortisone 0.5-2.5%	Betamethasone valerate 0.025% (Betnovate RD) Clobetasone butyrate 0.05% (Eumovate)	Fluticasone propionate 0.05% (Cutivate) Betamethasone valerate 0.1% (Betnovate)	Clobetasol propionate 0.05% (Dermovate)

Finger tip rule
- 1 finger tip unit (FTU) = 0.5 g, sufficient to treat a skin area about twice that of the flat of an adult hand

Topical steroid doses for eczema in adults

Area of skin	Fingertip units per dose
Hand and fingers (front and back)	1.0
A foot (all over)	2.0
Front of chest and abdomen	7.0
Back and buttocks	7.0
Face and neck	2.5
An entire arm and hand	4.0
An entire leg and foot	8.0

Question 32 of 117

A 54-year-old woman with a history of type 1 diabetes mellitus presents with unsightly toenails affecting the lateral three nails of the left foot. On examination the nails and brown and break easily. Nail scrapings demonstrate Trichophyton rubrum infection. What is the treatment of choice?

- A. Oral terbinafine for 12 weeks
- B. Oral itraconazole for 4 weeks
- C. Topical itraconazole for 2 weeks
- D. Topical amorolfine for 6 weeks
- E. Oral itraconazole for 1 weeks

Question 32 of 117

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- C. Topical itraconazole for 2 weeks
- D. Topical amorolfine for 6 weeks
- E. Oral itraconazole for 1 weeks

Dermatophyte nail infections - use oral terbinafine

Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by

- dermatophytes - mainly Trichophyton rubrum, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

Features

- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

Investigation

- nail clippings
- scrapings of the affected nail

Management

- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

Question 33 of 117

A 34-year-old man presents with a three week history of an intensely itchy rash on the back of his elbows. On examination he has a symmetrical vesicular rash on the extensor aspects of his arms. Which one of the following antibodies is most likely to be positive?

- A. Anti-mitochondrial antibody
- B. Anti-gliadin antibody
- C. Anti-nuclear antibody
- D. Anti-neutrophil cytoplasmic antibody
- E. Anti-Jo-1 antibody

Question 33 of 117

A 34-year-old man presents with a three week history of an intensely itchy rash on the back of his elbows. On examination he has a symmetrical vesicular rash on the extensor aspects of his arms. Which one of the following antibodies is most likely to be positive?

- A. Anti-mitochondrial antibody
- B. Anti-gliadin antibody
- C. Anti-nuclear antibody
- D. Anti-neutrophil cytoplasmic antibody
- E. Anti-Jo-1 antibody

Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

Features
- itchy, vesicular skin lesions on the extensor surfaces (e.g. Elbows, knees buttocks)

Diagnosis
- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

Management
- gluten-free diet
- dapsone

Question 34 of 117

You review a 50-year-old man who has psoriasis. Which one of the following medications is most likely exacerbate his condition?

- A. Nicorandil
- B. Simvastatin
- C. Verapamil
- D. Atenolol
- E. Isosorbide mononitrate

Question 34 of 117

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- A. Nicorandil
- B. Simvastatin
- C. Verapamil
- D. Atenolol
- E. Isosorbide mononitrate

Psoriasis: exacerbating factors

The following factors may exacerbate psoriasis:

- trauma
- alcohol
- drugs: beta blockers, lithium, antimalarials (chloroquine and hydroxychloroquine), NSAIDs and ACE inhibitors
- withdrawal of systemic steroids

Question 35 of 117

A 23-year-old man presents with an itchy skin condition. Which one of the following is least relevant when deciding whether a patient has atopic eczema?

- A. History of asthma
- B. Responds to topical steroids
- C. History of flexural involvement
- D. Onset below age 2 years
- E. History of generally dry skin

Question 35 of 117

A 23-year-old man presents with an itchy skin condition. Which one of the following is least relevant when deciding whether a patient has atopic eczema?

- A. History of asthma
- B. Responds to topical steroids
- C. History of flexural involvement
- D. Onset below age 2 years
- E. History of generally dry skin

Whilst response to topical steroids provides useful clinical information it is not part of the diagnostic criteria

Eczema: diagnosis

UK Working Party Diagnostic Criteria for Atopic Eczema

An itchy skin condition in the last 12 months

Plus three or more of
- onset below age 2 years*
- history of flexural involvement**
- history of generally dry skin
- personal history of other atopic disease***
- visible flexural dermatitis

*not used in children under 4 years

**or dermatitis on the cheeks and/or extensor areas in children aged 18 months or under
***in children aged under 4 years, history of atopic disease in a first degree relative may be included

Question 36 of 117

Which of the following skin disorders is least associated with tuberculosis?

- A. Scrofuloderma
- B. Erythema nodosum
- C. Lupus vulgaris
- D. Verrucosa cutis
- E. Lupus pernio

Question 36 of 117

Which of the following skin disorders is least associated with tuberculosis?

- A. Scrofuloderma
- B. Erythema nodosum
- C. Lupus vulgaris
- D. Verrucosa cutis
- E. Lupus pernio

Lupus pernio is sometimes seen in sarcoidosis but is not associated with tuberculosis

Skin disorders associated with TB

Possible skin disorders
- lupus vulgaris (accounts for 50% of cases)
- erythema nodosum
- scarring alopecia
- scrofuloderma: breakdown of skin overlying a tuberculous focus
- verrucosa cutis
- gumma

Lupus vulgaris is the most common form of cutaneous TB seen in the Indian subcontinent. It generally occurs on the face and is common around the nose and mouth. The initial lesion is an erythematous flat plaque which gradually becomes elevated and may ulcerate later

Question 37 of 117

Which of the following statements regarding psoriasis is incorrect?

- A. Often occurs on extensor surfaces
- B. Psoriatic arthropathy may occur prior to the development of skin lesions
- C. Mediated by type 2 helper T cells
- D. Abnormal T cell activity stimulates keratinocyte proliferation
- E. Nail signs include pitting and onycholysis

Question 37 of 117

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- C. Mediated by type 2 helper T cells
- D. Abnormal T cell activity stimulates keratinocyte proliferation
- E. Nail signs include pitting and onycholysis

Psoriasis is mediated by type 1 helper T cells which are involved in the cell mediated response, rather than type 2 helper T cells

Psoriasis

Psoriasis can be divided into type 1 and 2:

Type 1
- presents < 40 years old
- positive family history
- associated with HLA-CW6

Type 2
- presents > 50 years old
- no family history

Cause
- abnormal T cell activity stimulates keratinocyte proliferation (rather than an actual primary keratinocyte disorder)
- mediated by type 1 helper T cells

Features
- red, scaly plaques
- scalp, extensor surfaces elbows/knees, sacrum
- nail signs: pitting, onycholysis
- arthritis

Complications
- psoriatic arthropathy (around 10%)
- psychological distress
- increased incidence of cardiovascular disease

Question 38 of 117

Which one of the following statements regarding acne vulgaris is incorrect?

- A. Follicular epidermal hyperproliferation results in obstruction of the pilosebaceous follicle
- B. Acne vulgaris affects at least 80% of teenagers
- C. Propionibacterium acnes is an anaerobic bacterium
- D. Typical lesions include comedones and pustules
- E. Beyond the age of 25 years acne vulgaris is more common in males

Question 38 of 117

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B. Acne vulgaris affects at least 80% of teenagers
C. Propionibacterium acnes is an anaerobic bacterium
D. Typical lesions include comedones and pustules
E. Beyond the age of 25 years acne vulgaris is more common in males

Acne is actually more common in females after the age of 25 years

Acne vulgaris

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Epidemiology

- affects around 80-90% of teenagers, 60% of whom seek medical advice
- acne may also persist beyond adolescence, with 10-15% of females and 5% of males over 25 years old being affected

Pathophysiology is multifactorial

- follicular epidermal hyperproliferation resulting in the formation of a keratin plug. This in turn causes obstruction of the pilosebaceous follicle. Activity of sebaceous glands may be controlled by androgen, although levels are often normal in patients with acne
- colonisation by the anaerobic bacterium Propionibacterium acnes
- inflammation

Question 39 of 117

A 81-year-old man is investigated after he develops a number of itchy blisters on his trunk. A skin biopsy suggests a diagnosis bullous pemphigoid. This is most likely to be caused by antibodies directed against:

- A. Adherens
- B. Desmoglein-3
- C. Hemidesmosomal BP antigens
- D. Occludin-2
- E. Desmoglein-1

Question 39 of 117

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- B. Desmoglein-3
- C. Hemidesmosomal BP antigens
- D. Occludin-2
- E. Desmoglein-1

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 40 of 117

A 62-year-old male is referred to dermatology with a lesion over his shin. On examination shiny, painless areas of yellow skin over the shin are found with abundant telangiectasia. What is the most likely diagnosis?

- A. Pretibial myxoedema
- B. Necrobiosis lipoidica diabeticorum
- C. Erythema nodosum
- D. Pyoderma gangrenosum
- E. Syphilis

Question 40 of 117

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- E. Syphilis

Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 41 of 117

A 17-year-old man presents with a 2 week history of abdominal pain, diarrhoea and repeated episodes of flushing. Examination reveals urticarial skin lesions on the trunk. What test is most likely to reveal the diagnosis?

- A. Chest x-ray
- B. Urinary catecholamines
- C. Serum amylase
- D. Urinary 5-HIAA
- E. Urinary histamine

Question 41 of 117

A 17-year-old man presents with a 2 week history of abdominal pain, diarrhoea and repeated episodes of flushing. Examination reveals urticarial skin lesions on the trunk. What test is most likely to reveal the diagnosis?

- A. Chest x-ray
- B. Urinary catecholamines
- C. Serum amylase
- D. Urinary 5-HIAA
- E. Urinary histamine

Urinary histamine is used to diagnose systemic mastocytosis

Given the history of diarrhoea and flushing a diagnosis of carcinoid syndrome should be considered, which would be investigated with urinary 5-HIAA levels. This would not however explain the urticarial skin lesions. In a young person a diagnosis of systemic mastocytosis should be considered. Another factor against carcinoid syndrome is the age of the patient - the average age of a patient with a carcinoid tumour is 61 years

Systemic mastocytosis

Systemic mastocytosis results from a neoplastic proliferation of mast cells

Features
- urticaria pigmentosa - produces a wheal on rubbing (Darier's sign)
- flushing
- abdominal pain
- monocytosis on the blood film

Diagnosis
- raised serum tryptase levels
- urinary histamine

Question 42 of 117

A 54-year-old man presents with a two month history of a rapidly growing lesion on his right forearm. The lesion initially appeared as a red papule but in the last two weeks has become a crater filled centrally with yellow/brown material. On examination the man has skin type II, the lesion is 4 mm in diameter and is morphologically as described above. What is the most likely diagnosis?

- A. Seborrhoeic keratosis
- B. Keratoacanthoma
- C. Pyoderma gangrenosum
- D. Basal cell carcinoma
- E. Malignant melanoma

Question 42 of 117

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- A. Seborrhoeic keratosis
- B. Keratoacanthoma
- C. Pyoderma gangrenosum
- D. Basal cell carcinoma
- E. Malignant melanoma

Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

Question 43 of 117

A 62-year-old with a history of acne rosacea presents for advice regarding treatment. Which one of the following interventions has the least role in management?

- A. Camouflage creams
- B. Topical metronidazole
- C. Low-dose topical corticosteroids
- D. Laser therapy
- E. Use of high-factor sun block

Question 43 of 117

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- C. Low-dose topical corticosteroids
- D. Laser therapy
- E. Use of high-factor sun block

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 44 of 117

A 49-year-old man is reviewed in the dermatology clinic complaining of losing hair. Examination reveals generalised scalp hair loss that does not follow the typical male-pattern distribution. Which one of the following medications is least likely to be responsible?

- A. Colchicine
- B. Cyclophosphamide
- C. Heparin
- D. Carbimazole
- E. Phenytoin

Question 44 of 117

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- C. Heparin
- D. Carbimazole
- E. Phenytoin

Phenytoin is a recognised cause of hirsuitism, rather than alopecia

Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

Scarring alopecia
- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis*

Non-scarring alopecia
- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

*scarring would develop in untreated tinea capitis if a kerion develops

Question 45 of 117

A 26-year-old male presents with a rash. Examination reveals erythematous oval lesions on his back and upper arms which have a slight scale just inside the edge. They vary in size from 1 to 5 cm in diameter. What is the most likely diagnosis?

- A. Lichen planus
- B. Guttate psoriasis
- C. Lichen sclerosus
- D. Pityriasis rosea
- E. Pityriasis versicolor

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- C. Lichen sclerosus
- D. Pityriasis rosea
- E. Pityriasis versicolor

The skin lesions seen in pityriasis rosea are generally larger than those found in guttate psoriasis and scaling is typically confined to just inside the edges

Pityriasis rosea

Overview
- cause unknown, herpes hominis virus 7 (HHV-7) a possibility
- tends to affect young adults

Features
- herald patch (usually on trunk)
- followed by erythematous, oval, scaly patches which follow a characteristic distribution with the longitudinal diameters of the oval lesions running parallel to the line of Langer. This may produce a 'fir-tree' appearance

Management
- self-limiting, usually disappears after 4-6 weeks

Question 46 of 117

A 25-year-old male presents with extensive patches of altered pigmentation on his front, back, face and thighs. There is mild pruritus. A diagnosis of extensive pityriasis versicolor is made. What is the most appropriate management?

- A. Oral metronidazole
- B. Topical terbinafine
- C. Oral itraconazole
- D. Topical selenium sulphide
- E. Oral terbinafine

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- C. Oral itraconazole
- D. Topical selenium sulphide
- E. Oral terbinafine

Given the extensive nature of the lesions systemic therapy is indicated in this case

Pityriasis versicolor

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by Malassezia furfur (formerly termed Pityrosporum ovale)

Features
- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

Predisposing factors
- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

Management
- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

Question 47 of 117

A 64-year-old woman presents with severe mucosal ulceration associated with the development of blistering lesions over her torso and arms. On examination the blisters are flaccid and easily ruptured when touched. What is the most likely diagnosis?

- A. Pemphigus vulgaris
- B. Pemphigoid
- C. Dermatitis herpetiformis
- D. Psoriasis
- E. Epidermolysis bullosa

Question 47 of 117

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- C. Dermatitis herpetiformis
- D. Psoriasis
- E. Epidermolysis bullosa

Blisters/bullae
- no mucosal involvement: bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

Features
- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

Management
- steroids
- immunosuppressants

Question 48 of 117

A 21-year-old woman who is 16 weeks pregnant present with worsening acne which she is finding distressing. She is currently using topical benzyl peroxide with limited effect. On examination there is widespread non-inflammatory lesions and pustules on her face. What is the most appropriate next management step?

- A. Oral trimethoprim
- B. Oral lymecycline
- C. Oral erythromycin
- D. Topical retinoid
- E. Oral doxycycline

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- B. Oral lymecycline
- C. Oral erythromycin
- D. Topical retinoid
- E. Oral doxycycline

Oral erythromycin may be used for acne in pregnancy. The other drugs are contraindicated

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 49 of 117

Which one of the following factors would predispose a patient to forming keloid scars?

- A. Having white skin
- B. Incisions along relaxed skin tension lines
- C. Being aged 20-40 years
- D. Being female
- E. Having a wound on the lower back

Question 49 of 117

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- A. Having white skin
- B. Incisions along relaxed skin tension lines
- C. Being aged 20-40 years
- D. Being female
- E. Having a wound on the lower back

Keloid scars - more common in young, black, male adults

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 50 of 117

A 26-year-old man who is HIV positive is noted to have developed seborrhoeic dermatitis. Which of the following two complications are most associated with this condition?

- A. Alopecia and otitis externa
- B. Blepharitis and otitis externa
- C. Photosensitivity and alopecia
- D. Photosensitivity and blepharitis
- E. Blepharitis and alopecia

Question 50 of 117

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- C. Photosensitivity and alopecia
- D. Photosensitivity and blepharitis
- E. Blepharitis and alopecia

Alopecia is not commonly seen in seborrhoeic dermatitis, but may develop if a severe secondary infection develops

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 51 of 117

A 65-year-old woman presents with bullae on her forearms following a recent holiday in Spain. She also notes that the skin on her hands is extremely fragile and tears easily. In the past the patient has been referred to dermatology due to troublesome hypertrichosis. What is the most likely diagnosis?

- A. Pellagra
- B. Pemphigus vulgaris
- C. Epidermolysis bullosa
- D. Bullous pemphigoid
- E. Porphyria cutanea tarda

Question 51 of 117

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- C. Epidermolysis bullosa
- D. Bullous pemphigoid
- E. Porphyria cutanea tarda

Porphyria cutanea tarda
- blistering photosensitive rash
- hypertrichosis
- hyperpigmentation

Porphyria cutanea tarda

Porphyria cutanea tarda is the most common hepatic porphyria. It is due to an inherited defect in uroporphyrinogen decarboxylase or caused by hepatocyte damage e.g. alcohol, oestrogens

Features
- classically presents with photosensitive rash with blistering and skin fragility on the face and dorsal aspect of hands (most common feature)
- hypertrichosis
- hyperpigmentation

Investigations
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp

Management
- chloroquine
- venesection

Question 52 of 117

A 60-year-old woman presents with a swelling just proximal to the nailbed on the left ring finger. She has a history of osteoarthritis but is usually well. On examination a 4mm, firm dome-shaped swelling is seen. What is the most likely diagnosis?

- A. Fibrokeratoma
- B. Epidermoid cyst
- C. Orf
- D. Myxoid cyst
- E. Rheumatoid nodule

Question 52 of 117

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- A. Fibrokeratoma
- B. Epidermoid cyst
- C. Orf
- D. Myxoid cyst
- E. Rheumatoid nodule

Myxoid cyst

Myxoid cysts (also known as mucous cysts) are benign ganglion cysts usually found on the distal, dorsal aspect of the finger. There is usually osteoarthritis in the surrounding joint. They are more common in middle-aged women.

Question 53 of 117

A 23-year-old man presents as he is concerned over recent hair loss. Examination reveals a discrete area of hair loss on the left temporal region with no obvious abnormality of the underlying scalp. What is the most likely diagnosis?

- A. Telogen effluvium
- B. Alopecia areata
- C. Tinea capitis
- D. Male-pattern baldness
- E. Discoid lupus erythematous

Question 53 of 117

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- C. Tinea capitis
- D. Male-pattern baldness
- E. Discoid lupus erythematous

Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

Question 54 of 117

Which of the following skin conditions associated with malignancy are not correctly paired?

- A. Necrolytic migratory erythema and glucagonoma
- B. Migratory thrombophlebitis and pancreatic cancer
- C. Erythema gyratum repens and lymphoma
- D. Acanthosis nigricans and gastrointestinal cancer
- E. Erythroderma and lymphoma

Question 54 of 117

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- E. Erythroderma and lymphoma

Erythema gyratum repens is generally associated with solid organ malignancies such as lung and breast cancer

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	**Associated malignancies**
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 55 of 117

Which one of the following conditions is least associated with pruritus?

- A. Pemphigus vulgaris
- B. Iron-deficiency anaemia
- C. Polycythaemia
- D. Chronic renal failure
- E. Scabies

Question 55 of 117

Which one of the following conditions is least associated with pruritus?

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- B. Iron-deficiency anaemia
- C. Polycythaemia
- D. Chronic renal failure
- E. Scabies

Pemphigus vulgaris is an autoimmune bullous disease of the skin. It is not commonly associated with pruritus

Pruritus

The table below lists the main characteristics of the most important causes of pruritus

Liver disease	History of alcohol excess Stigmata of chronic liver disease: spider naevi, bruising, palmar erythema, gynaecomastia etc Evidence of decompensation: ascites, jaundice, encephalopathy
Iron deficiency anaemia	Pallor Other signs: koilonychia, atrophic glossitis, post-cricoid webs, angular stomatitis
Polycythaemia	Pruritus particularly after warm bath 'Ruddy complexion' Gout Peptic ulcer disease
Chronic kidney disease	Lethargy & pallor Oedema & weight gain Hypertension
Lymphoma	Night sweats Lymphadenopathy Splenomegaly, hepatomegaly Fatigue

Other causes:

- hyper- and hypothyroidism
- diabetes
- pregnancy
- 'senile' pruritus
- urticaria
- skin disorders: eczema, scabies, psoriasis, pityriasis rosea

Question 56 of 117

A 24-year-old woman presents due to a rash on her neck and forehead. She returned from a holiday in Cyprus 1 week ago and had her hair dyed 2 days ago. On examination there is a weepy, vesicular rash around her hairline although the scalp itself is not badly affected. What is the most likely diagnosis?

- A. Cutaneous leishmaniasis
- B. Irritant contact dermatitis
- C. Allergic contact dermatitis
- D. Syphilis
- E. Photocontact dermatitis

Question 56 of 117

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- C. Allergic contact dermatitis
- D. Syphilis
- E. Photocontact dermatitis

Contact dermatitis

There are two main types of contact dermatitis

- irritant contact dermatitis: common - non-allergic reaction due to weak acids or alkalis (e.g. detergents). Often seen on the hands. Erythema is typical, crusting and vesicles are rare
- allergic contact dermatitis: type IV hypersensitivity reaction. Uncommon - often seen on the head following hair dyes. Presents as an acute weeping eczema which predominately affects the margins of the hairline rather than the hairy scalp itself. Topical treatment with a potent steroid is indicated

Cement is a frequent cause of contact dermatitis. The alkaline nature of cement may cause an irritant contact dermatitis whilst the dichromates in cement also can cause an allergic contact dermatitis

Question 57 of 117

A 24-year-old female with a history of anorexia nervosa presents with red crusted lesions around the corner of her mouth and below her lower lip. What is she most likely to be deficient in?

- A. Zinc
- B. Tocopherol
- C. Pantothenic acid
- D. Thiamine
- E. Magnesium

Question 57 of 117

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- C. Pantothenic acid
- D. Thiamine
- E. Magnesium

Vitamin B12 deficiency may also cause angular cheilosis

Zinc deficiency

Features
- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Question 58 of 117

Which of the following conditions is least likely to exhibit the Koebner phenomenon?

- A. Vitiligo
- B. Molluscum contagiosum
- C. Lichen planus
- D. Psoriasis
- E. Lupus vulgaris

Question 58 of 117

Which of the following conditions is least likely to exhibit the Koebner phenomenon?

- A. Vitiligo
- B. Molluscum contagiosum
- C. Lichen planus
- D. Psoriasis
- E. Lupus vulgaris

Lupus vulgaris is not associated with the Koebner phenomenon

Koebner phenomenon

The Koebner phenomenon describes skin lesions which appear at the site of injury. It is seen in:

- psoriasis
- vitiligo
- warts
- lichen planus
- lichen sclerosus
- molluscum contagiosum

Question 59 of 117

A 34-year-old female is reviewed in the dermatology clinic with a skin rash under her new wrist watch. An allergy to nickel is suspected. What is the best investigation?

- A. Skin prick test
- B. Skin patch test
- C. Skin biopsy
- D. Serum IgE
- E. Serum nickel antibodies

Question 59 of 117

A 34-year-old female is reviewed in the dermatology clinic with a skin rash under her new wrist watch. An allergy to nickel is suspected. What is the best investigation?

- A. Skin prick test
- B. Skin patch test
- C. Skin biopsy
- D. Serum IgE
- E. Serum nickel antibodies

Nickel dermatitis

Nickel is a common cause allergic contact dermatitis and is an example of a type IV hypersensitivity reaction. It is often caused by jewellery such as watches

It is diagnosed by a skin patch test

Question 60 of 117

A 45-year-old man with a history of seborrhoeic dermatitis presents in late winter due a flare in his symptoms, affecting both his face and scalp. Which one of the following agents is least likely to be beneficial?

- A. Topical ketoconazole
- B. Selenium sulphide shampoo
- C. Topical hydrocortisone
- D. Tar shampoo
- E. Aqueous cream

Question 60 of 117

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- C. Topical hydrocortisone
- D. Tar shampoo
- E. Aqueous cream

There is less of a role for emollients in the management of seborrhoeic dermatitis than in other chronic skin disorders

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 61 of 117

An 84-year-old woman with a history of ischaemic heart disease is reviewed in the dermatology clinic. She has developed tense blistering lesions on her legs. Each lesion is around 1 to 3 cm in diameter and she reports that they are slightly pruritic. Examination of her mouth and vulva is unremarkable. What is the most likely diagnosis?

- A. Pemphigus
- B. Drug reaction to aspirin
- C. Epidermolysis bullosa
- D. Scabies
- E. Bullous pemphigoid

Question 61 of 117

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- A. Pemphigus
- B. Drug reaction to aspirin
- C. Epidermolysis bullosa
- D. Scabies
- E. Bullous pemphigoid

Blisters/bullae
- no mucosal involvement (in exams at least*): bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 62 of 117

A woman presents with painful erythematous lesions on her shins. Which one of the following is least associated with this presentation?

- A. Pregnancy
- B. Behcet's syndrome
- C. Streptococcal infection
- D. Penicillin
- E. Amyloidosis

Question 62 of 117

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- B. Behcet's syndrome
- C. Streptococcal infection
- D. Penicillin
- E. Amyloidosis

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 63 of 117

A 23-year-old man presents with a 4 day history of an itchy and sore right ear. He has recently returned from holiday in Spain. On examination the right ear canal is inflamed but no debris is seen. The tympanic membrane is clearly visible and is unremarkable. What is the most appropriate management?

- A. Topical corticosteroid + aminoglycoside
- B. Topical corticosteroid
- C. Refer to ENT
- D. Topical corticosteroid + clotrimazole
- E. Oral flucloxacillin

Question 63 of 117

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- B. Topical corticosteroid
- C. Refer to ENT
- D. Topical corticosteroid + clotrimazole
- E. Oral flucloxacillin

This patient has otitis externa. The first line management is either a topical antibiotic or a combined topical antibiotic and steroid

Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes of otitis externa include:
- infection: bacterial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*) or fungal
- seborrhoeic dermatitis
- contact dermatitis (allergic and irritant)

Features
- ear pain, itch, discharge
- otoscopy: red, swollen, or eczematous canal

The recommend initial management of otitis externa is:
- topical antibiotic or a combined topical antibiotic with steroid
- if the tympanic membrane is perforated aminoglycosides should not be used
- if there is canal debris then consider removal
- if the canal is extensively swollen then an ear wick is sometimes inserted

Second line options include
- consider contact dermatitis secondary to neomycin
- oral antibiotics if the infection is spreading
- taking a swab inside the ear canal
- empirical use of an antifungal agent

Malignant otitis externa is more common in elderly diabetics. In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal. Intravenous antibiotics may be required.

Question 64 of 117

A 45-year-old woman is presents with itchy, violaceous papules on the flexor aspects of her wrists. She is normally fit and well and has not had a similar rash previously. Given the likely diagnosis, what other feature is she most likely to have?

- A. Onycholysis
- B. Raised ESR
- C. Mucous membrane involvement
- D. Pain in small joints
- E. Microscopic haematuria

Question 64 of 117

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- D. Pain in small joints
- E. Microscopic haematuria

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

Mucous membrane involvement is common in lichen planus

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 65 of 117

A 78-year-old nursing home resident is reviewed due to the development of an intensely itchy rash. On examination white linear lesions are seen on the wrists and elbows, and red papules are present on the penis. What is the most appropriate management?

- A. Topical permethrin
- B. Referral to GUM clinic
- C. Topical betnovate
- D. Topical ketoconazole
- E. Topical selenium sulphide

Question 65 of 117

A 78-year-old nursing home resident is reviewed due to the development of an intensely itchy rash. On examination white linear lesions are seen on the wrists and elbows, and red papules are present on the penis. What is the most appropriate management?

- A. Topical permethrin
- B. Referral to GUM clinic
- C. Topical betnovate
- D. Topical ketoconazole
- E. Topical selenium sulphide

Lichen planus may give a similar picture but the intense itching is more characteristic of scabies. It is also less common for lichen planus to present in the elderly - it typical affects patients aged 30-60 years.

Scabies

Scabies is caused by the mite Sarcoptes scabiei and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8–12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Question 66 of 117

A 72-year-old woman is diagnosed with a number of erythematous, rough lesions on the back of her hands. A diagnosis of actinic keratoses is made. What is the most appropriate management?

- A. Reassurance
- B. Urgent referral to a dermatologist
- C. Topical fluorouracil cream
- D. Review in 3 months
- E. Topical betnovate

Question 66 of 117

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- A. Reassurance
- B. Urgent referral to a dermatologist
- C. Topical fluorouracil cream
- D. Review in 3 months
- E. Topical betnovate

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 67 of 117

A 15-year-old male returns to the dermatology clinic for review. He has a past history of acne and is currently treated with oral lymecycline. There has been no response to treatment and examination reveals evidence of scarring on his face. What is the most suitable treatment?

- A. Oral doxycycline
- B. Oral cyproterone acetate
- C. Oral retinoin
- D. IV retinoin
- E. Topical retinoids

Question 67 of 117

A 15-year-old male returns to the dermatology clinic for review. He has a past history of acne and is currently treated with oral lymecycline. There has been no response to treatment and examination reveals evidence of scarring on his face. What is the most suitable treatment?

- A. Oral doxycycline
- B. Oral cyproterone acetate
- C. Oral retinoin
- D. IV retinoin
- E. Topical retinoids

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 68 of 117

Each one of the following is associated with yellow nail syndrome except:

- A. Chronic sinus infections
- B. Bronchiectasis
- C. Azoospermia
- D. Congenital lymphoedema
- E. Pleural effusions

Question 68 of 117

Each one of the following is associated with yellow nail syndrome except:

- A. Chronic sinus infections
- B. Bronchiectasis
- C. Azoospermia
- D. Congenital lymphoedema
- E. Pleural effusions

Yellow nail syndrome

Slowing of nail growth leads to the characteristic thickened and discoloured nails seen in yellow nail syndrome

Associations

- congenital lymphoedema
- pleural effusions
- bronchiectasis
- chronic sinus infections

Question 69 of 117

A 29-year-old man presents due to the development of 'hard skin' on his scalp. On examination he has a 4cm circular, white, hyperkeratotic lesion on the crown of his head. He has no past history of any skin or scalp disorder. Skin scrapings are reported as follows:

No fungal elements seen

What is the most likely diagnosis?

- A. Psoriasis
- B. Dissecting cellulitis
- C. Kerion
- D. Systemic lupus erythematous
- E. Seborrhoeic dermatitis

Question 69 of 117

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No fungal elements seen

What is the most likely diagnosis?

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- B. Dissecting cellulitis
- C. Kerion
- D. Systemic lupus erythematous
- E. Seborrhoeic dermatitis

As the skin scraping is negative for fungi the most likely diagnosis is psoriasis. Scalp psoriasis may occur in isolation in patients with no history of psoriasis elsewhere. Please see the link for more information.

The white appearance of the lesion is secondary to the 'silver scale' covering the psoriatic plaque.

Psoriasis

Psoriasis can be divided into type 1 and 2:

Type 1
- presents < 40 years old
- positive family history
- associated with HLA-CW6

Type 2
- presents > 50 years old
- no family history

Cause
- abnormal T cell activity stimulates keratinocyte proliferation (rather than an actual primary keratinocyte disorder)
- mediated by type 1 helper T cells

Features
- red, scaly plaques
- scalp, extensor surfaces elbows/knees, sacrum
- nail signs: pitting, onycholysis
- arthritis

Complications
- psoriatic arthropathy (around 10%)
- psychological distress
- increased incidence of cardiovascular disease

Question 70 of 117

A 54-year-old woman is prescribed topical fusidic acid for a small patch of impetigo around her nose. She has recently been discharged from hospital following varicose vein surgery. Seven days after starting treatment there has been no change in her symptoms. Examination reveals a persistent small, crusted area around the right nostril. Whilst awaiting the results of swabs, what is the most appropriate management?

- A. Oral vancomycin
- B. Oral erythromycin
- C. Topical metronidazole
- D. Topical mupirocin
- E. Oral flucloxacillin

Question 70 of 117

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- B. Oral erythromycin
- C. Topical metronidazole
- D. Topical mupirocin
- E. Oral flucloxacillin

MRSA should be considered given the recent hospital stay and lack of response to fusidic acid. Topical mupirocin is therefore the most appropriate treatment.

Impetigo: management

Limited, localised disease
- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease
- oral flucloxacillin
- oral erythromycin if penicillin allergic

Question 71 of 117

A 63-year-old man who is known to have type 2 diabetes mellitus presents with a number of lesions over his shins. On examination there are a number of 3-4 mm smooth, firm, papules which are hyperpigmented and centrally depressed. What is the most likely diagnosis?

- A. Lupus vulgaris
- B. Necrobiosis lipoidica diabeticorum
- C. Guttate psoriasis
- D. Granuloma annulare
- E. Pyoderma gangrenosum

Question 71 of 117

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- C. Guttate psoriasis
- D. Granuloma annulare
- E. Pyoderma gangrenosum

Granuloma annulare

Basics

- papular lesions that are often slightly hyperpigmented and depressed centrally
- typically occur on the dorsal surfaces of the hands and feet, and on the extensor aspects of the arms and legs

A number of associations have been proposed to conditions such as diabetes mellitus but there is only weak evidence for this

Question 72 of 117

A 43-year-old presents with itchy lesions on the instep of both feet. These have been present for the past two months. On examination small blisters are seen with surrounding dry and cracked skin. What is the most likely diagnosis?

- A. Porphyria cutanea tarda
- B. Pustular psoriasis
- C. Pompholyx
- D. Bullous pemphigoid
- E. Pemphigus

Question 72 of 117

A 43-year-old presents with itchy lesions on the instep of both feet. These have been present for the past two months. On examination small blisters are seen with surrounding dry and cracked skin. What is the most likely diagnosis?

- A. Porphyria cutanea tarda
- B. Pustular psoriasis
- C. Pompholyx
- D. Bullous pemphigoid
- E. Pemphigus

Pompholyx

Pompholyx is a type of eczema which affects both the hands (cheiropompholyx) and the feet (pedopompholyx). It is also known as dyshidrotic eczema

Features
- small blisters on the palms and soles
- pruritic, sometimes burning sensation
- once blisters burst skin may become dry and crack

Management
- cool compresses
- emollients
- topical steroids

Question 73 of 117

Café-au-lait spots are seen in each of the following, except:

- A. McCune-Albright syndrome
- B. Friedreich's ataxia
- C. Neurofibromatosis
- D. Fanconi anaemia
- E. Tuberous sclerosis

Question 73 of 117

Café-au-lait spots are seen in each of the following, except:

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- B. Friedreich's ataxia
- C. Neurofibromatosis
- D. Fanconi anaemia
- E. Tuberous sclerosis

Café-au-lait spots

Hyperpigmented lesions that vary in colour from light brown to dark brown, with borders that may be smooth or irregular

Causes

- neurofibromatosis type I & II
- tuberous sclerosis
- Fanconi anaemia
- McCune-Albright syndrome

Question 74 of 117

A 58-year-old woman presents with a persistent erythematous rash on her cheeks and a 'red nose'. She describes occasional episodes of facial flushing. On examination erythematous skin is noted on the nose and cheeks associated with occasional telangiectasia. What is the most appropriate management?

- A. Topical metronidazole
- B. Topical isotretinoin
- C. Benzyl peroxide
- D. Daktacort
- E. Topical hydrocortisone

Question 74 of 117

A 58-year-old woman presents with a persistent erythematous rash on her cheeks and a 'red nose'. She describes occasional episodes of facial flushing. On examination erythematous skin is noted on the nose and cheeks associated with occasional telangiectasia. What is the most appropriate management?

A. Topical metronidazole

B. Topical isotretinoin

C. Benzyl peroxide

D. Daktacort

E. Topical hydrocortisone

Given that this woman has mild symptoms, topical metronidazole should be used first line

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 75 of 117

A 34-year-old man with a history of polyarthralgia, back pain and diarrhoea is found to have a 3 cm red lesion on his shin which is starting to ulcerate. What is the most likely diagnosis?

- A. Systemic *Shigella* infection
- B. Syphilis
- C. Metastatic colon cancer
- D. Erythema nodosum
- E. Pyoderma gangrenosum

Question 75 of 117

A 34-year-old man with a history of polyarthralgia, back pain and diarrhoea is found to have a 3 cm red lesion on his shin which is starting to ulcerate. What is the most likely diagnosis?

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- B. Syphilis
- C. Metastatic colon cancer
- D. Erythema nodosum
- E. Pyoderma gangrenosum

This patient is likely to have ulcerative colitis, which has a known association with large-joint arthritis, sacroilitis and pyoderma gangrenosum

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 76 of 117

A 48-year-old man with a history of psoriasis develops plaques on his face. Of the following options, which one is the most appropriate treatment?

- A. Hydrocortisone 1%
- B. Calcipotriol
- C. Coal tar
- D. Dithranol
- E. Tacrolimus

Question 76 of 117

A 48-year-old man with a history of psoriasis develops plaques on his face. Of the following options, which one is the most appropriate treatment?

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- B. Calcipotriol
- C. Coal tar
- D. Dithranol
- E. Tacrolimus

Difficult question, particularly as there is an emphasis on patient-doctor choice when deciding upon treatment in psoriasis. Vitamin D analogues can be used in this situation but calcipotriol is not recommended as it may cause irritation - calcitriol and tacalcitol are alternatives. Mild potency topical steroids are useful for the management of facial psoriasis. Coal tar is smelly and messy - most patients would not tolerate facial application

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 77 of 117

Which one of the following conditions is least associated with photosensitivity?

- A. Discoid lupus erythematous
- B. Systemic lupus erythematous
- C. Herpes labialis
- D. Acute intermittent porphyria
- E. Xeroderma pigmentosum

Question 77 of 117

Which one of the following conditions is least associated with photosensitivity?

- A. Discoid lupus erythematous
- B. Systemic lupus erythematous
- C. Herpes labialis
- D. Acute intermittent porphyria
- E. Xeroderma pigmentosum

Photosensitivity is not a feature of acute intermittent porphyria unlike porphyria cutanea tarda

Photosensitive skin disorders

Diseases aggravated by exposure to sunlight

- systemic lupus erythematosus, discoid lupus
- porphyria (not acute intermittent)
- herpes labialis (cold sores)
- pellagra
- xeroderma pigmentosum
- solar urticaria
- polymorphic light eruption

Question 78 of 117

A 20-year-old man presents with acute gingivitis assoociated with oral ulceration. A diagnosis of primary herpes simplex infection is suspected. Which one of the following types of rash is he most likely to go an develop?

- A. Erythema ab igne
- B. Erythema nodosum
- C. Erythema chronicum migrans
- D. Erythema marginatum
- E. Erythema multiforme

Question 78 of 117

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- D. Erythema marginatum
- E. Erythema multiforme

Erythema multiforme

Erythema multiforme
- target lesions (typically worse on peripheries e.g. palms and soles)
- severe = Stevens-Johnson syndrome (blistering and mucosal involvement)

Causes
- viruses: herpes simplex virus, Orf
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

Question 79 of 117

A 17-year-old female originally from Nigeria presents due to a swelling around her earlobe. She had her ears pierced around three months ago and has noticed the gradual development of an erythematous swelling since. On examination a keloid scar is seen. What is the most appropriate management?

- A. Intralesional diclofenac
- B. Advise no treatment is available
- C. Intralesional triamcinolone
- D. Advise will spontaneously regress within 4-6 months
- E. Intralesional sclerotherapy

Question 79 of 117

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- E. Intralesional sclerotherapy

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 80 of 117

A 22-year-old male is referred to dermatology clinic with a longstanding problem of bilateral excessive axillary sweating. He is otherwise well but the condition is affecting his confidence and limiting his social life. What is the most appropriate management?

- A. Non-sedating antihistamine
- B. Topical hydrocortisone 1%
- C. Perform thyroid function tests
- D. Topical aluminium chloride
- E. Trial of desmopressin

Question 80 of 117

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- C. Perform thyroid function tests
- D. Topical aluminium chloride
- E. Trial of desmopressin

Hyperhidrosis

Hyperhidrosis describes the excessive production of sweat

Management options include

- topical aluminium chloride preparations are first-line. Main side effect is skin irritation
- iontophoresis: particularly useful for patients with palmar, plantar and axillary hyperhidrosis
- botulinum toxin: currently licensed for axillary symptoms
- surgery: e.g. Endoscopic transthoracic sympathectomy. Patients should be made aware of the risk of compensatory sweating

Question 81 of 117

A 15-year-old girl presents with an urticarial rash, angioedema and wheezing. Her mother states that she has just come from her younger sister's party where she had been helping to blow up balloons. What is the most likely diagnosis?

- A. C1-esterase deficiency (hereditary angioedema)
- B. Allergic contact dermatitis
- C. Peanut allergy
- D. Latex allergy
- E. Irritant contact dermatitis

Question 81 of 117

A 15-year-old girl presents with an urticarial rash, angioedema and wheezing. Her mother states that she has just come from her younger sister's party where she had been helping to blow up balloons. What is the most likely diagnosis?

- A. C1-esterase deficiency (hereditary angioedema)
- B. Allergic contact dermatitis
- C. Peanut allergy
- D. Latex allergy
- E. Irritant contact dermatitis

This is a typical history of latex allergy. Adrenaline should be given immediately and usual anaphylaxis management followed

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 82 of 117

A 29-year-old man consults you regarding a rash he has noticed around his groin. It has been present for the past 3 months and is asymptomatic. On examination there is a symmetrical well-demarcated, brown-red macular rash around the groin. What is the most likely diagnosis?

- A. Erythrasma
- B. Pityriasis versicolor
- C. Secondary syphilis
- D. Acanthosis nigricans
- E. *Candida*l intertrigo

Question 82 of 117

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- B. Pityriasis versicolor
- C. Secondary syphilis
- D. Acanthosis nigricans
- E. *Candida*l intertrigo

Erythrasma

Erythrasma is a generally asymptomatic, flat, slightly scaly, pink or brown rash usually found in the groin or axillae. It is caused by an overgrowth of the diphtheroid Corynebacterium minutissimum

Examination with Wood's light reveals a coral-red fluorescence.

Topical miconazole or antibacterial are usually effective. Oral erythromycin may be used for more extensive infection

Question 83 of 117

A patient who is suspected of having dermatitis herpetiformis undergoes a skin biopsy. Which one of the following antibodies is most likely to be found in the dermis?

- A. IgM
- B. IgA
- C. IgD
- D. IgE
- E. IgG

Question 83 of 117

A patient who is suspected of having dermatitis herpetiformis undergoes a skin biopsy. Which one of the following antibodies is most likely to be found in the dermis?

- A. IgM
- B. IgA
- C. IgD
- D. IgE
- E. IgG

Dermatitis herpetiformis - caused by IgA deposition in the dermis

Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

Features
- itchy, vesicular skin lesions on the extensor surfaces (e.g. Elbows, knees buttocks)

Diagnosis
- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

Management
- gluten-free diet
- dapsone

Question 84 of 117

Which one of the following is least recognised as a cause of erythroderma in the UK?

- A. Lymphoma
- B. Drug eruption
- C. Lichen planus
- D. Psoriasis
- E. Eczema

Question 84 of 117

Which one of the following is least recognised as a cause of erythroderma in the UK?

- A. Lymphoma
- B. Drug eruption
- C. Lichen planus
- D. Psoriasis
- E. Eczema

Erythroderma

Erythroderma is a term used when more than 95% of the skin is involved in a rash of any kind

Causes of erythroderma

- eczema
- psoriasis
- drugs e.g. gold
- lymphoma, leukaemia
- idiopathic

Erythrodermic psoriasis

- may result from progression of chronic disease to an exfoliative phase with plaques covering most of the body. Associated with mild systemic upset
- more serious form is an acute deterioration. This may be triggered by a variety of factors such as withdrawal of systemic steroids. Patients need to be admitted to hospital for management

Question 85 of 117

A patient develops an eczematous, weeping rash on his wrist following the purchase of a new watch. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

Question 85 of 117

A patient develops an eczematous, weeping rash on his wrist following the purchase of a new watch. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

This patient has allergic contact dermatitis, which is commonly precipitated by nickel

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
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In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 86 of 117

A 62-year-old woman mentions in diabetes clinic that she has a 'volcano' like spot on her left cheek, which has appeared over the past 3 months. She initially thought it may be a simple spot but it has not gone away. On examination she has a 5 mm red, raised lesion with a central keratin filled crater. A clinical diagnosis of probable keratoacanthoma is made. What is the most suitable management?

- A. Reassure will spontaneously involute within 3 months
- B. Urgent referral to dermatology
- C. Topical 5-FU
- D. Non-urgent referral to dermatology
- E. Oral prednisolone

Question 86 of 117

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- A. Reassure will spontaneously involute within 3 months
- B. Urgent referral to dermatology
- C. Topical 5-FU
- D. Non-urgent referral to dermatology
- E. Oral prednisolone

Whilst keratoacanthoma is a benign lesion it is difficult clinically to exclude squamous cell carcinoma so urgent excision is advised

Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

Question 87 of 117

A 67-year-old man with recurrent actinic keratoses on his scalp is reviewed. Which one of the following is not a treatment option for the management of this condition?

- A. Topical diclofenac
- B. Topical betnovate
- C. Topical fluorouracil
- D. Topical imiquimod
- E. Cryotherapy

Question 87 of 117

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- B. Topical betnovate
- C. Topical fluorouracil
- D. Topical imiquimod
- E. Cryotherapy

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 88 of 117

A 69-year-old woman with a history of learning difficulties is reviewed in clinic. She is known to have erythema ab igne on her legs but according to her carer still spends long hours in front of her electric fire. Which one of the following skin lesions is she at risk of developing?

- A. Squamous cell carcinoma
- B. Cutaneous T-cell lymphoma of the skin
- C. Dermatofibrosarcoma protuberans
- D. Basal cell carcinoma
- E. Malignant melanoma

Question 88 of 117

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- A. Squamous cell carcinoma
- B. Cutaneous T-cell lymphoma of the skin
- C. Dermatofibrosarcoma protuberans
- D. Basal cell carcinoma
- E. Malignant melanoma

Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

Question 89 of 117

A 31-year-old female with polycystic ovarian syndrome consults you as she is troubled with excessive facial hair. Switching her combined oral contraceptive pill to co-cyprindiol has had no effect. On examination she has hirsuitism affecting her moustache, beard, and temple areas. What is the most appropriate treatment?

- A. Topical salicylic acid
- B. Topical adapalene
- C. Oral clomifene
- D. Topical eflornithine
- E. Topical tazarotene

Question 89 of 117

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- D. Topical eflornithine
- E. Topical tazarotene

Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based

General
- weight reduction if appropriate
- if a women requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

Hirsuitism and acne
- a COC pill may be used help manage hirsuitism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

Infertility
- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen* therapies such as clomifene
- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

Question 90 of 117

A 72-year-old man is investigated for oral ulceration. A biopsy suggests pemphigus vulgaris. This is most likely to be caused by antibodies directed against:

- A. Hemidesmosomal BP180
- B. Occludin-2
- C. Hemidesmosomal BP230
- D. Desmoglein
- E. Adherens

Question 90 of 117

A 72-year-old man is investigated for oral ulceration. A biopsy suggests pemphigus vulgaris. This is most likely to be caused by antibodies directed against:

- A. Hemidesmosomal BP180
- B. Occludin-2
- C. Hemidesmosomal BP230
- D. Desmoglein
- E. Adherens

Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

Features

- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

Management

- steroids
- immunosuppressants

Question 91 of 117

Which one of the following drugs is most likely to result in a photosensitive rash?

- A. Gentamicin
- B. Erythromycin
- C. Penicillin
- D. Tetracycline
- E. Amoxicillin

Question 91 of 117

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- D. Tetracycline
- E. Amoxicillin

Drugs causing photosensitivity

Causes of drug-induced photosensitivity

- thiazides
- tetracyclines, sulphonamides, ciprofloxacin
- amiodarone
- NSAIDs e.g. piroxicam
- psoralens
- sulphonylureas

Question 92 of 117

A 17-year-old female presents with multiple comedones, pustules and papules on her face. Which one of the following is least likely to improve her condition?

- A. Topical retinoids
- B. Dietary advice
- C. Sunlight
- D. Oral trimethoprim
- E. Ethinylestradiol with cyproterone acetate

Question 92 of 117

A 17-year-old female presents with multiple comedones, pustules and papules on her face. Which one of the following is least likely to improve her condition?

- A. Topical retinoids
- B. Dietary advice
- C. Sunlight
- D. Oral trimethoprim
- E. Ethinylestradiol with cyproterone acetate

There is no role for dietary modification in patients with acne vulgaris. Ethinylestradiol with cyproterone acetate (Dianette) is useful in some female patients with acne unresponsive to standard treatment. Oral trimethoprim is useful in patients on long-term antibiotics who develop Gram negative folliculitis

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 93 of 117

Which one of the following is least likely to cause a bullous rash?

- A. Frusemide
- B. Friction
- C. Lichen planus
- D. Insect bite
- E. Epidermolysis bullosa

Question 93 of 117

Which one of the following is least likely to cause a bullous rash?

- A. Frusemide
- B. Friction
- C. Lichen planus
- D. Insect bite
- E. Epidermolysis bullosa

The bullous variant of lichen planus is extremely rare

Bullous disorders

Causes of skin bullae
- congenital: epidermolysis bullosa
- autoimmune: bullous pemphigoid, pemphigus
- insect bite
- trauma/friction
- drugs: barbiturates, furosemide

Question 94 of 117

A 64-year-old female is referred to dermatology due to a non-healing skin ulcer on her lower leg. This has been present for around 6 weeks and the appearance didn't improve following a course of oral flucloxacillin. What is the most important investigation to perform first?

- A. MRI
- B. Rheumatoid factor titres
- C. Ankle-brachial pressure index
- D. Swab of ulcer for culture and sensitivity
- E. X-ray

Question 94 of 117

A 64-year-old female is referred to dermatology due to a non-healing skin ulcer on her lower leg. This has been present for around 6 weeks and the appearance didn't improve following a course of oral flucloxacillin. What is the most important investigation to perform first?

- A. MRI
- B. Rheumatoid factor titres
- C. Ankle-brachial pressure index
- D. Swab of ulcer for culture and sensitivity
- E. X-ray

An ankle-brachial pressure index measurement would help exclude arterial insufficiency as a contributing factor. If this was abnormal then a referral to the vascular surgeons should be considered.

If the ulcer fails to heal with active management (e.g. Compression bandaging) then referral for consideration of biopsy to exclude a malignancy should be made.

Ongoing infection is not a common cause of non-healing leg ulcers.

Venous ulceration

Venous ulceration is typically seen above the medial malleolus

Investigations
- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

Management
- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

Question 95 of 117

A 14-year-old male is reviewed due to a patch of scaling and hair loss on the right side of his head. A skin scraping is sent which confirms a diagnosis of tinea capitis. Which organism is most likely to be responsible?

- A. Trichophyton tonsurans
- B. Microsporum distortum
- C. Trichophyton verrucosum
- D. Microsporum audouinii
- E. Microsporum canis

Question 95 of 117

A 14-year-old male is reviewed due to a patch of scaling and hair loss on the right side of his head. A skin scraping is sent which confirms a diagnosis of tinea capitis. Which organism is most likely to be responsible?

- A. Trichophyton tonsurans
- B. Microsporum distortum
- C. Trichophyton verrucosum
- D. Microsporum audouinii
- E. Microsporum canis

Tinea

Tinea is a term given to dermatophyte fungal infections. Three main types of infection are described depending on what part of the body is infected

- tinea capitis - scalp
- tinea corporis - trunk, legs or arms
- tinea pedis - feet

Tinea capitis (scalp ringworm)

- a cause of scarring alopecia mainly seen in children
- if untreated a raised, pustular, spongy/boggy mass called a kerion may form
- most common cause is Trichophyton tonsurans in the UK and the USA
- may also be caused by Microsporum canis acquired from cats or dogs
- diagnosis: lesions due to Microsporum canis green fluorescence under Wood's lamp*. However the most useful investigation is scalp scapings
- management (based on CKS guidelines): oral antifungals: terbinafine for Trichophyton tonsurans infections and griseofulvin for Microsporum infections. Topical ketoconazole shampoo should be given for the first two weeks to reduce transmission

Tinea corporis

- causes include Trichophyton rubrum and Trichophyton verrucosum (e.g. From contact with cattle)
- well-defined annular, erythematous lesions with pustules and papules
- may be treated with oral fluconazole

Tinea pedis (athlete's foot)

- characterised by itchy, peeling skin between the toes
- common in adolescence

*lesions due to Trichophyton species do not readily fluoresce under Wood's lamp

Question 96 of 117

Each of the following drugs may be used in psoriasis, except:

- A. Interferon alpha
- B. Infliximab
- C. Retinoids
- D. Methotrexate
- E. Ciclosporin

Question 96 of 117

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Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 97 of 117

A 34-year-old female with a history of discoid lupus erythematous is reviewed in clinic. The erythematous, scaly rash on her face has not responded to topical steroid creams. What is the most appropriate next step in management?

- A. UV light therapy
- B. Oral hydroxychloroquine
- C. Topical dapsone
- D. Oral prednisolone
- E. Topical hydroxychloroquine

Question 97 of 117

A 34-year-old female with a history of discoid lupus erythematous is reviewed in clinic. The erythematous, scaly rash on her face has not responded to topical steroid creams. What is the most appropriate next step in management?

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- E. Topical hydroxychloroquine

Discoid lupus erythematous - topical steroids --> oral hydroxychloroquine

Discoid lupus erythematous

Discoid lupus erythematous is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematous is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

Features
- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Management
- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure

Question 98 of 117

A 33-year-old woman is reviewed in the dermatology clinic with patchy, well demarcated hair loss on the scalp. This is affecting around 20% of her total scalp, and causing significant psychological distress. A diagnosis of alopecia areata is suspected. Which one of the following is an appropriate management plan?

- A. Topical 5-FU cream
- B. Autoimmune screen
- C. Topical ketoconazole
- D. Topical corticosteroid
- E. Autoimmune screen + topical ketoconazole

Question 98 of 117

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- A. Topical 5-FU cream
- B. Autoimmune screen
- C. Topical ketoconazole
- D. Topical corticosteroid
- E. Autoimmune screen + topical ketoconazole

Watchful waiting for spontaneous remission is another option. Neither the British Association of Dermatologists or Clinical Knowledge Summaries recommend screening for autoimmune disease

Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

Question 99 of 117

A 33-year-old is investigated for lethargy. The full blood count is reported as follows:

Hb 10.1 g/dl

Plt 156 * 10^9/l

WBC 3.7 * 10^9/l

His daughter was unwell one week previously with a pyrexial illness associated with a red rash on her cheeks. What is the most likely cause?

- A. Measles
- B. Coxsackie a16
- C. Group A haemolytic streptococci
- D. Parvovirus B19
- E. HHV-6 (Human Herpesvirus-6)

Question 99 of 117

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Parvovirus B19

Parvovirus B19 is a DNA virus which causes a variety of clinical presentations. It was identified in the 1980's as the cause of erythema infectiosum

Erythema infectiosum (also known as fifth disease or 'slapped-cheek syndrome')

- most common presenting illness
- systemic symptoms: lethargy, fever, headache
- 'slapped-cheek' rash spreading to proximal arms and extensor surfaces

Other presentations

- asymptomatic
- pancytopaenia in immunosuppressed patients
- aplastic crises e.g. in sickle-cell disease (parvovirus B19 suppresses erythropoiesis for about a week so aplastic anaemia is rare unless there is a chronic haemolytic anaemia)

Question 100 of 117

A 35-year-old female presents tender, erythematous nodules over her forearms. Blood tests reveal:

Calcium 2.78 mmol/l

What is the most likely diagnosis?

- A. Granuloma annulare
- B. Erythema nodosum
- C. Lupus pernio
- D. Erythema multiforme
- E. Necrobiosis lipoidica

Question 100 of 117

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- C. Lupus pernio
- D. Erythema multiforme
- E. Necrobiosis lipoidica

The likely underlying diagnosis is sarcoidosis

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 101 of 117

A 72-year-old woman who is known to have type 2 diabetes mellitus and heart failure is reviewed. One week ago she was treated with oral flucloxacillin and penicillin V for a right lower limb cellulitis. Unfortunately there has been no response to treatment. What is the most appropriate next line antibiotic?

- A. Co-amoxiclav
- B. Erythromycin
- C. Clindamycin
- D. Vancomycin
- E. Gentamicin

Question 101 of 117

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- A. Co-amoxiclav
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- C. Clindamycin
- D. Vancomycin
- E. Gentamicin

Cellulitis: management

The BNF recommends penicillin + flucloxacillin as first-line treatment for cellulitis. Erythromycin is recommend in patients allergic to penicillin. Treatment failure is now commonly treated with oral clindamycin.

Question 102 of 117

A 78-year-old woman asks you for cream to treat a lesion on her left cheek. It has been present for the past nine months and is asymptomatic. On examination you find a 2 * 3 cm area of flat brown pigmentation with a jagged, irregular edge. The pigmentation on the anterior aspect of the lesion is a darker brown. What is the most likely diagnosis?

- A. Solar lentigo
- B. Dermatofibroma
- C. Lentigo maligna
- D. Bowen's disease
- E. Seborrhoeic keratosis

Question 102 of 117

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- A. Solar lentigo
- B. Dermatofibroma
- C. Lentigo maligna
- D. Bowen's disease
- E. Seborrhoeic keratosis

These lesions often present a diagnostic dilemma. The asymmetrical nature of the lesion would however point away from a diagnosis of solar lentigo.

Lentigo maligna

Lentigo maligna is a type of melanoma in-situ. It typically progresses slowly but may at some stage become invasive causing lentigo maligna melanoma.

Question 103 of 117

A 36-year-old female with a history of ulcerative colitis is diagnosed as having pyoderma gangrenosum. She presented 4 days ago with a 1 cm lesion on her right shin which rapidly ulcerated and is now painful. What is the most appropriate management?

- A. Topical hydrocortisone
- B. Oral prednisolone
- C. Surgical debridement
- D. Topical tacrolimus
- E. Infliximab

Question 103 of 117

A 36-year-old female with a history of ulcerative colitis is diagnosed as having pyoderma gangrenosum. She presented 4 days ago with a 1 cm lesion on her right shin which rapidly ulcerated and is now painful. What is the most appropriate management?

- A. Topical hydrocortisone
- B. Oral prednisolone
- C. Surgical debridement
- D. Topical tacrolimus
- E. Infliximab

Topical therapy does have a role in pyoderma gangrenosum and it may seem intuitive to try this first before moving on to systemic treatment. However, pyoderma gangrenosum has the potential to evolve rapidly and for this reason oral prednisolone is usually given as initial treatment. For a review see BMJ 2006;333:181-184

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 104 of 117

Each one of the following is associated with hypertrichosis, except:

- A. Anorexia nervosa
- B. Porphyria cutanea tarda
- C. Psoriasis
- D. Minoxidil
- E. Ciclosporin

Question 104 of 117

Each one of the following is associated with hypertrichosis, except:

- A. Anorexia nervosa
- B. Porphyria cutanea tarda
- C. Psoriasis
- D. Minoxidil
- E. Ciclosporin

Hirsuitism and hypertrichosis

Hirsuitism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Causes of hirsuitism
- polycystic ovarian syndrome
- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

Causes of hypertrichosis
- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa

Question 105 of 117

A 19-year-old man is started on isotretinoin for severe nodulo-cystic acne. Which one of the following side-effects is most likely to occur?

- A. Low mood
- B. Thrombocytopaenia
- C. Raised plasma triglycerides
- D. Reversible alopecia
- E. Dry skin

Question 105 of 117

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- A. Low mood
- B. Thrombocytopaenia
- C. Raised plasma triglycerides
- D. Reversible alopecia
- E. Dry skin

Dry skin is the most common side-effect of isotretinoin

Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

Adverse effects

- teratogenicity: females MUST be using two forms of contraception (e.g. combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Question 106 of 117

A 45-year-old man who presented with itchy lesions on his hands is diagnosed with scabies. It is decided to treat him with permethrin 5%. You have explained the need to treat all members of the household and hot wash all bedding and clothes. What advice should be given about applying the cream?

- A. From neck down + leave for 12 hours
- B. All skin including scalp + leave for 12 hours + retreat in 2 days
- C. All skin including scalp + leave for 12 hours + retreat in 7 days
- D. From neck down + leave for 4 hours
- E. From neck down + leave for 12 hours + retreat in 7 days

Question 106 of 117

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- C. All skin including scalp + leave for 12 hours + retreat in 7 days
- D. From neck down + leave for 4 hours
- E. From neck down + leave for 12 hours + retreat in 7 days

Scabies - permethrin treatment: all skin including scalp + leave for 12 hours + retreat in 7 days

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation (and common practice).

Scabies

Scabies is caused by the mite Sarcoptes scabiei and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8–12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Question 107 of 117

Which one of the following antibiotics is most associated with the development of Stevens-Johnson syndrome?

- A. Co-trimoxazole
- B. Ethambutol
- C. Chloramphenicol
- D. Ciprofloxacin
- E. Gentamicin

Question 107 of 117

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- E. Gentamicin

Stevens-Johnson syndrome

Stevens-Johnson syndrome severe form of erythema multiforme associated with mucosal involvement and systemic symptoms

Features
- rash is typically maculopapular with target lesions being characteristic. May develop into vesicles or bullae
- mucosal involvement
- systemic symptoms: fever, arthralgia

Causes
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- viruses: herpes simplex virus, Orf
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill
- connective tissue disease e.g. SLE
- sarcoidosis
- malignancy

Question 108 of 117

A 33-year-old man presents complaining of an itchy scalp and dandruff. On examination he is noted to have eczema on his scalp, behind his ears and around his nose. He has tried 'Head and Shoulders' and 'Neutrogen T-gel' but with poor results. Which one of the following is the most appropriate treatment for his scalp?

- A. Topical hydrocortisone
- B. Oral metronidazole
- C. Topical selenium sulphide
- D. Oral terbinafine
- E. Topical ketoconazole

Question 108 of 117

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Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 109 of 117

A 34-year-old patient who is known to have psoriasis presents with erythematous skin in the groin and genital area. He also has erythematous skin in the axilla. In the past he has expressed a dislike of messy or cumbersome creams. What is the most appropriate treatment?

- A. Topical steroid
- B. Topical dithranol
- C. Topical clotrimazole
- D. Coal tar
- E. Topical calcipotriol

Question 109 of 117

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- B. Topical dithranol
- C. Topical clotrimazole
- D. Coal tar
- E. Topical calcipotriol

Flexural psoriasis - topical steroid

This patient has flexual psoriasis which responds well to topical steroids. Topical calcipotriol is usually irritant in flexures. Mild tar preparations are an option but may be messy and cumbersome.

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
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- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 110 of 117

A 50-year-old man presents with shiny, flat-topped papules on the palmar aspect of the wrists. He is mainly bothered by the troublesome and persistent itching. A diagnosis of lichen planus is suspected. What is the most appropriate treatment?

- A. Refer for punch biopsy
- B. Emollients + oral antihistamine
- C. Topical dapsone
- D. Topical clotrimazole
- E. Topical clobetasone butyrate

Question 110 of 117

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- C. Topical dapsone
- D. Topical clotrimazole
- E. Topical clobetasone butyrate

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 111 of 117

A 17-year-old male is reviewed six weeks after starting an oral antibiotic for acne vulgaris. He stopped taking the drug two weeks ago due to perceived alteration in his skin colour, and denies been exposed to strong sunlight for the past six months. On examination he has generalised increased skin pigmentation, including around the buttocks. Which one of the following antibiotics was he likely to be taking?

- A. Doxycycline
- B. Oxytetracycline
- C. Tetracycline
- D. Erythromycin
- E. Minocycline

Question 111 of 117

A 17-year-old male is reviewed six weeks after starting an oral antibiotic for acne vulgaris. He stopped taking the drug two weeks ago due to perceived alteration in his skin colour, and denies been exposed to strong sunlight for the past six months. On examination he has generalised increased skin pigmentation, including around the buttocks. Which one of the following antibiotics was he likely to be taking?

- A. Doxycycline
- B. Oxytetracycline
- C. Tetracycline
- D. Erythromycin
- E. Minocycline

Minocycline can cause irreversible skin pigmentation and is now considered a second line drug in acne. Photosensitivity secondary to tetracycline/doxycycline is less likely given the generalised distribution of the pigmentation and the failure to improve following drug withdrawal

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 112 of 117

A 30-year-old man presents with painful, purple coloured lesions on his shins. Some of these lesions have started to heal and no evidence of scarring is seen. These have been present for the past 2 weeks. There is no past medical history of note and he takes no regular medications. What is the most useful next investigation?

- A. Liver function tests
- B. Anti-nuclear antibody
- C. ECG
- D. HIV test
- E. Chest x-ray

Question 112 of 117

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- A. Liver function tests
- B. Anti-nuclear antibody
- C. ECG
- D. HIV test
- E. Chest x-ray

The likely diagnosis here is erythema nodosum (EN). All these tests may have a place but a chest x-ray is important as it helps exclude sarcoidosis and tuberculosis, two important cause of EN

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 113 of 117

A 67-year-old man is diagnosed with actinic keratoses on his right temple and prescribed fluorouracil cream. One week later he presents as the skin where he is applying treatment has become red and sore. On examination there is no sign of weeping or blistering. What is the most appropriate action?

- A. Continue fluorouracil cream + review in 1 week
- B. Complete a 'Yellow Card'
- C. Stop fluorouracil cream + prescribe topical hydrocortisone
- D. Continue fluorouracil cream + prescribe topical hydrocortisone to use concurrently
- E. Stop fluorouracil cream

Question 113 of 117

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This is a normal reaction to treatment. Fluorouracil should be continued for at least another week before starting topical steroids.

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features
- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include
- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 114 of 117

A 65-year-old woman with blistering lesions on her leg is diagnosed as having bullous pemphigoid. What is the most appropriate initial management?

- A. Reassurance
- B. Topical corticosteroids
- C. Oral itraconazole
- D. Screen for solid-tumour malignancies
- E. Oral corticosteroids

Question 114 of 117

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- D. Screen for solid-tumour malignancies
- E. Oral corticosteroids

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 115 of 117

Which one of the following statements regarding fungal nail infections is incorrect?

- A. *Candida* accounts for less than 10% of cases
- B. Diagnosis should be confirmed by microbiology before starting treatment
- C. Treatment is successful in around 90-95% of people
- D. Thickened, rough, opaque nails are typical
- E. Suitable investigations include nail clippings

Question 115 of 117

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- E. Suitable investigations include nail clippings

Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by
- dermatophytes - mainly Trichophyton rubrum, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

Features
- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

Investigation
- nail clippings
- scrapings of the affected nail

Management
- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

Question 116 of 117

Which of the following skin conditions associated with malignancy are not correctly paired?

- A. Erythroderma and lymphoma
- B. Necrolytic migratory erythema and gastrinoma
- C. Acanthosis nigricans and gastrointestinal cancer
- D. Sweet's syndrome and myelodysplasia
- E. Erythema gyratum repens and lung cancer

Question 116 of 117

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- E. Erythema gyratum repens and lung cancer

Necrolytic migratory erythema is associated with glucagonomas

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	**Associated malignancies**
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 117 of 117

A man presents with an area of dermatitis on his left wrist. He thinks he may be allergic to nickel. Which one of the following is the best test to investigate this possibility?

- A. Skin patch test
- B. Radioallergosorbent test (RAST)
- C. Nickel IgG levels
- D. Skin prick test
- E. Nickel IgM levels

Question 117 of 117

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- D. Skin prick test
- E. Nickel IgM levels

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 1 of 138

Which one of the following is a recognised cause of hypokalaemia associated with hypertension

- A. Liddle's syndrome
- B. Bartter's syndrome
- C. Gitelman syndrome
- D. Ciclosporin
- E. Renal tubular acidosis

Question 1 of 138

Which one of the following is a recognised cause of hypokalaemia associated with hypertension

- A. Liddle's syndrome
- B. Bartter's syndrome
- C. Gitelman syndrome
- D. Ciclosporin
- E. Renal tubular acidosis

Liddle's syndrome: hypokalaemia + hypertension

Liddle's syndrome is an autosomal dominant disorder that mimics hyperaldosteronism, resulting in hypokalaemia associated with hypertension.

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension.

Gitelman's syndrome is due to a defect in the thiazide-sensitive Na^+ Cl- transporter in the distal convoluted tubule. It is associated with hypokalaemia and normotension.

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 2 of 138

A 15-year-old girl is investigated for primary amenorrhoea, despite having developed secondary sexual characteristics at 11 years of age. On examination she has well developed breasts with scanty pubic hair and small bilateral groin swellings. What is the most likely diagnosis?

- A. Congenital adrenal hyperplasia
- B. Polycystic ovarian syndrome
- C. Turner's syndrome
- D. Complete androgen insensitivity syndrome
- E. Mullerian duct agenesis

Question 2 of 138

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- B. Polycystic ovarian syndrome
- C. Turner's syndrome
- D. Complete androgen insensitivity syndrome
- E. Mullerian duct agenesis

Androgen insensitivity syndrome

Androgen insensitivity syndrome is an X-linked recessive condition due to end-organ resistance to testosterone causing genotypically male children (46XY) to have a female phenotype. Complete androgen insensitivity syndrome is the new term for testicular feminisation syndrome

Features
- 'primary amennorhoea'
- undescended testes causing groin swellings
- breast development may occur as a result of conversion of testosterone to oestradiol

Diagnosis
- buccal smear or chromosomal analysis to reveal 46XY genotype

Management
- counselling - raise child as female
- bilateral orchidectomy (increased risk of testicular cancer due to undescended testes)
- oestrogen therapy

Question 3 of 138

A 48-year-old man who was diagnosed with type 2 diabetes mellitus presents for review. During his annual review he was noted to have the following results:

Total cholesterol	5.3 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	3.1 mmol/l
Triglyceride	1.7 mmol/l
HbA1c	6.4%

His current medication is metformin 500mg tds. According to recent NICE guidelines, what is the most appropriate action?

- A. Simvastatin 40mg on
- B. Lifestyle advice, repeat lipid profile in 3 months
- C. Nicotinic acid
- D. Atorvastatin 40mg on
- E. Increase his metformin slowly to 1g tds

Question 3 of 138

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- D. Atorvastatin 40mg on
- E. Increase his metformin slowly to 1g tds

Patients over the age of 40 years with type 2 diabetes mellitus should be started on a statin if they have any other risk factors for cardiovascular disease, such as smoking and hypertension. This patient has a 'high-risk lipid profile' and should therefore be offered statin therapy. Please see the link for more details.

Question 4 of 138

A 45-year-old man is referred to the acute medical unit. He had presented earlier in the day to the GP complaining of ongoing fatigue and polydipsia. A BM taking in the surgery was 22.3. On examination he is an obese man (BMI 36) with a pulse of 84 bpm and blood pressure of 144/84 mmHg. Blood tests reveal the following:

Na^+	140 mmol/l
K^+	3.9 mmol/l
Bicarbonate	23 mmol/l
Urea	5.2 mmol/l
Creatinine	101 µmol/l
Glucose	21.2 mmol/l

What is the most appropriate initial management?

- A. Gliclazide
- B. Pioglitazone
- C. Weight loss
- D. Metformin
- E. Commence insulin therapy

Question 4 of 138

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Weight reduction alone would be insufficient in this patient with frank diabetes

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis* with severe liver disease or renal failure

Contraindications**

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 5 of 138

A 46-year-old man with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.7
2	7.6

How should these results be interpreted?

- A. Normal
- B. Impaired fasting glucose and impaired glucose tolerance
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Question 5 of 138

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How should these results be interpreted?

- A. Normal
- B. Impaired fasting glucose and impaired glucose tolerance
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Both the fasting and two-hour glucose are within normal limits.

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.
Diabetes mellitus

If the patient is symptomatic:
- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:
- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 6 of 138

A 45-year-old man is investigated following referral to the endocrinology clinic with polydipsia. Plasma glucose and calcium are normal. A water deprivation test is performed with the following results:

Starting plasma osm.	292 mOsmol/l
Final urine osm.	142 mOsmol/l
Urine osm. post-DDAVP	885 mOsmol/l

What is the most likely diagnosis?

- A. Psychogenic polydipsia
- B. Nephrogenic diabetes insipidus
- C. Primary hyperparathyroidism
- D. Pseudohypoparathyroidism
- E. Cranial diabetes insipidus

Question 6 of 138

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- C. Primary hyperparathyroidism
- D. Pseudohypoparathyroidism
- E. Cranial diabetes insipidus

A dramatic improvement is seen in the ability of the kidneys to concentrate urine following the administration of DDAVP. This points towards a diagnosis of cranial diabetes insipidus

Water deprivation test

Method

- prevent patient drinking water
- ask patient to empty bladder
- hourly urine and plasma osmolalities

	Starting plasma osm.	**Final urine osm.**	**Urine osm. post-DDAVP**
Normal	Normal	> 600	> 600
Psychogenic polydipsia	Low	> 400	> 400
Cranial DI	High	< 300	> 600
Nephrogenic DI	High	< 300	< 300

Question 7 of 138

A 56-year-old man is reviewed in the Cardiology outpatient clinic following a myocardial infarction one year previously. During his admission he was found to be hypertensive and diabetic. He complains that he has put on 5kg in weight in the past 6 months. Which of his medications may be contributing to his weight gain?

- A. Metformin
- B. Losartan
- C. Clopidogrel
- D. Gliclazide
- E. Simvastatin

Question 7 of 138

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- A. Metformin
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- D. Gliclazide
- E. Simvastatin

Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present.

Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- increased appetite and weight gain

Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- photosensitivity
- peripheral neuropathy

Sulfonylureas should be avoided in breast feeding and pregnancy

Question 8 of 138

What causes increased sweating in patients with acromegaly?

A. Increased sodium content in sweat

B. Decreased LH and FSH secondary to hypopituitarism

C. Episodic hypoglycaemia

D. Low-grade chronic pyrexia

E. Sweat gland hypertrophy

Question 8 of 138

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- C. Episodic hypoglycaemia
- D. Low-grade chronic pyrexia
- E. Sweat gland hypertrophy

Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

Features
- coarse, oily skin , large tongue, prognathism, interdental spaces
- spade-like hands, increase in shoe size
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

Complications
- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Question 9 of 138

Each one of the following is a cause of cranial diabetes insipidus, except:

- A. Pituitary surgery
- B. Lithium
- C. Histiocytosis X
- D. Craniopharyngioma
- E. Post head-injury

Question 9 of 138

Each one of the following is a cause of cranial diabetes insipidus, except:

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- B. Lithium
- C. Histiocytosis X
- D. Craniopharyngioma
- E. Post head-injury

Lithium causes a nephrogenic diabetes insipidus

Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 10 of 138

Which one of the following statements regarding maturity-onset diabetes of the young (MODY) is true?

- A. There is usually a strong family history
- B. Body mass index is typically > 30
- C. Doesn’t respond to glimepiride
- D. Autosomal recessive inheritance
- E. Frequent episodes of diabetic ketoacidosis are typical

Question 10 of 138

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- D. Autosomal recessive inheritance
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MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

MODY 3
- 60% of cases
- due to a defect in the HNF-1 alpha gene

MODY 2
- 20% of cases
- due to a defect in the glucokinase gene

Question 11 of 138

A 45-year-old woman is investigated for weight gain. She had had been unwell for around four months and described a combination of symptoms including depression, facial male-pattern hair growth and reduced libido. During the work-up she was found to be hypertensive with a blood pressure of 170/100 mmHg. Which one of the following tests is most likely to be diagnostic?

- A. Renin:aldosterone levels
- B. High-dose dexamethasone suppression test
- C. Pelvic ultrasound
- D. Overnight dexamethasone suppression test
- E. 24 hr urinary free cortisol

Question 11 of 138

A 45-year-old woman is investigated for weight gain. She had had been unwell for around four months and described a combination of symptoms including depression, facial male-pattern hair growth and reduced libido. During the work-up she was found to be hypertensive with a blood pressure of 170/100 mmHg. Which one of the following tests is most likely to be diagnostic?

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The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

This patient has Cushing's syndrome as evidenced by the weight gain, hirsuitism, depression and hypertension. Polycystic ovarian syndrome may give some of these features but would not cause such an elevated blood pressure.

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 12 of 138

A 9-year-old boy is investigated for lethargy. Examination is unremarkable with a blood pressure of 102/62 mmHg. Blood tests reveal:

Na^+	140 mmol/l
K^+	2.6 mmol/l
Bicarbonate	33 mmol/l
Urea	4.2 mmol/l
Creatinine	91 µmol/l

Which one of the following conditions is most likely to be responsible?

- A. Cushing's syndrome
- B. Conn's syndrome
- C. 11-beta hydroxylase deficiency
- D. Bartter's syndrome
- E. Liddle's syndrome

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Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

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- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 13 of 138

A 35-year-old female who has recently being diagnosed with Grave's disease presents for review 3 months after starting a 'block and replace' regime with carbimazole and thyroxine. She is concerned about developing thyroid eye disease. What is the best way that her risk of developing thyroid eye disease can be reduced?

- A. Reduce alcohol intake
- B. A diet rich in omega-3 fatty acids
- C. Regular exercise
- D. Stop smoking
- E. Lose weight

Question 13 of 138

A 35-year-old female who has recently being diagnosed with Grave's disease presents for review 3 months after starting a 'block and replace' regime with carbimazole and thyroxine. She is concerned about developing thyroid eye disease. What is the best way that her risk of developing thyroid eye disease can be reduced?

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- B. A diet rich in omega-3 fatty acids
- C. Regular exercise
- D. Stop smoking
- E. Lose weight

Smoking is the most important modifiable risk factor for the development of thyroid eye disease

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 14 of 138

A 46-year-old woman is referred to endocrine with a tender neck swelling. Blood results are as follows:

TSH <0.1 mU/l

T4 188 nmol/l

Hb 14.2 g/dl

Plt 377 * 10^9/l

WBC 6.4 * 10^9/l

ESR 65 mm/hr

Technetium thyroid scan shows decreased uptake globally

What is the most likely diagnosis?

- A. Sick thyroid syndrome
- B. Acute bacterial thyroiditis
- C. Hashimoto's thyroiditis
- D. Subacute thyroiditis
- E. Toxic multinodular goitre

Question 14 of 138

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- D. Subacute thyroiditis
- E. Toxic multinodular goitre

Subacute thyroiditis is suggested by the tender goitre, hyperthyroidism and raised ESR. The globally reduced uptake on technetium thyroid scan is also typical

Subacute (De Quervain's) thyroiditis

Subacute thyroiditis (also known as De Quervain's thyroiditis) is thought to occur following viral infection and typically presents with hyperthyroidism

Features

- hyperthyroidism
- painful goitre
- raised ESR
- globally reduced uptake on iodine-131 scan

Management

- usually self-limiting - most patients do not require treatment
- thyroid pain may respond to aspirin or other NSAIDs
- in more severe cases steroids are used, particularly if hypothyroidism develops

Question 15 of 138

A 68-year-old woman is found to have the following blood tests:
TSH 0.05 mu/l
Free T4 19 pmol/l (range 9-25 pmol/l)
Free T3 7 pmol/l (range 3-9 pmol/l)

If left untreated, what are the most likely possible consequences?

- A. Supraventricular arrhythmias and osteoporosis
- B. Supraventricular arrhythmias and hyperlipidaemia
- C. Hypothyroidism and impaired glucose tolerance
- D. Myasthenia gravis and hypothyroidism
- E. Impaired glucose tolerance and hyperlipidaemia

Question 15 of 138

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- D. Myasthenia gravis and hypothyroidism
- E. Impaired glucose tolerance and hyperlipidaemia

Subclinical hyperthyroidism

Subclinical hyperthyroidism is an entity which is gaining increasing recognition. It is defined as:

- normal serum free thyroxine and triiodothyronine levels
- with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l)

Causes

- multinodular goitre, particularly in elderly females
- excessive thyroxine may give a similar biochemical picture

The importance in recognising subclinical hyperthyroidism lies in the potential effect on the cardiovascular system (atrial fibrillation) and bone metabolism (osteoporosis). It may also impact on quality of life and increase the likelihood of dementia

Management

- TSH levels often revert back to normal - therefore levels must be persistently low to warrant intervention
- a reasonable treatment option is a therapeutic trial of low-dose antithyroid agents for approximately 6 months in an effort to induce a remission

Question 16 of 138

A 61-year-old man presents as he developed enlargement of his breast tissue. He has become very self-conscious and is worried about going on holiday in the summer. Which one of the following drugs is most likely to be responsible?

- A. Amitriptyline
- B. Isoniazid
- C. Verapamil
- D. Methyldopa
- E. Spironolactone

Question 16 of 138

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- D. Methyldopa
- E. Spironolactone

All the above drugs may cause gynaecomastia but spironolactone is the most common cause.

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia
- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

Drug causes of gynaecomastia
- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia
- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

Question 17 of 138

A 53 year man presents as his wife has noticed a change in his appearance. He has also noticed his hands seem larger. On examination blood pressure is 170/94 and he is noted to have bitemporal hemianopia. What is the most appropriate first-line treatment?

- A. Octreotide
- B. External irradiation
- C. Pegvisomant
- D. Trans-sphenoidal surgery
- E. Bromocriptine

Question 17 of 138

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- C. Pegvisomant
- D. Trans-sphenoidal surgery
- E. Bromocriptine

Trans-sphenoidal surgery is the treatment of choice in acromegaly. There is no significant evidence base supporting the use of pre-operative octreotide

Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists
- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue
- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant
- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

Question 18 of 138

A 45-year-old female is admitted to the Emergency Department with abdominal pain associated with vomiting. She has a past medical history of hypothyroidism and takes thyroxine. On examination she is pyrexial at 37.6ºC. Pulse is 110 bpm with a blood pressure of 100/64 mmHg. Blood results show the following:

Na^+	131 mmol/l
K^+	4.9 mmol/l
Urea	8.1 mmol/l
Creatinine	110 µmol/l
Glucose	3.3 mmol/l

What treatment should be given first?

- A. Ceftriaxone + benzylpenicillin
- B. Glucagon
- C. Propranolol
- D. Triiodothyronine
- E. Hydrocortisone

Question 18 of 138

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This is a typical history of Addison's. Patients may have a history of other autoimmune conditions such as thyroid disorders. Steroids should be given as soon as possible

Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

Features

- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

Other causes of hypoadrenalism

Primary causes

- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

Secondary causes

- pituitary disorders (e.g. tumours, irradiation, infiltration)

Exogenous glucocorticoid therapy

Question 19 of 138

A 46-year-old man presents as he is concerned about reduced libido, erectile dysfunction and excessive thirst. His wife also reports that he has 'no energy' and is generally listless. During the review of systems he also complains of pains in both hands. Which one of the following investigations is most likely to reveal the diagnosis?

- A. Ferritin
- B. Testosterone
- C. Cortisol
- D. Blood glucose
- E. Prolactin

Question 19 of 138

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- B. Testosterone
- C. Cortisol
- D. Blood glucose
- E. Prolactin

The above patient has symptoms consistent with haemochromatosis. The excessive thirst is secondary to untreated diabetes mellitus. Diabetes mellitus itself would not normally cause reduced libido or arthralgia.

Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 20 of 138

In patients with suspected insulinoma, which one of the following is considered the best investigation?

- A. Oral glucose tolerance test
- B. Insulin tolerance test
- C. Early morning C-peptide levels
- D. Glucagon stimulation test
- E. Supervised fasting

Question 20 of 138

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- E. Supervised fasting

Insulinoma is diagnosed with supervised prolonged fasting

CT of the pancreas is also useful in demonstrating a lesion

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 21 of 138

A diabetic man is diagnosed as having painful diabetic neuropathy in his feet. He has no other medical history of note. What is the most suitable first-line treatment to relieve his pain?

- A. Duloxetine
- B. Gabapentin
- C. Carbamazepine
- D. Referral to pain management clinic
- E. Pregabalin

Question 21 of 138

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- C. Carbamazepine
- D. Referral to pain management clinic
- E. Pregabalin

Diabetic neuropathy

NICE updated it's guidance on the management of diabetic neuroopathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

Question 22 of 138

An 18-year-old girl is admitted to the Emergency Department with an episode of sweating and dizziness. She is brought in by her father who has type 2 diabetes mellitus as he is worried she may be diabetic. He describes a number of similar episodes for the past two weeks. Her BM on admission is 1.9 mmol/l so the following bloods are taken:

Plasma glucose	1.8 mmol/l
Insulin	15 mg/ml (6-10 mg/ml)
Proinsulin	22% (22-24%)
C-peptide	0.15 nmol/l (0.2-0.4 nmol/l)

What is the most likely diagnosis?

- A. Diabetes mellitus
- B. Insulinoma
- C. Nesidioblastosis
- D. Insulin abuse
- E. Sulfonylurea abuse

Question 22 of 138

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- A. Diabetes mellitus
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- C. Nesidioblastosis
- D. Insulin abuse
- E. Sulfonylurea abuse

The raised insulin with low c-peptide level points to a diagnosis of insulin abuse. C-peptide levels would be raised in a patient following sulfonylurea abuse

Hypoglycaemia

Causes
- insulinoma - increased ratio of proinsulin to insulin
- self-administration of insulin/sulphonylureas
- liver failure
- Addison's disease
- alcohol

Other possible causes in children
- nesidioblastosis - beta cell hyperplasia

Question 23 of 138

A 55-year-old woman is investigated following an osteoporotic hip fracture. The following results are obtained:

TSH < 0.05 mu/l

Free T4 29 pmol/l

Which one of the following autoantibodies is most likely to be present?

- A. Anti-TSH receptor stimulating autoantibodies
- B. Anti-nuclear antibodies
- C. Anti-thyroglobulin autoantibodies
- D. Anti-microsomal antibodies
- E. Anti-thyroid peroxidase autoantibodies

Question 23 of 138

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Anti-TSH receptor stimulating autoantibodies (often referred to as Thyroid Stimulating Immunoglobulins) are almost diagnostic of Graves' disease, the most common cause of thyrotoxicosis in the UK

Graves' disease: features

Features seen in Graves' but not in other causes of thyrotoxicosis
- eye signs: exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

Autoantibodies
- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

Question 24 of 138

Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

- A. Diabetes mellitus
- B. Bendrofluazide
- C. Nephrotic syndrome
- D. Alcohol
- E. Obesity

Question 24 of 138

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- A. Diabetes mellitus
- B. Bendrofluazide
- C. Nephrotic syndrome
- D. Alcohol
- E. Obesity

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia
- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia
- nephrotic syndrome
- cholestasis
- hypothyroidism

Question 25 of 138

A 71-year-old woman with a history of type 2 diabetes mellitus presents with lethargy and polyuria. A diagnosis of hyperosmolar hyperglycaemic state is considered. Which one of the following findings would be least consistent with this diagnosis?

- A. pH of 7.38
- B. Ketones 1+ in urine
- C. Serum osmolality of 310 mosmol/kg
- D. Serum bicarbonate of 19 mmol/l
- E. Glucose of 45 mmol/l

Question 25 of 138

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- C. Serum osmolality of 310 mosmol/kg
- D. Serum bicarbonate of 19 mmol/l
- E. Glucose of 45 mmol/l

A trace of ketones may be found in hyperosmolar hyperglycaemic state. Serum osmolality is typically > 320 mosmol/kg

Hyperosmolar hyperglycaemic state

The American Diabetes Association criteria for the diagnosis of hyperosmolar hyperglycaemic state (HHS) is as follows:

- glucose > 33.3 mmol/l
- pH > 7.30
- serum bicarbonate > 15 mmol/l
- serum osmolality > 320 mosmol/kg
- traces of ketones may be present in urines

Question 26 of 138

A 64-year-old man with a history of type 2 diabetes mellitus is admitted with chest pain to the Emergency Department. An ECG shows ST elevation in the anterior leads and he is thrombolysed and transferred to the Coronary Care Unit (CCU). His usual medication includes simvastatin, gliclazide and metformin. How should his diabetes be managed whilst in CCU?

- A. Stop metformin + continue gliclazide at a higher dose
- B. Subcutaneous insulin: basal-bolus regime
- C. Continue metformin + gliclazide at same dose
- D. Intravenous insulin
- E. Subcutaneous insulin: biphasic insulin regime

Question 26 of 138

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The benefits of tight glycaemic control following a myocardial infarction were initially established by the DIGAMI study.

Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO2) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO2 of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO2 of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Question 27 of 138

A 28-year-old woman with polycystic ovarian syndrome consults you as she is having problems becoming pregnant. She has a past history of oligomenorrhea and has previously recently stopped taking a combined oral contraceptive pill. Despite stopping the pill 6 months ago she is still not having regular periods. Her body mass index is 28 kg/m^2. Apart from advising her to lose weight, which one of the following interventions is most effective in increasing her chances of conceiving?

- A. Metformin
- B. Bromocriptine
- C. Laparoscopic ovarian cautery
- D. Clomifene
- E. Orlistat

Question 27 of 138

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- C. Laparoscopic ovarian cautery
- D. Clomifene
- E. Orlistat

Infertility in PCOS - clomifene is superior to metformin

Whilst metformin has a role in the management of infertility it should be used second-line to anti-oestrogens such as clomifene. Similar questions to this often appear in which clomifene is not an option, in this case metformin is clearly the right answer.

Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based

General

- weight reduction if appropriate
- if a women requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

Hirsuitism and acne

- a COC pill may be used help manage hirsuitism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

Infertility

- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen* therapies such as clomifene
- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

Question 28 of 138

What is the mechanism of action of rosiglitazone?

- A. PPAR-gamma receptor antagonist
- B. PPAR-alpha receptor antagonist
- C. PPAR-alpha receptor agonist
- D. PPAR-gamma receptor agonist
- E. Increases endogenous insulin secretion

Question 28 of 138

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- D. PPAR-gamma receptor agonist
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Glitazones are agonists of PPAR-gamma receptors

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 29 of 138

A 45-year-old female is reviewed in the medical clinic with a two month history of lethargy. Blood tests reveal the following:

Na^+	129 mmol/l
K^+	5.1 mmol/l
Urea	5.3 mmol/l
Creatinine	99 µmol/l
Total T4	66 nmol/l

Which one of the following investigations is most likely to reveal the diagnosis?

- A. Serum glucose
- B. TSH
- C. Free T4
- D. Overnight dexamethasone suppression test
- E. Short synacthen test

Question 29 of 138

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- E. Short synacthen test

The short synacthen test is the best test to diagnose Addison's disease

Hyponatraemia and a high potassium in a patient with lethargy is highly suggestive of Addison's disease. The thyroxine level is slightly low and she may indeed have co-existing hypothyroidism but this would not explain the high potassium

Many labs have an upper reference range for potassium of 5.5 mmol/l, but in the context of the other results hypoadrenalism should be suspected

Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a short ACTH test. Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Question 30 of 138

A 45-year-old man is reviewed in the diabetes clinic. The following results are obtained:

Urinalysis NAD

HbA1c 8.6%

Gliclazide is added to the metformin he already takes. What is the minimum time period after which the HbA1c should be repeated ?

- A. 6 months
- B. 1 month
- C. 2 weeks
- D. 3 months
- E. 4 months

Question 30 of 138

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HbA1C - recheck after 2-3 months

A more accurate answer would probably be 2 months but this is not given as an option. See the explanation below

Glycosylated haemoglobin

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HBA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose = (2 * HbA1c) - 4.5

Question 31 of 138

A 36-year-old woman presents with feeling tired and cold all the time. On examination a firm, non-tender goitre is noted. Blood tests reveal the following:

TSH 24.2 mU/l

Free T4 5.4 pmol/l

What is the most likely diagnosis?

- A. Primary atrophic hypothyroidism
- B. Pituitary failure
- C. De Quervain's thyroiditis
- D. Iodine deficiency
- E. Hashimoto's thyroiditis

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- D. Iodine deficiency
- E. Hashimoto's thyroiditis

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

The combination of a goitre with hypothyroidism points to a diagnosis of Hashimoto's.

Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

Features

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

Question 32 of 138

Which one of the following is not part of the diagnostic criteria for the metabolic syndrome?

- A. High triglycerides
- B. Low HDL
- C. High LDL
- D. Central obesity
- E. Hypertension

Question 32 of 138

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High LDL levels are not part of the World Health Organization or International Diabetes Federation diagnostic criteria

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 33 of 138

A 45-year-old man presents with bitemporal hemianopia and spade-like hands. What is the definite test to confirm the diagnosis?

- A. Early morning growth hormone
- B. Insulin tolerance test
- C. Oral glucose tolerance with growth hormone measurements
- D. Random insulin-like growth factor 1 (IGF-!)
- E. Short ACTH test

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- E. Short ACTH test

The diagnostic test for acromegaly is an oral glucose tolerance with growth hormone measurements

Acromegaly: investigations

Growth hormone (GH) levels vary during the day and are therefore not diagnostic. The definitive test is the oral glucose tolerance (OGTT) with serial GH measurements. Serum IGF-1 may also be used as a screening test and is sometimes used to monitor disease

Oral glucose tolerance test

- in normal patients GH is suppressed to < 2 mu/L with hyperglycaemia
- in acromegaly there is no suppression of GH
- may also demonstrate impaired glucose tolerance which is associated with acromegaly

A pituitary MRI may demonstrate a pituitary tumour

Question 34 of 138

A 54-year-old woman presents to the Emergency Department with confusion and fever. She has a past history of thyrotoxicosis previously treated with radioiodine therapy. On examination she has a pulse of 120/min regular, blood pressure 150/90 mmHg, temperature of 39.1ºC and a respiratory rate of 18/min. Examination of the cardiorespiratory system is unremarkable and urine dipstick is clear. Blood results showed the following:

Free T4 84 pmol/l (normal range 10–22 pmol/l)

Free T3 29 pmol/l (2.5–5.5 pmol/l)

TSH < 0.01 mU/l (0.5–4.0 mU/l)

Which one of the following does not have a role in the subsequent management?

- A. Lugol's iodine
- B. Propranolol
- C. Propylthiouracil
- D. Bicarbonate
- E. Dexamethasone

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- C. Propylthiouracil
- D. Bicarbonate
- E. Dexamethasone

There is no indication for giving bicarbonate in this scenario.

Thyroid storm

Thyroid storm is a rare but life-threatening complication of thyrotoxicosis. It is typically seen in patients with established thyrotoxicosis and is rarely seen as the presenting feature. Iatrogenic thyroxine excess does not usually result in thyroid storm

Clinical features include:

- fever > 38.5ºC
- tachycardia
- confusion and agitation
- nausea and vomiting
- hypertension
- heart failure
- abnormal liver function test

Management

- symptomatic treatment e.g. paracetamol
- treatment of underlying precipitating event
- anti-thyroid drugs: e.g. methimazole or propylthiouracil
- Lugol's iodine
- dexamethasone - e.g. 4mg IV qds - blocks the conversion of T4 to T3
- propranolol

Question 35 of 138

Which one of the following is not associated with primary hyperparathyroidism?

- A. Hypotension
- B. Multiple endocrine neoplasia type 1
- C. Multiple endocrine neoplasia type 2a
- D. Depression
- E. Pancreatitis

Question 35 of 138

Which one of the following is not associated with primary hyperparathyroidism?

- A. Hypotension
- B. Multiple endocrine neoplasia type 1
- C. Multiple endocrine neoplasia type 2a
- D. Depression
- E. Pancreatitis

Primary hyperparathyroidism is associated with hypertension

Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism
- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'
- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations
- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations
- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment
- total parathyroidectomy

Question 36 of 138

A 25-year-old Asian woman who is 26 weeks pregnant has an oral glucose tolerance test (OGTT). This was requested due to a combination of her ethnicity and a background of obesity. A recent ultrasound shows that the fetus is large for dates. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	9.2
2	14.2

What is the most appropriate management?

- A. Start insulin
- B. Give advice about a diabetic diet
- C. Give advice about a diabetic diet + repeat OGTT in 4 weeks
- D. Start metformin
- E. Start insulin + aspirin

Question 36 of 138

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- D. Start metformin
- E. Start insulin + aspirin

Insulin should be started straight away given the blood glucose levels and evidence of macrosomia

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes

- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 37 of 138

A 36-year-old female with a BMI of 34 kg/m^2 is reviewed after managing to lose 3 kg in the past month. She asks about the possibility of starting a drug to help her lose weight. What is the primary mode of action of orilistat?

- A. Leptin antagonist
- B. Pancreatic lipase inhibitor
- C. Blocks intestinal absorption of lipids
- D. HMG-CoA reductase inhibitor
- E. Centrally-acting appetite suppressant

Question 37 of 138

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The primary mode of action of orilistat is to inhibit pancreatic lipases, which in turn will decrease the absorption of lipids from the intestine

Obesity: therapeutic options

The management of obesity consists of a step-wise approach:
- conservative: diet, exercise
- medical
- surgical

Orlistat is a pancreatic lipase inhibitor used in the management of obesity. Adverse effects include faecal urgency/incontinence and flatulence. A lower dose version is now available without prescription ('Alli'). NICE have defined criteria for the use of orlistat. It should only be prescribed as part of an overall plan for managing obesity in adults who have:
- BMI of 28 kg/m^2 or more with associated risk factors, or
- BMI of 30 kg/m^2 or more
- continued weight loss e.g. 5% at 3 months
- orlistat is normally used for < 1 year

Sibutramine
- withdrawn January 2010 by the European Medicines Agency due to an increased risk of cardiovascular events
- centrally acting appetite suppressant (inhibits uptake of serotonin and noradrenaline at hypothalamic sites that regular food intake)
- adverse effects include hypertension (monitor blood pressure and pulse during treatment), constipation, headache, dry mouth, insomnia and anorexia
- contraindicated in psychiatric illness, hypertension, IHD, stroke, arrhythmias

Rimonabant, a specific CB1 cannabinoid receptor antagonist, was withdrawn in October 2008 after the European Medicines Agency warned of serious psychiatric problems including suicide

Question 38 of 138

A 27-year-old female develops eye pain and reduced visual acuity following the initiation of treatment for her recently diagnosed Grave's disease. Which one of the following treatments is likely to have been started?

- A. Radioiodine treatment
- B. Thyroidectomy
- C. Propylthiouracil
- D. Carbimazole and thyroxine
- E. Carbimazole

Question 38 of 138

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- C. Propylthiouracil
- D. Carbimazole and thyroxine
- E. Carbimazole

Radioiodine treatment may lead to the development / worsening of thyroid eye disease in up to 15% of patients with Grave's disease

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 39 of 138

Which one of the following statements regarding polycystic ovarian syndrome (PCOS) is incorrect?

- A. A slightly elevated prolactin is consistent with a diagnosis of PCOS
- B. Luteinizing hormone levels are usually raised
- C. Hyperinsulinaemia is seen
- D. Acanthosis nigricans may be seen
- E. Affects between 2-3% of women of reproductive age

Question 39 of 138

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- E. Affects between 2-3% of women of reproductive age

Polycystic ovarian syndrome is extremely common, affecting between 5-20% of women of reproductive age

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features
- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations
- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 40 of 138

A 22-year-old female presents with recurrent painful oral ulceration. Examination reveals signs of oral *Candida*l infection. Which one of the following would most suggest type 1 polyglandular syndrome?

- A. Hypocalcaemia
- B. Rheumatoid arthritis
- C. Type II diabetes mellitus
- D. Coeliac disease
- E. Hypercalcaemia

Question 40 of 138

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- B. Rheumatoid arthritis
- C. Type II diabetes mellitus
- D. Coeliac disease
- E. Hypercalcaemia

Primary hypoparathyroidism is usually the first endocrine manifestation of type 1 autoimmune polyendocrinopathy syndrome. The contrast to multiple endocrine neoplasia (MEN), where hyperparathyroidism is a common finding, should be noted

The question gives a slightly atypical history as this is the upper end of the age range in which patients would be expected to present

Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

Question 41 of 138

A 33-year-old female is referred to endocrinology with thyrotoxicosis. Following a discussion of management options she elects to have radioiodine therapy. Which one of the following is the most likely adverse effect?

- A. Hypothyroidism
- B. Thyroid malignancy
- C. Agranulocytosis
- D. Oesophagitis
- E. Precipitation of thyroid eye disease

Question 41 of 138

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- A. Hypothyroidism
- B. Thyroid malignancy
- C. Agranulocytosis
- D. Oesophagitis
- E. Precipitation of thyroid eye disease

It is well documented that radioiodine therapy can precipitate thyroid eye disease but a majority of patients will eventually require thyroxine replacement

Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

Question 42 of 138

A 64-year-old patient is prescribed pegvisomant for the treatment of acromegaly. What is the mechanism of action of pegvisomant?

- A. IGF-1 receptor antagonist
- B. Growth hormone receptor antagonist
- C. IGF-1 receptor agonist
- D. Growth hormone receptor agonist
- E. Long-acting somatostatin analogue

Question 42 of 138

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Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists
- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue
- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant
- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

Question 43 of 138

A 24-year-old female with a history of type 1 diabetes mellitus presents to the Emergency Department with vomiting and abdominal pain. Finger-prick testing estimates the blood sugar to be 25 mmol/l. Arterial blood gases record a pH of 7.22. On examination the patient is dehydrated and weighs 84 kg. An intravenous line is sited and bloods are sent. One litre of 0.9% saline is infused and an intravenous insulin pump is set-up. What rate should insulin be initially given?

- A. 10 unit / hour
- B. 1 unit / hour
- C. 2 unit / hour
- D. 8 unit / hour
- E. 6 unit / hour

Question 43 of 138

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- D. 8 unit / hour
- E. 6 unit / hour

Diabetic ketoacidosis

The most common precipitating factors of diabetic ketoacidosis (DKA) are infection, missed insulin doses and myocardial infarction

American Diabetes Association diagnostic criteria are as follows:

- blood glucose >13.8 mmol/l
- pH < 7.30
- serum bicarbonate
- anion gap > 10
- ketonaemia

Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially
- insulin: an intravenous infusion should be started at 6u/hour. Once blood glucose is < 15 mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

Complications of DKA and its treatment

- gastric stasis
- cerebral oedema
- thromboembolism
- acute respiratory distress syndrome
- acute renal failure

Question 44 of 138

Liddle's syndrome is associated with each one of the following, except:

- A. Alkalosis
- B. Response to treatment with amiloride
- C. Hypertension
- D. Autosomal recessive inheritance
- E. Hypokalaemia

Question 44 of 138

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- A. Alkalosis
- B. Response to treatment with amiloride
- C. Hypertension
- D. Autosomal recessive inheritance
- E. Hypokalaemia

Question 45 of 138

Each one of the following is associated with pseudohypoparathyroidism, except:

A. Low calcium levels

B. Low PTH levels

C. Shortened 4th and 5th metacarpals

D. Low IQ

E. Short stature

Question 45 of 138

Each one of the following is associated with pseudohypoparathyroidism, except:

- A. Low calcium levels
- B. Low PTH levels
- C. Shortened 4th and 5th metacarpals
- D. Low IQ
- E. Short stature

Hypoparathyroidism

Primary hypoparathyroidism
- decrease PTH secretion
- e.g. secondary to thyroid surgery
- low calcium, high phosphate
- treat with alfacalcidol

Pseudohypoparathyroidism
- target cells being insensitive to PTH
- due to abnormality in a G protein
- associated with low IQ, short stature, shortened 4th and 5th metacarpals
- low calcium, high phosphate, high PTH
- diagnosis is made by measuring urinary cAMP and phosphate levels following an infusion of PTH. In hypoparathyroidism this will cause an increase in both cAMP and phosphate levels. In pseudohypoparathyroidism type I neither cAMP nor phosphate levels are increased whilst in pseudohypoparathyroidism type II only cAMP rises.

Pseudopseudohypoparathyroidism
- similar phenotype to pseudohypoparathyroidism but normal biochemistry

Question 46 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypercalcaemia
- B. Demeclocycline
- C. Histiocytosis X
- D. Lithium
- E. Hypokalaemia

Question 46 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypercalcaemia
- B. Demeclocycline
- C. Histiocytosis X
- D. Lithium
- E. Hypokalaemia

Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 47 of 138

Which one of the following is not an indication for treating a patient with subclinical hypothyroidism?

- A. Previous treatment of Graves' disease
- B. TSH > 10
- C. Raised ESR
- D. Positive thyroid autoantibodies
- E. Other autoimmune disorder

Question 47 of 138

Which one of the following is not an indication for treating a patient with subclinical hypothyroidism?

- A. Previous treatment of Graves' disease
- B. TSH > 10
- C. Raised ESR
- D. Positive thyroid autoantibodies
- E. Other autoimmune disorder

Subclinical hypothyroidism

Basics
- TSH raised but T3, T4 normal
- no obvious symptoms

Significance
- risk of progressing to overt hypothyroidism is 2-5% per year (higher in men)
- risk increased by presence of thyroid autoantibodies

Treat if
- TSH > 10
- thyroid autoantibodies positive
- other autoimmune disorder
- previous treatment of Graves' disease

Question 48 of 138

The first-line treatment in remnant hyperlipidaemia (dysbetalipoproteinaemia) is:

- A. Ursodeoxycholic acid
- B. Vitamin A
- C. Statins
- D. Fish oil
- E. Fibrates

Question 48 of 138

The first-line treatment in remnant hyperlipidaemia (dysbetalipoproteinaemia) is:

- A. Ursodeoxycholic acid
- B. Vitamin A
- C. Statins
- D. Fish oil
- E. Fibrates

Remnant hyperlipidaemia

Overview
- rare cause of mixed hyperlipidaemia (raised cholesterol and triglyceride levels)
- also known as Fredrickson type III hyperlipidaemia, broad-beta disease and dysbetalipoproteinaemia
- associated with apo-e2 homozygosity
- high incidence of ischaemic heart disease and peripheral vascular disease
- thought to be caused by impaired removal of intermediate density lipoprotein from the circulation by the liver

Features
- yellow palmar creases
- palmer xanthomas
- tuberous xanthomas

Management
- fibrates are first line treatment

Question 49 of 138

A 45-year-old man is reviewed in the diabetic clinic. His current medication is basal bolus insulin regime combined with ramipril 10mg od, amlodipine 10mg od, simvastatin 40mg on and aspirin 75mg od. On examination blood pressure is 134/84 mmHg. The following results are obtained:

HbA1c	7.3%
Albumin:Creatinine ratio	10.5

What is the most appropriate change to his treatment?

- A. Stop aspirin
- B. Increase dose of ramipril
- C. Add an angiotensin-II receptor antagonist
- D. Add doxazosin
- E. Stop ramipril

Question 49 of 138

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- A. Stop aspirin
- B. Increase dose of ramipril
- C. Add an angiotensin-II receptor antagonist
- D. Add doxazosin
- E. Stop ramipril

The patient is on the maximum daily dose of ramipril. Given the persistently raised albumin:creatinine ratio dual blockade with an angiotensin-II receptor antagonist is indicated

Diabetic nephropathy: management

Screening
- all patients should be screened annually
- albumin:creatinine ratio (ACR) in early morning specimen
- ACR > 2.5 = microalbuminuria

Management
- dietary protein restriction
- tight glycaemic control
- BP control: aim for < 130/80 mmHg
- benefits independent of blood pressure control have been demonstrated for ACE inhibitors and angiotensin II receptor blockers - these may be used alone or in combination
- control dyslipidaemia e.g. Statins

Question 50 of 138

A 51-year-old woman who is known to have poorly controlled type 1 diabetes mellitus is reviewed. Her main presenting complaint is bloating and vomiting after eating. She also notes that her blood glucose readings have become more erratic recently. Which one of the following medications is most likely to be beneficial?

- A. *Helicobacter pylori* eradication therapy
- B. Lansoprazole
- C. Amitriptyline
- D. Metoclopramide
- E. Cyclizine

Question 50 of 138

A 51-year-old woman who is known to have poorly controlled type 1 diabetes mellitus is reviewed. Her main presenting complaint is bloating and vomiting after eating. She also notes that her blood glucose readings have become more erratic recently. Which one of the following medications is most likely to be beneficial?

- A. *Helicobacter pylori* eradication therapy
- B. Lansoprazole
- C. Amitriptyline
- D. Metoclopramide
- E. Cyclizine

Diabetic neuropathy

NICE updated it's guidance on the management of diabetic neuroopathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

Question 51 of 138

Which one of the following skin disorders is least associated with hypothyroidism?

- A. Xanthomata
- B. Pruritus
- C. Pretibial myxoedema
- D. Eczema
- E. Dry, coarse hair

Question 51 of 138

Which one of the following skin disorders is least associated with hypothyroidism?

- A. Xanthomata
- B. Pruritus
- C. Pretibial myxoedema
- D. Eczema
- E. Dry, coarse hair

For the purposes of postgraduate exams pretibial myxoedema is associated with thyrotoxicosis. There are however case reports of it been found in hypothyroid patients, especially the diffuse non-pitting variety

Skin disorders associated with thyroid disease

Skin manifestations of hypothyroidism
- dry (anhydrosis), cold, yellowish skin
- non-pitting oedema (e.g. hands, face)
- dry, coarse scalp hair, loss of lateral aspect of eyebrows
- eczema
- xanthomata

Skin manifestations of hyperthyroidism
- pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli
- thyroid acropachy: clubbing
- scalp hair thinning
- increased sweating

Pruritus can occur in both hyper- and hypothyroidism

Question 52 of 138

A 53-year-old female with a history of primary atrophic hypothyroidism is assessed two months following a change in her dose of levothyroxine. Which one of the following best describes what the TSH should ideally be?

- A. Between 0.5 to 1.0 mU/l
- B. Between 0.5 to 2.5 mU/l
- C. Between 2.5 to 4.5 mU/l
- D. Between 1.5 to 3.5 mU/l
- E. Between 3.5 to 5.5 mU/l

Question 52 of 138

A 53-year-old female with a history of primary atrophic hypothyroidism is assessed two months following a change in her dose of levothyroxine. Which one of the following best describes what the TSH should ideally be?

- A. Between 0.5 to 1.0 mU/l
- B. Between 0.5 to 2.5 mU/l
- C. Between 2.5 to 4.5 mU/l
- D. Between 1.5 to 3.5 mU/l
- E. Between 3.5 to 5.5 mU/l

A TSH value between 0.5 to 2.5 mU/l is now considered preferable. Dosage changes should of course also take account of symptoms

Hypothyroidism: management

Key points

- initial starting dose of levothyroxine should be lower in elderly patients and those with ischaemic heart disease (e.g. 25–50 mcg/day)
- following a change in thyroxine dose thyroid function tests should be checked after 6-8 weeks
- the therapeutic goal is 'normalisation' of the thyroid stimulating hormone (TSH) level. As the majority unaffected people have a TSH value 0.5–2.5 mU/l it is now thought preferable to aim for a TSH in this range
- there is no evidence to support combination therapy with levothyroxine and liothyronine

Side-effects of thyroxine therapy

- hyperthyroidism: due to over treatment
- reduced bone mineral density
- worsening of angina
- atrial fibrillation

Question 53 of 138

A 36-year-old woman who presented with a goitre is diagnosed with autoimmune thyroiditis. Which one of the following types of thyroid cancer is she predisposed to developing?

- A. Anaplastic
- B. Lymphoma
- C. Medullary
- D. Follicular
- E. Papillary

Question 53 of 138

A 36-year-old woman who presented with a goitre is diagnosed with autoimmune thyroiditis. Which one of the following types of thyroid cancer is she predisposed to developing?

- A. Anaplastic
- B. Lymphoma
- C. Medullary
- D. Follicular
- E. Papillary

Hashimoto's thyroiditis is associated with thyroid lymphoma

Thyroid cancer

Features of hyperthyroidism or hypothyroidism are not commonly seen in patients with thyroid malignancies as they rarely secrete thyroid hormones

Type	**Percentage**	
Papillary	70%	Often young females - excellent prognosis
Follicular	20%	
Medullary	5%	Cancer of parafollicular cells, secrete calcitonin, part of MEN-2
Anaplastic	1%	Not responsive to treatment, can cause pressure symptoms
Lymphoma	Rare	Associated with Hashimoto's

Management of papillary and follicular cancer

- total thyroidectomy
- followed by radioiodine (I-131) to kill residual cells
- yearly thyroglobulin levels to detect early recurrent disease

Question 54 of 138

Which one of the following features is not seen in carcinoid syndrome?

- A. Flushing
- B. Diarrhoea
- C. Bronchospasm
- D. Hypertension
- E. Pellagra

Question 54 of 138

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- C. Bronchospasm
- D. Hypertension
- E. Pellagra

Flushing, diarrhoea, bronchospasm, tricuspid stenosis, pellagra --> carcinoid with liver mets - diagnosis: urinary 5-HIAA

Hypo- not hypertension is seen in carcinoid syndrome secondary to serotonin release

Carcinoid tumours

Carcinoid syndrome
- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

Features
- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation
- urinary 5-HIAA
- plasma chromogranin A y

Management
- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help

Question 55 of 138

A 47-year-old woman is referred to the general medical clinic. She has gained 10 kg in weight in the past 3 months but her main problem is episodic sweating. These episodes of sweating are associated with double vision and typically occur early in the morning. Clinical examination is unremarkable. What is the most likely diagnosis?

- A. Bronchial carcinoid
- B. Hashimoto's thyroiditis
- C. Menopause
- D. Cushing's syndrome
- E. Insulinoma

Question 55 of 138

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- A. Bronchial carcinoid
- B. Hashimoto's thyroiditis
- C. Menopause
- D. Cushing's syndrome
- E. Insulinoma

This is a typical presentation of insulinoma

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 56 of 138

A 56-year-old female is admitted to ITU with a severe pneumonia. Thyroid function tests are most likely to show:

- A. TSH normal; thyroxine high; T3 high
- B. TSH normal / low; thyroxine low; T3 low
- C. TSH high; thyroxine low; T3 low
- D. TSH low; thyroxine high; T3 high
- E. TSH high; thyroxine normal; T3 high

Question 56 of 138

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- A. TSH normal; thyroxine high; T3 high
- B. TSH normal / low; thyroxine low; T3 low
- C. TSH high; thyroxine low; T3 low
- D. TSH low; thyroxine high; T3 high
- E. TSH high; thyroxine normal; T3 high

Sick euthyroid syndrome

In sick euthyroid syndrome (now referred to as non-thyroidal illness) it is often said that everything (TSH, thyroxine and T3) is low. In the majority of cases however the TSH level is within the normal range (inappropriately normal given the low thyroxine and T3).

Changes are reversible upon recovery from the systemic illness.

Question 57 of 138

A 30-year-old female is diagnosed with having Grave's disease. What is her chance of developing thyroid eye disease?

- A. 2-5%
- B. 5-10&
- C. 10-15%
- D. 15-25%
- E. 25-50%

Question 57 of 138

A 30-year-old female is diagnosed with having Grave's disease. What is her chance of developing thyroid eye disease?

- A. 2-5%
- B. 5-10&
- C. 10-15%
- D. 15-25%
- E. 25-50%

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 58 of 138

A 43-year-old man is found to have a phaeochromocytoma. Which anti-hypertensive medication should be started first?

- A. Propranolol
- B. Ramipril
- C. Atenolol
- D. Phenoxybenzamine
- E. Doxazosin

Question 58 of 138

A 43-year-old man is found to have a phaeochromocytoma. Which anti-hypertensive medication should be started first?

- A. Propranolol
- B. Ramipril
- C. Atenolol
- D. Phenoxybenzamine
- E. Doxazosin

PHaeochromocytoma - give **PH**enoxybenzamine before beta-blockers

Phenoxybenzamine is a non-selective alpha-adrenoceptor antagonist and should be started before a beta-blocker is introduced

There is ongoing debate about the optimal medical management of phaeochromocytoma, with the suggestion that antihypertensive treatment regimes other than nonspecific alpha-blockade are just as effective and safe. There are however no trials to provide an answer to this question yet

Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

Basics
- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

Tests
- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:
- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

Question 59 of 138

A 69-year-old man who had a stroke 6 months ago is reviewed. After his diagnosis he was started on simvastatin 40mg on for secondary prevention of further cardiovascular disease. A fasting lipid profile taken one week ago is reported as follows:

Total cholesterol	5.4 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	4.1 mmol/l
Triglyceride	1.5 mmol/l

According to recent NICE guidelines, what is the most appropriate action?

- A. Switch to simvastatin 80mg on
- B. No change in medication, repeat lipid profile in 6 months
- C. Add nicotinic acid
- D. Switch to atorvastatin 80mg on
- E. Add ezetimibe

Question 59 of 138

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- B. No change in medication, repeat lipid profile in 6 months
- C. Add nicotinic acid
- D. Switch to atorvastatin 80mg on
- E. Add ezetimibe

Nicotinic acid can raise HDL levels by up to 30% but in practice its use is limited by flushing. Any change to treatment should of course be in conjunction with continued lifestyle advice.

The increased risk of myopathy with the 80mg dose of simvastatin was recently highlighted by the Medicines and Healthcare products Regulatory Agency. Please see the link for more details.

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 60 of 138

A 62-year-old HGV driver is reviewed. He was diagnosed last year with type 2 diabetes mellitus. Following weight loss and metformin his HbA1c has decreased from 8.8% to 8.4%. What is the most suitable next step in management?

- A. Add exenatide
- B. Make no changes to management
- C. Add gliclazide
- D. Stop metformin for a period to ensure hypoglycaemic awareness is not lost
- E. Add pioglitazone

Question 60 of 138

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- C. Add gliclazide
- D. Stop metformin for a period to ensure hypoglycaemic awareness is not lost
- E. Add pioglitazone

Pioglitazone is the best option here as it would not put him at risk of hypoglycaemia, which obviously could be dangerous given his job.

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c

- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 61 of 138

Which one of the following statements regarding impaired glucose regulation is correct?

- A. All patient should have a repeat oral glucose tolerance test every 2 years
- B. Patients with impaired glucose tolerance are more likely to develop diabetes than patients with impaired fasting glycaemia
- C. Impaired glucose tolerance (IGT) is defined as a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l
- D. Around 1 in 20 adults in the UK have impaired glucose regulation
- E. Patients should be offered metformin if lifestyle changes fail to improve their glucose profile

Question 61 of 138

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- D. Around 1 in 20 adults in the UK have impaired glucose regulation
- E. Patients should be offered metformin if lifestyle changes fail to improve their glucose profile

Impaired glucose regulation

Impaired glucose regulation (IGR) may also be referred to as non-diabetic hyperglycaemia (NDH) or prediabetes. It describes blood glucose levels which are above the normal range but not high enough for a diagnosis of diabetes mellitus. Diabetes UK estimate that around 1 in 7 adults in the UK have IGR. Many individuals with IGR will progress on to developing type 2 diabetes mellitus (T2DM) and they are therefore at greater risk of microvascular and macrovascular complications.

There are two main types of IGR:

- impaired fasting glucose (IFG) - due to hepatic insulin resistance
- impaired glucose tolerance (IGT) - due to muscle insulin resistance
- patients with IGT are more likely to develop T2DM and cardiovascular disease than patients with IFG

Definitions

- a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)
- impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l
- the role of HbA1c is diagnosing IGR and diabetes is currently under review
- people with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT

Management

- Diabetes UK suggests using the term 'prediabetes' when discussing the condition with patients as research has shown that this term has the most impact and is most easily understood
- lifestyle modification: weight loss, increased exercise, change in diet
- drug therapy is not currently licensed or recommended for patients with IGR in the UK
- at least yearly follow-up with blood tests is recommended

Question 62 of 138

Which of the following results establishes a diagnosis of diabetes mellitus?

- A. Asymptomatic patient with fasting glucose 7.9 mmol/L on one occasion
- B. Symptomatic patient with fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria +++
- D. Asymptomatic patient with random glucose 22.0 mmol/L on one occasion
- E. Symptomatic patient with random glucose 12.0 mmol/L on one occasion

Question 62 of 138

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- B. Symptomatic patient with fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria +++
- D. Asymptomatic patient with random glucose 22.0 mmol/L on one occasion
- E. Symptomatic patient with random glucose 12.0 mmol/L on one occasion

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 63 of 138

A 56-year-old lady with a BMI of 27 is reviewed in the diabetic clinic due to poor glycaemic control. She is currently being treated with gliclazide 160mg bd. Her latest bloods show:

Na^+	139 mmol/l
K^+	4.1 mmol/l
Urea	8.4 mmol/l
Creatinine	170 µmol/l
ALT	25 iu/l
yGT	33 iu/l
HbA1c	9.4%

Which one of the following medications should be added next?

- A. Guar gum
- B. Pioglitazone
- C. Metformin
- D. Acarbose
- E. Repaglinide

Question 63 of 138

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Which one of the following medications should be added next?

- A. Guar gum
- B. Pioglitazone
- C. Metformin
- D. Acarbose
- E. Repaglinide

Given that she is overweight metformin would be a natural choice to add. The creatinine however is elevated so pioglitazone is the next best option

One possible drawback of using pioglitazone is that it may lead to weight gain, especially given her BMI is already 27

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 64 of 138

A 34-year-old female with a history of Addison's disease presents for review in endocrinology clinic. She is generally well but complains of a decrease in her libido. On examination there is a slight loss of pubic hair. What is the most likely cause?

- A. Adverse effect of hydrocortisone therapy
- B. 11-hydroxylase deficiency
- C. Diethylstilbestrol deficiency
- D. Oestrogen deficiency
- E. Dehydroepiandrosterone (DHEA) deficiency

Question 64 of 138

A 34-year-old female with a history of Addison's disease presents for review in endocrinology clinic. She is generally well but complains of a decrease in her libido. On examination there is a slight loss of pubic hair. What is the most likely cause?

- A. Adverse effect of hydrocortisone therapy
- B. 11-hydroxylase deficiency
- C. Diethylstilbestrol deficiency
- D. Oestrogen deficiency
- E. Dehydroepiandrosterone (DHEA) deficiency

Dehydroepiandrosterone is the most abundant circulating adrenal steroid. Adrenal glands are the main source of dehydroepiandrosterone in females - loss of functioning adrenal tissue as in Addison's disease may result in symptoms secondary to androgen deficiency, such as loss of libido. Research is ongoing as to whether routine replacement of DHEA is beneficial

Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

Features
- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

Other causes of hypoadrenalism

Primary causes
- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

Secondary causes
- pituitary disorders (e.g. tumours, irradiation, infiltration)

Exogenous glucocorticoid therapy

Question 65 of 138

Which one of the following is most likely to be seen in a patient with multiple endocrine neoplasia (MEN) type I?

- A. Phaeochromocytoma
- B. Insulinoma
- C. Marfanoid body habitus
- D. Medullary thyroid carcinoma
- E. RET gene

Question 65 of 138

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Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	**MEN type IIa**	**MEN type IIb**
Mnemonic 'three P's': • parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia • pituitary (70%) • pancreas (50%, e.g. insulinoma, gastrinoma) • also: adrenal and thyroid	• phaeochromocytoma (95%, e.g. Phaeochromocytoma) • medullary thyroid cancer (70%) • parathyroid (60%)	• medullary thyroid cancer • phaeochromocytoma • marfanoid body habitus • neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene

MEN is inherited as an autosomal dominant disorder

Question 66 of 138

Cushing's syndrome is most typically associated with which one of the following abnormalities:

- A. Hypokalaemic metabolic acidosis
- B. Hyperkalaemic metabolic alkalosis
- C. Hypocalcaemic metabolic acidosis
- D. Hypokalaemic metabolic alkalosis
- E. Hyperkalaemic metabolic acidosis

Question 66 of 138

Cushing's syndrome is most typically associated with which one of the following abnormalities:

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- D. Hypokalaemic metabolic alkalosis
- E. Hyperkalaemic metabolic acidosis

Cushing's syndrome - hypokalaemic metabolic alkalosis

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:
- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test
- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation
- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 67 of 138

An insulin stress test is most useful in the investigation of:

- A. Glucagonoma
- B. Insulinoma
- C. Addison's disease
- D. Hypopituitarism
- E. Diabetes mellitus

Question 67 of 138

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Insulin stress tests are also occasionally used to differentiate Cushing's from pseudo-Cushing's

Insulin stress test

Basics

- used in investigation of hypopituitarism
- IV insulin given, GH and cortisol levels measured
- with normal pituitary function GH and cortisol should rise

Contraindications

- epilepsy
- ischaemic heart disease
- adrenal insufficiency

Question 68 of 138

A 23-year-old woman presents for review. She has not a normal period for around 8 months now. A recent pregnancy test was negative. Blood tests are ordered:

FSH	2.2 IU/L (0-20 IU/L)
Oestradiol	84 pmol/l (100-500 pmol/l)
Thyroid stimulating hormone	3.1 mIU/L
Prolactin	2 ng/ml (0-10 ng/ml)
Free androgen index	3 (< 7)

What is the most likely cause of her symptoms?

- A. Prolactinoma
- B. Premature ovarian failure
- C. Polycystic ovarian syndrome
- D. Addison's disease
- E. Excessive exercise

Question 68 of 138

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- C. Polycystic ovarian syndrome
- D. Addison's disease
- E. Excessive exercise

The bloods show a hypothalamic amenorrhoea which may be caused by stress or excessive exercise. The FSH would be raised in premature ovarian failure.

Amenorrhoea

Amenorrhoea may be divided into primary (failure to start menses by the age of 16 years) or secondary (cessation of established, regular menstruation for 6 months or longer).

Causes of primary amenorrhoea
- Turner's syndrome
- testicular feminisation
- congenital adrenal hyperplasia
- congenital malformations of the genital tract

Causes of secondary amenorrhoea (after excluding pregnancy)
- hypothalamic amenorrhoea (e.g. Stress, excessive exercise)
- polycystic ovarian syndrome (PCOS)
- hyperprolactinaemia
- premature ovarian failure
- thyrotoxicosis*

Initial investigations
- exclude pregnancy with urinary or serum bHCG
- gonadotrophins: low levels indicate a hypothalamic cause where as raised levels suggest an ovarian problem (e.g. Premature ovarian failure)
- prolactin
- androgen levels: raised levels may be seen in PCOS
- oestradiol
- thyroid function tests

*hypothyroidism may also cause amenorrhoea

Question 69 of 138

Which one of the following is the most common non-iatrogenic cause of Cushing's syndrome?

- A. Ectopic ACTH production
- B. Adrenal adenoma
- C. Micronodular adrenal dysplasia
- D. Adrenal carcinoma
- E. Pituitary tumour

Question 69 of 138

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- A. Ectopic ACTH production
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- C. Micronodular adrenal dysplasia
- D. Adrenal carcinoma
- E. Pituitary tumour

Cushing's disease is the most common, non-iatrogenic, cause of Cushing's syndrome

Cushing's syndrome: causes

ACTH dependent causes
- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes
- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's
- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Question 70 of 138

Which one of the following may be associated with galactorrhoea?

- A. Primary hypothyroidism
- B. Addison's disease
- C. Cushing's syndrome
- D. Grave's disease
- E. Bromocriptine

Question 70 of 138

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Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin
- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin
- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin
- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

Question 71 of 138

A 54-year-old man with type 2 diabetes mellitus is found on annual review to have new vessel formation at the optic disc. Visual acuity in both eyes is not affected (6/9). Blood pressure is155/84 mmHg.

HbA1c 8.4%

What is the most important intervention in this patient?

- A. Follow-up ophthalmoscopy in 3 months
- B. Add aspirin
- C. Blood pressure control
- D. Tight glycaemic control
- E. Laser therapy

Question 71 of 138

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- E. Laser therapy

This patient has proliferative diabetic retinopathy and urgent referral to an ophthalmologist for panretinal photocoagulation is indicated

Diabetic retinopathy

Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovasculization is thought to be caused by the production of growth factors in response to retinal ischaemia

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proposed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	**New classification**
Background retinopathy • microaneurysms (dots) • blot haemorrhages (=3) • hard exudates Pre-proliferative retinopathy • cotton wool spots (soft exudates; ischaemic nerve fibres) • > 3 blot haemorrhages • venous beading/looping • deep/dark cluster haemorrhages • more common in Type I DM, treat with laser photocoagulation	Mild NPDR • 1 or more microaneurysm Moderate NPDR • microaneurysms • blot haemorrhages • hard exudates • cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR Severe NPDR • blot haemorrhages and microaneurysms in 4 quadrants • venous beading in at least 2 quadrants • IRMA in at least 1 quadrant

Proliferative retinopathy

- retinal neovascularisation - may lead to vitrous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

Maculopathy

- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

Question 72 of 138

Which of the following is least recognised as a potential complication of acromegaly?

- A. Colorectal cancer
- B. Hypertension
- C. Cardiomyopathy
- D. Diabetes mellitus
- E. Pulmonary hypertension

Question 72 of 138

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- B. Hypertension
- C. Cardiomyopathy
- D. Diabetes mellitus
- E. Pulmonary hypertension

Acromegaly is associated with systemic rather than pulmonary hypertension.

Secondary causes of pulmonary hypertension include COPD, congenital heart disease (Eisenmenger's syndrome), recurrent pulmonary embolism, HIV and sarcoidosis.

Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

Features
- coarse, oily skin , large tongue, prognathism, interdental spaces
- spade-like hands, increase in shoe size
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

Complications
- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Question 73 of 138

A 29-year-old female who is 14 weeks into her first pregnancy is investigated for excessive sweating and tremor. Blood tests reveal the following:

TSH < 0.05 mu/l

T4 188 nmol/l

What is the most appropriate management?

- A. Immediate surgery
- B. Carbimazole
- C. Surgery at start of third trimester
- D. Propylthiouracil
- E. Radioiodine

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- B. Carbimazole
- C. Surgery at start of third trimester
- D. Propylthiouracil
- E. Radioiodine

Propylthiouracil is traditionally taught as the antithyroid drug of choice in pregnancy. This approach was supported by the 2007 Endocrine Society consensus guidelines. It also has the advantage of being excreted to a lesser extent than carbimazole in breast milk.

Despite this some endocrinologists use carbimazole and the BNF states both drugs may be used in pregnancy. Carbimazole has rarely been associated with aplasia cutis of the neonate

Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

Thyrotoxicosis
Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

Management
- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

Hypothyroidism
Key points
- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

Question 74 of 138

Which one of the following features of haemochromatosis may be reversible with treatment?

- A. Cardiomyopathy
- B. Hypogonadotrophic hypogonadism
- C. Diabetes mellitus
- D. Arthropathy
- E. Liver cirrhosis

Question 74 of 138

Which one of the following features of haemochromatosis may be reversible with treatment?

- A. Cardiomyopathy
- B. Hypogonadotrophic hypogonadism
- C. Diabetes mellitus
- D. Arthropathy
- E. Liver cirrhosis

Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 75 of 138

Which one of the following statements regarding the metabolic syndrome is correct?

- A. The WHO criteria are used to define impaired glucose tolerance
- B. The central pathophysiological change is thought to be reduced insulin production
- C. A diagnosis cannot be made without weighing the patient
- D. A raised LDL concentration is one of the key criteria in most definitions
- E. Decisions on cardiovascular risk factor modification should be made regardless of whether patients meet the criteria for metabolic syndrome

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D. A raised LDL concentration is one of the key criteria in most definitions

E. Decisions on cardiovascular risk factor modification should be made regardless of whether patients meet the criteria for metabolic syndrome

Decisions on primary prevention of cardiovascular disease should be made using standard tools and are not dependant on whether a diagnosis of metabolic syndrome is made.

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 76 of 138

A 43-year-old man requests a 'medical' as he is concerned about his risk of heart disease. His father died at the age of 45-years following a myocardial infarction. His lipid profile is as follows:

HDL	1.4 mmol/l
LDL	5.7 mmol/l
Triglycerides	2.3 mmol/l
Total cholesterol	8.2 mmol/l

Clinical examination reveals tendon xanthomata around his ankles. What is the most likely diagnosis?

- A. Familial hypercholesterolaemia (heterozygous)
- B. Nephrotic syndrome
- C. Mixed hyperlipidaemia
- D. Familial hypercholesterolaemia (homozygous)
- E. Hypothyroidism

Question 76 of 138

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- B. Nephrotic syndrome
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- D. Familial hypercholesterolaemia (homozygous)
- E. Hypothyroidism

The presence of tendon xanthomata and cholesterol levels meet the diagnostic criteria for familial hypercholesterolaemia. Homozygous familial hypercholesterolaemia is exceedingly rare - most patients die in their teenage years from a myocardial infarction.

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Question 77 of 138

A 49-year-old man with type 2 diabetes mellitus is reviewed. Despite weight loss and therapy with metformin and gliclazide his last HbA1c is 7.2%. Which one of the following factors would suggest that the patient may benefit from a meglitinide?

- A. Obesity
- B. Not adhering to diabetic diet
- C. Problems with hypoglycaemia from gliclazide
- D. Erratic lifestyle
- E. Elderly and frail patients

Question 77 of 138

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- D. Erratic lifestyle
- E. Elderly and frail patients

Meglitinides - stimulate insulin release - good for erratic lifestyle

Meglitinides stimulate insulin release and are particularly useful for post-prandial hyperglycaemia or an erratic eating schedule, as patients take them shortly before meals

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin

- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 78 of 138

What is the mode of inheritance of haemochromatosis?

- A. Autosomal recessive
- B. X-linked dominant
- C. Mitochondrial inheritance
- D. Autosomal dominant
- E. X-linked recessive

Question 78 of 138

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- arthritis (especially of the hands)

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*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 79 of 138

Which one of the following is least characteristic of Addison's disease?

- A. Hypoglycaemia
- B. Metabolic alkalosis
- C. Hyponatraemia
- D. Hyperkalaemia
- E. Positive short ACTH test

Question 79 of 138

Which one of the following is least characteristic of Addison's disease?

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- B. Metabolic alkalosis
- C. Hyponatraemia
- D. Hyperkalaemia
- E. Positive short ACTH test

Addison's disease is associated with a metabolic acidosis

Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a short ACTH test. Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Question 80 of 138

A 26-year-old obese female is investigated for menstrual disturbance. A diagnosis of polycystic ovarian syndrome is made. Which of the following findings is most consistently seen in polycystic ovarian syndrome?

- A. Obesity
- B. Hirsuitism
- C. Ovarian cysts on ultrasound
- D. Raised LH:FSH ratio
- E. Clitoromegaly

Question 80 of 138

A 26-year-old obese female is investigated for menstrual disturbance. A diagnosis of polycystic ovarian syndrome is made. Which of the following findings is most consistently seen in polycystic ovarian syndrome?

- A. Obesity
- B. Hirsuitism
- C. Ovarian cysts on ultrasound
- D. Raised LH:FSH ratio
- E. Clitoromegaly

Polycystic ovarian syndrome - ovarian cysts are the most consistent feature

Whilst all of the features listed above may be seen in polycystic ovarian syndrome, ovarian cysts are the most consistent feature.

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features
- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations
- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 81 of 138

Dynamic pituitary function tests may be used to assess each one of the following, except:

- A. Cortisol
- B. Prolactin
- C. Growth hormone
- D. Follicular stimulating hormone
- E. Antidiuretic hormone

Question 81 of 138

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- A. Cortisol
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Dynamic pituitary function tests

A dynamic pituitary function test is used to assess patients with suspected primary pituitary dysfunction

Insulin, TRH and LHRH are given to the patient following which the serum glucose, cortisol, growth hormone, TSH, LH and FSH levels are recorded at regular intervals. Prolactin levels are also sometimes measured*

A normal dynamic pituitary function test has the following characteristics:

- GH level rises > 20mu/l
- cortisol level rises > 550 mmol/l
- TSH level rises by > 2 mu/l from baseline level
- LH and FSH should double

*dopamine antagonist tests using metoclopramide may also be used in the investigation of hyperprolactinaemia. A normal response is at least a twofold rise in prolactin. A blunted prolactin response suggests a prolactinoma

Question 82 of 138

Which of the following statements is true regarding the pathophysiology of diabetes mellitus?

A. Concordance between identical twins is higher in type 2 diabetes mellitus than type 1

B. Patients with type 1 diabetes mellitus are rarely HLA-DR4 positive

C. Type 2 diabetes mellitus is associated with HLA-DR3

D. Haemochromatosis is an example of primary diabetes

E. Type 1 diabetes mellitus is thought to be inherited in an autosomal dominant fashion

Question 82 of 138

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C. Type 2 diabetes mellitus is associated with HLA-DR3

D. Haemochromatosis is an example of primary diabetes

E. Type 1 diabetes mellitus is thought to be inherited in an autosomal dominant fashion

Type 1 diabetes mellitus is caused by autoimmune destruction of the Beta-cells of the pancreas. Identical twins show a genetic concordance of 40%. It is associated with HLA-DR3 and DR4. It is inherited in a polygenic fashion

Type 2 diabetes mellitus is thought to be caused by a relative deficiency of insulin and the phenomenon of insulin resistance. Age, obesity and ethnicity are important aetiological factors. There is almost 100% concordance in identical twins and no HLA associations.

Haemochromatosis is an example of secondary diabetes

Diabetes: pathophysiology

Type 1 DM

- autoimmune disease
- antibodies against beta cells of pancreas
- HLA DR4 > HLA DR3
- various antibodies such as islet-associated antigen (IAA) antibody and glutamic acid decarboxylase (GAD) antibody are detected in patients who later go on to develop type 1 DM - their prognostic significance is not yet clear

Question 83 of 138

A 49-year-old woman is investigated for thyrotoxicosis. On examination she is noted to have a goitre containing multiple irregular nodules. Nuclear scintigraphy with technetium 99m reveals patchy uptake. What is the treatment of choice?

- A. Corticosteroids
- B. Radioiodine
- C. Block-and-replace regime
- D. Surgery
- E. Anti-thyroid drug titration regime

Question 83 of 138

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- C. Block-and-replace regime
- D. Surgery
- E. Anti-thyroid drug titration regime

Toxic multinodular goitre

Toxic multinodular goitre describes a thyroid gland that contains a number of autonomously functioning thyroid nodules that secrete excess thyroid hormones

Nuclear scintigraphy reveals patchy uptake

The treatment of choice is radioiodine therapy

Question 84 of 138

A 52-year-old woman who was diagnosed as having primary atrophic hypothyroidism 12 months ago is reviewed following recent thyroid function tests (TFTs):

TSH 12.5 mU/l

Free T4 14 pmol/l

She is currently taking 75mcg of levothyroxine once a day. How should these results be interpreted?

- A. Poor compliance with medication
- B. Taking extra thyroxine
- C. Evidence of recent systemic steroid therapy
- D. Keep on same dose
- E. T4 to T3 conversion disorder

Question 84 of 138

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- C. Evidence of recent systemic steroid therapy
- D. Keep on same dose
- E. T4 to T3 conversion disorder

Thyroid function tests

The interpretation of thyroid function tests is usually straightforward:

	TSH	**Free T4**	
Thyrotoxicosis (e.g. Graves' disease)	Low	High	In T3 thyrotoxicosis the free T4 will be normal
Primary hypothyroidism (primary atrophic hypothyroidism)	High	Low	
Secondary hypothyroidism	Low	Low	Replacement steroid therapy is required prior to thyroxine
Sick euthyroid syndrome*	Low**	Low	Common in hospital inpatients
Poor compliance with thyroxine	High	Normal / high	
Steroid therapy	Low	Normal	

*now referred to as non-thyroidal illness

**TSH may be normal in some cases

Question 85 of 138

A 54-year-old female presents to the Emergency Department concerned about double vision. She is noted to have exophthalmos and conjunctival oedema on examination and a diagnosis of thyroid eye disease is suspected. What can be said regarding her thyroid status?

- A. Hyper- or euthyroid
- B. Hypothyroid
- C. Hyperthyroid
- D. Hypo- or euthyroid
- E. Eu-, hypo- or hyperthyroid

Question 85 of 138

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- C. Hyperthyroid
- D. Hypo- or euthyroid
- E. Eu-, hypo- or hyperthyroid

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 86 of 138

A 45-year woman who you have treated for obesity comes for review. Despite ongoing lifestyle interventions and trials of orlistat and sibutramine she has failed to lose a significant amount of weight. She is currently taking ramipril for hypertension but a recent fasting glucose was normal. For this patient, what is the cut-off body mass index (BMI) that would trigger a referral for consideration of bariatric surgery?

- A. BMI > 35 kg/m^2
- B. BMI > 40 kg/m^2
- C. BMI > 30 kg/m^2
- D. BMI > 38 kg/m^2
- E. BMI > 45 kg/m^2

Question 87 of 138

Which one of the following is the most common cause of hypothyroidism in the UK?

- A. Pituitary failure
- B. Dietary iodine deficiency
- C. Lithium therapy
- D. Primary atrophic hypothyroidism
- E. Hashimoto's thyroiditis

Question 87 of 138

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- C. Lithium therapy
- D. Primary atrophic hypothyroidism
- E. Hashimoto's thyroiditis

In European countries primary atrophic hypothyroidism is the most cause causes of hypothyroidism, whereas in North America Hashimoto's thyroiditis appears to account for the majority of cases. The reason for this discrepancy is unclear

Hypothyroidism: causes

Hypothyroidism affects around 1-2% of women in the UK and is around 5-10 times more common in females than males.

Primary hypothyroidism

Primary atrophic hypothyroidism
- most common cause
- autoimmune disease, associated with IDDM, Addison's or pernicious anaemia
- 5 times more common in women

Hashimoto's thyroiditis
- autoimmune disease as above with goitre (positive microsomal antibodies)
- may cause transient thyrotoxicosis in the acute phase
- 10 times more common in women

After thyroidectomy or radioiodine treatment
Drug therapy (e.g. lithium, amiodarone or anti-thyroid drugs such as carbimazole)
Dietary iodine deficiency

Secondary hypothyroidism (rare)

From pituitary failure

Other associated conditions
- Down's syndrome
- Turner's syndrome
- coeliac disease

Question 88 of 138

Which one of the following features is least commonly seen in Gitelman's syndrome?

- A. Hypokalaemia
- B. Hypertension
- C. Metabolic alkalosis
- D. Hypocalciuria
- E. Hypomagnesaemia

Question 89 of 138

What is the most common cause of primary hyperaldosteronism?

- A. Pituitary tumour
- B. Adrenocortical adenoma
- C. Adrenal carcinoma
- D. Ectopic secretion
- E. Bilateral idiopathic adrenal hyperplasia

Question 89 of 138

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- B. Adrenocortical adenoma
- C. Adrenal carcinoma
- D. Ectopic secretion
- E. Bilateral idiopathic adrenal hyperplasia

bilateral idiopathic adrenal hyperplasia is the most common cause of primary hyperaldosteronism

Primary hyperaldosteronism

Primary hyperaldosteronism was previously thought to be most commonly caused by an adrenal adenoma, termed Conn's syndrome. However, recent studies have shown that bilateral idiopathic adrenal hyperplasia is the cause in up to 70% of cases. Differentiating between the two is important as this determines treatment. Adrenal carcinoma is an extremely rare cause of primary hyperaldosteronism

Features
- hypertension
- hypokalaemia (e.g. muscle weakness)
- alkalosis

Investigations
- high serum aldosterone
- low serum renin
- high-resolution CT abdomen

Management
- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

Question 90 of 138

A 24-year-old woman is found to have a blood pressure of 170/100 mmHg during a routine medical check. She is well and clinical examination is unremarkable. Blood tests show:

Na^+	140 mmol/l
K^+	2.6 mmol/l
Bicarbonate	31 mmol/l
Urea	3.4 mmol/l
Creatinine	77 µmol/l

Which one of the following investigations is most likely to be diagnostic?

- A. Renal ultrasound
- B. Overnight dexamethasone suppression test
- C. Renin:aldosterone ratio
- D. MR angiography
- E. 21-hydroxylase estimation

Question 90 of 138

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- C. Renin:aldosterone ratio
- D. MR angiography
- E. 21-hydroxylase estimation

Conn's syndrome is the likely diagnosis - a renin:aldosterone ratio would be an appropriate first-line investigation. A normal clinical examination makes a diagnosis of Cushing's syndrome less likely

Primary hyperaldosteronism

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- alkalosis

Investigations
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- low serum renin
- high-resolution CT abdomen

Management
- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

Question 91 of 138

A 62-year-old man who had a myocardial infarction six months ago presents for review. What should his target cholesterol levels be?

- A. Total cholesterol < 3.5 mmol/l; LDL < 1.5 mmol/l
- B. Total cholesterol < 4.0 mmol/l; LDL < 2.0 mmol/l
- C. Total cholesterol:HDL ratio < 5.0 mmol/l
- D. Total cholesterol:HDL ratio < 4.0 mmol/l
- E. Total cholesterol < 5.0 mmol/l; LDL < 3.0 mmol/l

Question 91 of 138

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- D. Total cholesterol:HDL ratio < 4.0 mmol/l
- E. Total cholesterol < 5.0 mmol/l; LDL < 3.0 mmol/l

NICE adopted the JBS2 targets for secondary prevention in the 2008 guidelines

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 92 of 138

A 54-year-old man with type 2 diabetes mellitus is started on exenatide. Which one of the following statements regarding exenatide is incorrect?

- A. Typically results in weight loss
- B. May be combined with a sulfonylurea
- C. The major adverse effect is flu-like symptoms
- D. May be combined with a thiazolidinedione
- E. Must be given by subcutaneous injection

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- D. May be combined with a thiazolidinedione
- E. Must be given by subcutaneous injection

Exenatide causes vomiting

The major adverse effect is nausea and vomiting

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 93 of 138

A 35-year-old female is referred to the endocrine clinic due to weight loss and palpitations. The following results are obtained:

TSH < 0.05 mu/l

T4 178 mmol/l

Which one of the following features would most suggest a diagnosis of Grave's disease?

- A. Atrial fibrillation
- B. Lid lag
- C. Family history of radioiodine treatment
- D. Pretibial myxoedema
- E. Multinodular goitre

Question 93 of 138

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- A. Atrial fibrillation
- B. Lid lag
- C. Family history of radioiodine treatment
- D. Pretibial myxoedema
- E. Multinodular goitre

Pretibial myxoedema is not seen in other causes of thyrotoxicosis and points towards a diagnosis of Graves'

Graves' disease: features

Features seen in Graves' but not in other causes of thyrotoxicosis
- eye signs: exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

Autoantibodies
- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

Question 94 of 138

A 52-year-old man has a set of fasting bloods as part of a work-up for hypertension. The fasting glucose comes back as 6.5 mmol/l. The test is repeated and reported as 6.7 mmol/l. He says he feels constantly tired but denies any polyuria or polydipsia. How should these results be interpreted?

- A. Impaired fasting glycaemia
- B. Suggestive of diabetes mellitus but not diagnostic
- C. Diabetes mellitus
- D. Normal
- E. Impaired glucose tolerance

Question 94 of 138

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- A. Impaired fasting glycaemia
- B. Suggestive of diabetes mellitus but not diagnostic
- C. Diabetes mellitus
- D. Normal
- E. Impaired glucose tolerance

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn’t have diabetes but does have IGT.'

Question 95 of 138

One of your patients is diagnosed with having the metabolic syndrome. Which one of the following is associated with this condition?

- A. Endometriosis
- B. Hypothyroidism
- C. Asymptomatic rise in amylase levels
- D. Elevated albumin levels
- E. Raised uric acid levels

Question 95 of 138

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- E. Raised uric acid levels

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 96 of 138

An 25-year-old male develops type 2 diabetes mellitus. Which one of the following genes is most likely to be responsible?

- A. Glucokinase
- B. HNF-1 alpha
- C. HNF-4 alpha
- D. HNF-1 beta
- E. IPF-1

Question 96 of 138

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- D. HNF-1 beta
- E. IPF-1

MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

MODY 3
- 60% of cases
- due to a defect in the HNF-1 alpha gene

MODY 2
- 20% of cases
- due to a defect in the glucokinase gene

Question 97 of 138

An 24-year-old woman is reviewed due to facial hirsuitism. You suspect a diagnosis of polycystic ovarian syndrome (PCOS). Which one of the following features would necessitate the need for further investigations before confidently making a diagnosis of PCOS?

- A. Clitoromegaly
- B. Acanthosis nigricans
- C. Obesity
- D. Amenorrhoea
- E. Acne

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- C. Obesity
- D. Amenorrhoea
- E. Acne

Clitoromegaly is seen occasionally in PCOS but is normally associated with very high androgen levels. If clitoromegaly is found then further investigations to exclude an ovarian or adrenal androgen secreting tumour are required.

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 98 of 138

Which one of the following drugs used in the management of type 2 diabetes mellitus has the Medicines and Healthcare products Regulatory Agency warned is associated with an increased risk of severe pancreatitis and renal impairment?

- A. Rosiglitazone
- B. Metformin
- C. Acarbose
- D. Exenatide
- E. Sitagliptin

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Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

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NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 99 of 138

A 52-year-old woman with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.9
2	8.4

How should these results be interpreted?

- A. Impaired fasting glucose and impaired glucose tolerance
- B. Normal
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Question 99 of 138

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2	8.4

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- B. Normal
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 100 of 138

What is the most appropriate screening investigation to exclude a phaeochromocytoma?

- A. Ultrasound adrenals
- B. Phenoxybenzamine suppression test
- C. 24 hour urinary collection of vanillylmandelic acid
- D. 24 hour urinary collection of catecholamines
- E. Plasma adrenaline (morning)

Question 100 of 138

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Phaeochromocytoma: do 24 hr urinary catecholamines, not VMA etc

A 24 hr urinary collection of catecholamines is preferred to one of vanillylmandelic acid as it has a higher sensitivity. Three 24 hour collections are needed as some patients have intermittently raised levels

Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

Basics
- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

Tests
- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:
- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

Question 101 of 138

An obese man presents as he is concerned about his risk of developing cardiovascular disease. Which one of the following sets of results would suggest a diagnosis of the metabolic syndrome using the Scottish Intercollegiate Guidelines Network (SIGN) criteria?

- A. Waist circumference = 98 cm; fasting glucose = 7.2 mmol/l; HDL = 1.2 mmol/l
- B. Triglycerides = 2.0 mmol/l; HDL = 1.2 mmol/l; fasting glucose = 5.4 mmol/l
- C. Blood pressure = 140/90 mmHg; waist circumference = 90 cm; HDL = 1.4 mmol/l
- D. Waist circumference = 110 cm; fasting glucose = 5.8 mmol/l; HDL = 0.8 mmol/l
- E. LDL = 3.0 mmol/l; blood pressure = 130/80; fasting glucose = 6.4 mmol/l

Question 101 of 138

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D. Waist circumference = 110 cm; fasting glucose = 5.8 mmol/l; HDL = 0.8 mmol/l

E. LDL = 3.0 mmol/l; blood pressure = 130/80; fasting glucose = 6.4 mmol/l

Whilst all the results contain at least one factor consistent with the metabolic syndrome only option D contains three of the criteria and would hence support a diagnosis.

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 102 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypocalcaemia
- B. Sickle-cell anaemia
- C. Lithium
- D. Hypokalaemia
- E. Demeclocycline

Question 102 of 138

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- D. Hypokalaemia
- E. Demeclocycline

Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 103 of 138

A 25-year-old man with a family history of multiple endocrine neoplasia type 1 is reviewed in clinic. What is the single most useful investigation to monitor such patients?

- A. Short synacthen test
- B. Urinary catecholamines
- C. Serum calcium
- D. Thyroid function tests
- E. Serum prolactin

Question 103 of 138

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- D. Thyroid function tests
- E. Serum prolactin

The high incidence of parathyroid tumours and hypercalcaemia make serum calcium a useful indicator of MEN type 1 in suspected individuals

Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	**MEN type IIa**	**MEN type IIb**
Mnemonic 'three P's': • parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia • pituitary (70%) • pancreas (50%, e.g. insulinoma, gastrinoma) • also: adrenal and thyroid	• phaeochromocytoma (95%, e.g. Phaeochromocytoma) • medullary thyroid cancer (70%) • parathyroid (60%)	• medullary thyroid cancer • phaeochromocytoma • marfanoid body habitus • neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene

MEN is inherited as an autosomal dominant disorder

Question 104 of 138

Which one of the following statements regarding the management of diabetes mellitus during pregnancy is incorrect?

- A. A previous macrosomic baby is a risk factor for gestational diabetes
- B. Diabetes complicates around 1 in 40 pregnancies
- C. A higher dose of folic acid (5 mg/day) should be used
- D. Metformin is contraindicated
- E. Tight glycaemic control reduces complication rates

Question 104 of 138

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- D. Metformin is contraindicated
- E. Tight glycaemic control reduces complication rates

There is increasing evidence that metformin is safe during pregnancy

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes
- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes
- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes
- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes
- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 105 of 138

Which one of the following regarding the management of thyroid problems during pregnancy is incorrect?

- A. Maternal free thyroxine levels should be kept in the upper third of the normal reference range when treating thyrotoxicosis
- B. Increased levels of thyroxine-binding globulin are seen in pregnancy
- C. Block-and-replace is preferable in pregnancy compared to antithyroid drug titration
- D. Breast feeding is safe whilst on thyroxine
- E. Untreated thyrotoxicosis increases the risk of premature labour

Question 105 of 138

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Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

Thyrotoxicosis

Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

Management

- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

Hypothyroidism

Key points

- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

Question 106 of 138

A 30-year-old female is started on carbimazole 20mg bd following a diagnosis of Grave's disease. What is the best biochemical marker to assess her response to treatment?

- A. Total T4
- B. TSH
- C. Free T4
- D. ESR
- E. Free T3

Question 106 of 138

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- B. TSH
- C. Free T4
- D. ESR
- E. Free T3

The answer the College are looking for is TSH. There is however a significant proportion of patients for whom TSH monitoring alone is insufficient. TSH may remain suppressed for several weeks as continued production of thyroid stimulating immunoglobulins seen in Grave's disease reduces the need for the pituitary to secrete TSH

Thyrotoxicosis

Graves' disease accounts for around 50-60% of cases of thyrotoxicosis.

Causes

- Graves' disease
- toxic nodular goitre
- subacute (de Quervain's) thyroiditis
- post-partum thyroiditis
- acute phase of Hashimoto's thyroiditis (later results in hypothyroidism)
- toxic adenoma (Plummer's disease)
- amiodarone therapy

Investigation

- TSH down, T4 and T3 up
- thyroid autoantibodies
- other investigations are not routinely done but includes isotope scanning

Question 107 of 138

Which one of the following statements regarding NICE guidance on the primary prevention of cardiovascular disease is incorrect?

- A. Premature coronary heart disease is defined as < 65 years in females
- B. A 10-year risk of 15% is used to identify patients who should be considered for lipid-lowering therapy
- C. Simvastatin 40mg on is the first line treatment in patients with a significant risk
- D. The 1991 Framingham equations are still recommended for calculating risk
- E. If a patient has a first degree relative with premature heart disease the risk should be multiplied by 1.5

Question 107 of 138

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Primary prevention CVD: 10-year risk of 20% is cut-off

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 108 of 138

A 23-year-old woman is diagnosed with Graves' disease. Which one of the following statements regarding treatment is correct?

- A. Block-and-replace regimes are usually of a shorter duration than carbimazole titration therapy
- B. Concurrent administration of propranolol and carbimazole should be avoided
- C. Patients on block-and-replace regimes have fewer side-effects than those using titration therapy
- D. Carbimazole should be started at no higher than 10mg/day for patients commencing a titration regime
- E. In the block-and-replace regime levothyroxine should be started at the same time as carbimazole

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- E. In the block-and-replace regime levothyroxine should be started at the same time as carbimazole

Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

Question 109 of 138

A 45-year-old woman presents with weight gain and recurrent 'dizzy' episodes. Over the past four months she has gained 20 kg. The episodes occur on an almost daily basis and are characterised by blurred vision, sweating, headaches and palpitations. Her GP checked a blood sugar during one of these episodes which was record as being 1.4 mmol/l. What is the single most useful test?

- A. Glucagon stimulation test
- B. Oral glucose tolerance test with growth hormone measurements
- C. Insulin + C-peptide levels during a hypoglycaemic episode
- D. Short ACTH test
- E. Insulin tolerance test

Question 109 of 138

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- C. Insulin + C-peptide levels during a hypoglycaemic episode
- D. Short ACTH test
- E. Insulin tolerance test

This patient has symptoms typical of an insulinoma. Whilst supervised fasting is normally the investigation of choice if this option is not given then insulin + C-peptide levels during an acute hypoglycaemic episode are useful.

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 110 of 138

A 53-year-old heavy goods vehicle driver with a history of type II diabetes mellitus is reviewed in the diabetes clinic. Despite maximal oral hypoglycaemic therapy his HbA1c is 9.7%. If insulin therapy is started then which one of the following is most appropriate with regards to his job?

- A. Cannot continue to drive heavy goods vehicle
- B. Inform DVLA and recommence driving once stable insulin dose achieved
- C. Can only drive during daylight hours
- D. As under 55 years of age then no requirement to inform DVLA
- E. Needs annual screening to exclude retinopathy or neuropathy

Question 110 of 138

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- E. Needs annual screening to exclude retinopathy or neuropathy

Patients on insulin cannot hold a HGV licence

DVLA: diabetes mellitus

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles (HGVs) tend to be much stricter

Specific rules

- if on insulin then cannot hold HGV licence*
- if on insulin then patient can drive a car as long as they have hypoglycaemic awareness and no relevant visual impairment
- if on tablets, exenatide or gliptin no need to notify DVLA
- if diet controlled alone and no relevant complications (e.g. Maculopathy) then no requirement to inform DVLA

*there are complex exceptions to this rule, but these are not relevant for the purposes of the exam

Question 111 of 138

Each one of the following is associated with Pendred's syndrome, except:

- A. Goitre
- B. Short 4th and 5th metacarpals
- C. Autosomal recessive inheritance
- D. Sensorineural deafness
- E. Euthyroid status

Question 111 of 138

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- C. Autosomal recessive inheritance
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- E. Euthyroid status

Pendred's syndrome

Autosomal recessive disorder of defective iodine uptake

Features
- sensorineural deafness
- goitre
- euthyroid or mild hypothyroidism

Question 112 of 138

Which one of the following combinations of treatments should be avoided in patients with type 2 diabetes mellitus?

A. Metformin + insulin + exenatide

B. Sulfonylurea + DPP-4 inhibitor

C. Metformin + sulfonylurea + exenatide

D. Metformin + DPP-4 inhibitor

E. Insulin + metformin + sulfonylurea

Question 112 of 138

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- C. Metformin + sulfonylurea + exenatide
- D. Metformin + DPP-4 inhibitor
- E. Insulin + metformin + sulfonylurea

Exenatide should only be used in combination with metformin, a sulfonylurea or both.

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 113 of 138

A 55-year-old woman with type 2 diabetes mellitus is reviewed. A decision is made to start thiazolidinedione therapy. Which one of the following points is it most relevant to consider before starting treatment?

- A. History of oesophageal problems
- B. Fracture risk
- C. History of depression
- D. History of cardiac arrhythmias
- E. Visual acuity

Question 113 of 138

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- B. Fracture risk
- C. History of depression
- D. History of cardiac arrhythmias
- E. Visual acuity

There is increasing evidence thiazolidinediones increase the risk of fractures

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 114 of 138

Which one of the following types of bariatric surgery is most likely to cause significant malabsorption?

- A. Laparoscopic-adjustable gastric banding
- B. Roux-en-Y gastric bypass surgery
- C. Biliopancreatic diversion with duodenal switch
- D. Sleeve gastrectomy
- E. Intragastric balloon

Question 114 of 138

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Biliopancreatic diversion with duodenal switch is a primarily malabsorptive procedure and reserved for patients who are very obese.

Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m2 in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m^2
- patients with a BMI > 40 kg/m^2 may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m^2)

Question 115 of 138

Which one of the following is most likely to be found in a patient with Hashimoto's thyroiditis?

- A. Raised ESR
- B. Anti-TSH receptor stimulating antibodies
- C. Anti-thyroid peroxidase antibodies
- D. Decreased TSH
- E. Co-existing type 2 diabetes mellitus

Question 115 of 138

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- D. Decreased TSH
- E. Co-existing type 2 diabetes mellitus

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

Features

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

Question 116 of 138

A 20-year-old man presents with a nine month history of weight gain. Prior to this he was of a normal weight and cannot identify any obvious lifestyle changes that would account for his obesity. On examination he is noted to have abdominal striae and a degree of proximal myopathy. Blood pressure is 130/80 mmHg. Bloods show the following:

Na^+	141 mmol/l
K^+	3.3 mmol/l
Bicarbonate	26 mmol/l
Urea	3.3 mmol/l
Creatinine	72 µmol/l

What is the most appropriate test to confirm the diagnosis?

- A. High-dose dexamethasone suppression test
- B. Plasma ACTH
- C. Short ACTH test
- D. 24 hour urinary free cortisol
- E. Renin:aldosterone ratio

Question 116 of 138

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The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

There is some debate as to whether a 24 hour urinary free cortisol or an overnight dexamethasone suppression test should be used to screen patients for Cushing's. The overnight (not high-dose) dexamethasone suppression test has however been shown to be more sensitive and is now much more commonly used in clinical practice. As this is not offered then 24 hour urinary free cortisol is the next best answer

For a review comparing diagnostic methods see 'Specificity of first-line tests for the diagnosis of Cushing's syndrome: assessment in a large series, J Clin Endocrinol Metab. 2007 Nov;92(11):4123-9'

The high-dose dexamethasone suppression test is used to help differentiate the cause of Cushing's syndrome

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test
- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation
- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 117 of 138

Each one of the following is associated with autoimmune polyendocrinopathy syndrome type 1, except:

A. Chronic mucocutaneous candidiasis

B. Addison's disease

C. Primary hyperparathyroidism

D. Autosomal recessive inheritance

E. A mutation of the AIRE1 gene on chromosome 21

Question 117 of 138

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Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

Question 118 of 138

A 62-year-old man is investigated for hypertension and proximal myopathy. On examination he is noted to have abdominal striae. Which one of the following is most associated with ectopic ACTH secretion?

- A. Carcinoid tumour
- B. Small cell lung cancer
- C. Cardiac myxoma
- D. Squamous cell lung cancer
- E. Adrenal carcinoma

Question 118 of 138

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- B. Small cell lung cancer
- C. Cardiac myxoma
- D. Squamous cell lung cancer
- E. Adrenal carcinoma

Small cell lung cancer accounts 50-75% of case of ectopic ACTH

Adrenal carcinoma and cardiac myxoma are causes of ACTH independent Cushing's syndrome

Cushing's syndrome: causes

ACTH dependent causes
- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes
- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's
- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Question 119 of 138

Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

- A. Hypothyroidism
- B. Obesity
- C. Liver disease
- D. Bendrofluazide
- E. Chronic renal failure

Question 119 of 138

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- D. Bendrofluazide
- E. Chronic renal failure

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia
- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia
- nephrotic syndrome
- cholestasis
- hypothyroidism

Question 120 of 138

A 54-year-old man with type 2 diabetes mellitus is reviewed in clinic. He is currently taking rosiglitazone, aspirin and simvastatin. Which one of the following problems is most likely caused by rosiglitazone?

- A. Photosensitivity
- B. Thrombocytopaenia
- C. Myalgia
- D. Peripheral oedema
- E. Hyponatraemia

Question 120 of 138

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- C. Myalgia
- D. Peripheral oedema
- E. Hyponatraemia

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 121 of 138

A 65-year-old man known to have a carcinoid tumour of the appendix is found to have hepatic metastases. If the patient develops carcinoid syndrome, which one of the following symptoms is most likely to occur first?

- A. Facial flushing
- B. Headache
- C. Vomiting
- D. Diarrhoea
- E. Palpitations

Question 121 of 138

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- D. Diarrhoea
- E. Palpitations

Carcinoid tumours

Carcinoid syndrome
- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

Features
- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation
- urinary 5-HIAA
- plasma chromogranin A y

Management
- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help

Question 122 of 138

A 49-year-old woman with type 2 diabetes mellitus is being considered for exenatide therapy. Which one of the following is not part of the NICE criteria for starting or continuing this drug?

- A. BMI > 35 kg/m^2
- B. Greater than 1.0 percentage point HbA1c reduction after 6 months
- C. Has failed with insulin therapy
- D. Has type 2 diabetes mellitus
- E. Weight loss > 3% at 6 months

Question 122 of 138

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C. Has failed with insulin therapy

D. Has type 2 diabetes mellitus

E. Weight loss > 3% at 6 months

Patients do not need to have been on insulin prior to using exenatide

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)
- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide
- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:
- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)
- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 123 of 138

Which one of the following conditions may cause hypokalaemia in association with hypertension?

- A. Gitelman syndrome
- B. 21-hydroxylase deficiency
- C. Bartter's syndrome
- D. Phaeochromocytoma
- E. 11-beta hydroxylase deficiency

Question 123 of 138

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- E. 11-beta hydroxylase deficiency

21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 124 of 138

A 52-year-old has a fasting lipid profile checked as part of an annual occupational health check. Combined with his blood pressure and current smoking status his 10-year risk of cardiovascular disease is calculated to be 23% percent. Following appropriate counselling he chooses to start simvastatin 40mg on. What should his target cholesterol be?

- A. Total cholesterol:HDL ratio < 5
- B. Total cholesterol < 5 mmol/l
- C. Target cholesterol is inappropriate in this situation
- D. Total cholesterol < 4 mmol/l
- E. Total cholesterol:HDL ratio < 4

Question 124 of 138

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- D. Total cholesterol < 4 mmol/l
- E. Total cholesterol:HDL ratio < 4

In primary prevention of CVD, a target cholesterol is not appropriate

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 125 of 138

A 55-year-old female is reviewed in the diabetes clinic. The following results are obtained:
Urinalysis protein +
HbA1c 10.0%

What average blood glucose level for the past 2 months is this most likely to represent?

- A. 9
- B. 10
- C. 11
- D. 15
- E. There is no relation between HbA1c and average blood glucose

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Glycosylated haemoglobin

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HBA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose = (2 * HbA1c) - 4.5

Question 126 of 138

Which one of the following increases the risk of developing peripheral oedema in a patient taking pioglitazone?

A. Concomitant use with gliclazide

B. Serum sodium < 140 mmol/l

C. Concomitant use with insulin

D. Concomitant use with metformin

E. Serum potassium < 4.0 mmol/l

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The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 127 of 138

Which one of the following statements regarding dipeptidyl peptidase-4 inhibitors in the management of type 2 diabetes mellitus is correct?

A. Metformin should always be co-prescribed

B. Do not cause weight gain

C. Is given via a subcutaneous injection

D. An example is exenatide

E. Patients should be warned that hypoglycaemia is the most common side-effect

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C. Is given via a subcutaneous injection

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E. Patients should be warned that hypoglycaemia is the most common side-effect

Hypoglycaemia is rare in patients taking dipeptidyl peptidase-4 inhibitors.

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

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NICE guidelines on the use of exenatide
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- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 128 of 138

A middle-aged man with type 2 diabetes mellitus is reviewed. Despite weight loss, metformin and gliclazide his HbA1c is 8.4%. The patient agrees to start insulin therapy. According to NICE guidelines which type of insulin should be tried initially?

- A. Basal bolus regime
- B. Isophane
- C. Biphasic insulin
- D. Glargine
- E. Detemir

Question 128 of 138

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Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 129 of 138

Which one of the following is least associated with gynaecomastia?

- A. Klinefelter's syndrome
- B. Seminoma
- C. Liver disease
- D. Puberty
- E. Hypothyroidism

Question 129 of 138

Which one of the following is least associated with gynaecomastia?

- A. Klinefelter's syndrome
- B. Seminoma
- C. Liver disease
- D. Puberty
- E. Hypothyroidism

Gynaecomastia is seen in up to a third of men with thyrotoxicosis, but is not a feature of hypothyroidism

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia
- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

Drug causes of gynaecomastia
- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia
- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

Question 130 of 138

A 54-year-old man has a routine medical for work. He is asymptomatic and clinical examination is unremarkable. Which of the following results establishes a diagnosis of impaired fasting glucose?

- A. Fasting glucose 7.1 mmol/L on one occasion
- B. Fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria ++
- D. 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L
- E. HbA1c of 6.7%

Question 130 of 138

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- D. 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L
- E. HbA1c of 6.7%

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

A 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L would imply impaired glucose tolerance rather than impaired fasting glucose

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 131 of 138

A 51-year-old woman is reviewed in the diabetes clinic. She was diagnosed with type 2 diabetes mellitus 12 months ago and still has poor glycaemic control. She has recently had to stop taking gliclazide due to repeated episodes of hypoglycaemia and is only taking maximum dose metformin. Her BMI is 26 kg/m^2. What is the most appropriate next step in management?

- A. Add either a thiazolidinedione or a DPP-4 inhibitor
- B. Refer her for a laparoscopic gastric band
- C. Refer her for insulin therapy
- D. Add either a thiazolidinedione or exenatide
- E. Add either a DPP-4 inhibitor or exenatide

Question 131 of 138

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Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c

- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only

if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 132 of 138

A 62-year-old male with a history of type 2 diabetes mellitus is investigated for lethargy. Blood tests are as follows:

Na^+	139 mmol/l
K^+	4.2 mmol/l
Bicarbonate	15 mmol/l
Chloride	105 mmol/l
Urea	15.2 mmol/l
Creatinine	267 µmol/l
Glucose	9.2 mmol/l

Which one of the following is most likely to be contributing to the low bicarbonate value?

- A. Vomiting due to gastroparesis
- B. Renal tubular acidosis
- C. Addison's disease
- D. Metformin
- E. Rosiglitazone

Question 132 of 138

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- D. Metformin
- E. Rosiglitazone

Whilst the decreased bicarbonate value may be worsened by deteriorating renal function, it is important to exclude lactic acidosis secondary to metformin.

The raised anion gap is against a diagnosis of renal tubular acidosis.

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis* with severe liver disease or renal failure

Contraindications**

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 133 of 138

A 29-year-old woman has just found out she is pregnant for the second time. Her first pregnancy was complicated by gestational diabetes. Following her first pregnancy she was told she was no longer diabetic. What is the most appropriate management?

- A. Start insulin
- B. Start metformin and do oral glucose tolerance test at 12-14 weeks
- C. Do oral glucose tolerance test at booking visit
- D. Do oral glucose tolerance test at 16-18 weeks
- E. Do fasting glucose at booking visit

Question 133 of 138

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- C. Do oral glucose tolerance test at booking visit
- D. Do oral glucose tolerance test at 16-18 weeks
- E. Do fasting glucose at booking visit

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes

- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 134 of 138

A 54-year-old obese man presents with lethargy and polyuria. A fasting blood sugar is requested:

Fasting glucose 8.4 mmol/l

He is given dietary advice and a decision is made to start metformin. What is the most appropriate prescription?

- A. Metformin 500mg od with food for 5 days then metformin 500mg bd for 5 days then metformin 500mg tds for 20 days then review
- B. Metformin 500mg tds with food
- C. Metformin 500mg od with food for 14 days then metformin 500mg bd for 14 days then review
- D. Metformin 1g tds with food
- E. Metformin 500mg tds taken at least 1 hour before meals

Question 134 of 138

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- D. Metformin 1g tds with food
- E. Metformin 500mg tds taken at least 1 hour before meals

Metformin should be titrated slowly, leave at least 1 week before increasing dose

Gastrointestinal side-effects are more likely to occur if metformin is not slowly titrated up. The BNF advises leaving at least 1 week before increasing the dose.

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
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Contraindications**

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**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 135 of 138

A 50-year-old man who is known to have obesity and hypertension comes for review. His current BMI is 38 kg/m^2 and blood pressure today is 154/92 mmHg despite ramipril and bendroflumethiazide. Lifestyle and a trial of orlistat have failed to reduce his weight. Which one of the following is the most suitable intervention?

- A. Biliopancreatic diversion with duodenal switch
- B. Laparoscopic-adjustable gastric banding
- C. Trial of sibutramine
- D. Referral for counselling to discuss his excessive eating
- E. Sleeve gastrectomy

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- E. Sleeve gastrectomy

A trial of sibutramine would not be appropriate given his poorly controlled hypertension. Laparoscopic-adjustable gastric banding is the intervention of choice in patients with a BMI < 40 kg/m^2.

Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m2 in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m^2
- patients with a BMI > 40 kg/m^2 may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m^2)

Question 136 of 138

A 56-year-old Muslim man with a history of type 2 diabetes asks for advice. He is due to start fasting for Ramadan soon and is unsure what he should do with regards to his diabetes medications. He currently takes metformin 500mg tds. What is the most appropriate advice?

- A. Switch to subcutaneous biphasic insulin for the duration of Ramadan
- B. 500 mg at the predawn meal + 1000 mg at the sunset meal
- C. No change to the metformin dose
- D. 1000 mg at the predawn meal + 500 mg at the sunset meal
- E. Stop metformin for the duration of Ramadan

Question 136 of 138

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Please see the Diabetes Care link for more details.

Metformin

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Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis* with severe liver disease or renal failure

Contraindications**

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
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**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 137 of 138

Which one of the following features is least associated with primary hyperparathyroidism?

- A. Depression
- B. Polydipsia
- C. Sensory loss
- D. Peptic ulceration
- E. Hypertension

Question 137 of 138

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Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism
- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'
- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations
- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations
- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment
- total parathyroidectomy

Question 138 of 138

A 7-year-old boy is being investigated for failure to thrive and generalised weakness. His blood pressure is normal. The following blood results are obtained:

Na^+	137 mmol/l
K^+	3.0 mmol/l
Urea	4.5 mmol/l
Creatinine	65 µmol/l
Bicarbonate	33 mmol/l

What is the most likely diagnosis?

- A. Conn's syndrome
- B. Bartter's syndrome
- C. Cushing's syndrome
- D. 21-hydroxylase deficiency
- E. Liddle's syndrome

Question 138 of 138

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Bartter's syndrome is associated with normotension

Bartter's syndrome is the most likely diagnosis. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency is associated with precocious puberty rather than failure to thrive in boys. Both Conn's and Cushing's are associated with hypertension and are not common in this age group.

Liddle's syndrome is a rare autosomal dominant condition that causes hypertension and hypokalaemic alkalosis. It is thought to be caused by disordered sodium channels in the distal tubules leading to increased reabsorption of sodium.

Bartter's syndrome

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension (unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome which are associated with hypertension)

Features

- usually presents in childhood, e.g. Failure to thrive
- polyuria, polydipsia
- hypokalaemia
- normotension
- weakness

Recommendations for Management of Diabetes During Ramadan

Before Ramadan	During Ramadan
Patients on diet and exercise control	No change needed (modify time and intensity of exercise), ensure adequate fluid intake
Patients on oral hypoglycemic agents	Ensure adequate fluid intake
Biguanide, metformin 500 mg three times a day, or sustained release metformin (glucophage R)	Metformin, 1,000 mg at the sunset meal (Iftar), 500 mg at the predawn meal (Suhur)
TZDs, pioglitazone or rosiglitazone once daily	No change needed
Sulfonylureas once a day, e.g., glimepiride 4 mg daily, gliclazide MR 60 mg daily	Dose should be given before the sunset meal (Iftar); adjust the dose based on the glycemic control and the risk of hypoglycemia
Sulfonylureas twice a day, e.g., glibenclamide 5 mg or gliclazide 80 mg, twice a day (morning and evening)	Use half the usual morning dose at the predawn meal (Suhur) and the full dose at the sunset meal (Iftar), e.g., glibenclamide 2.5 mg or gliclazide 40 mg in the morning, glibenclamide 5 mg or gliclazide 80 mg in evening
Patients on insulin	Ensure adequate fluid intake
70/30 premixed insulin twice daily, e.g., 30 units in morning and 20 units in evening	Use the usual morning dose at the sunset meal (Iftar) and half the usual evening dose at predawn (Suhur), e.g., 70/30 premixed insulin, 30 units in evening and 10 units in morning; also consider changing to glargine or detemir plus lispro or aspart

Question 1 of 142

A 54-year-old female presents with fatigue and xerostomia. Bloods tests reveal the following:

Hb	13.9 g/dl
WBC	6.1 *10^9/l
Platelets	246 *10^9/l
Bilirubin	33 µmol/l
ALP	292 u/l
ALT	47 u/l

What is the most likely diagnosis?

- A. Systemic lupus erythematous
- B. Infectious mononucleosis
- C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Sjogren's syndrome

Question 1 of 142

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- ✓ C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Sjogren's syndrome

Primary biliary cirrhosis - the **M** rule
- Ig**M**
- anti-**M**itochondrial antibodies, **M**2 subtype
- **M**iddle aged females

The dry mouth is this patient is due to sicca syndrome, which occurs in 70% of cases of primary biliary cirrhosis. The cholestatic liver function tests point towards primary biliary cirrhosis rather than Sjogren's syndrome

Primary biliary cirrhosis: features

Primary biliary cirrhosis is chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis, which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

Clinical features
- early: may be asymptomatic (e.g. raised ALP on routine LFTs) or fatigue, pruritus
- cholestatic jaundice
- hyperpigmentation, especially over pressure points
- xanthelasmas, xanthomata
- also: clubbing, hepatosplenomegaly
- late: may progress to liver failure

Complications
- malabsorption: osteomalacia, coagulopathy
- sicca syndrome occurs in 70% of cases
- portal hypertension: ascites, variceal haemorrhage
- hepatocellular cancer (20-fold increased risk)

Question 2 of 142

A 24-year-old man presents with rectal bleeding and pain on defecation. This has been present for the past two weeks. He has a tendency towards constipation and notices that when he wipes himself fresh blood is often on the paper. Rectal examination is limited due to pain but no external abnormalities are seen. What is the most likely diagnosis?

- A. Internal haemorrhoids
- B. Anal carcinoma
- C. Rectal polyp
- D. Anogenital herpes
- E. Anal fissure

Question 2 of 142

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- B. Anal carcinoma
- C. Rectal polyp
- D. Anogenital herpes
- ✓ E. Anal fissure

Superficial anal fissures may be difficult to see on examination.

Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks)

- dietary advice: high-fibre diet with high fluid intake
- bulk-forming laxatives are first line - if not tolerated then lactulose should be tried
- lubricants such as petroleum jelly may be tried before defecation
- topical anaesthetics
- sitz baths: hip baths in hot water for 2–5 minutes followed by cold water for 1 minute
- topical steroids do not provide significant relief

Management of a chronic anal fissure (> 6 weeks)

- the above techniques should be continued
- topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure
- if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

Question 3 of 142

A 54-year-old man with a long history of heartburn has an endoscopy to investigate his symptoms. A biopsy is taken from an abnormal area of mucosa in the lower oesophagus and reported as follows:

Non-dysplastic columnar-lined oesophagus

What is the most suitable management?

- A. Reassure and discharge
- B. Fundoplication
- C. Laser ablation
- D. Ivor-Lewis oesophagectomy
- E. High-dose proton pump inhibitor and follow-up

Question 3 of 142

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- D. Ivor-Lewis oesophagectomy
- ✓ E. High-dose proton pump inhibitor and follow-up

The 2005 British Society of Gastroenterology guidelines state that high-dose proton pump inhibitor therapy is first-line treatment in such patients. There is yet insufficient evidence to support the use of endoscopic ablation.

Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

Question 4 of 142

A 54-year-old woman presents with jaundice shortly after being discharged from hospital. Liver function tests are reported as follows:

Albumin	49 g/l
Bilirubin	89 µmol/l
Alanine transferase (ALT)	66 iu/l
Alkaline phosphatase (ALP)	245 µmol/l
Gamma glutamyl transferase (yGT)	529 u/l

Which of the following antibiotics is she most likely to have received?

- A. Flucloxacillin
- B. Gentamicin
- C. Ciprofloxacin
- D. Trimethoprim
- E. Ceftazidime

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Flucloxacillin + co-amoxiclav are well recognised causes of cholestasis

Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 5 of 142

A 35-year-old man who is usually fit and well presents with a 2 month history of indigestion. His weight is stable and there is no history of dysphagia. Examination of the abdomen is unremarkable. Of the following options, what is the most suitable initial management?

- A. Urea breath testing and non-urgent referral for endoscopy
- B. H pylori eradication therapy and full-dose proton pump inhibitor for three months
- C. Full-dose Proton pump inhibitor and immediate referral for endoscopy
- D. Three month course of a standard-dose proton pump inhibitor
- E. One month course of a full-dose proton pump inhibitor

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- C. Full-dose Proton pump inhibitor and immediate referral for endoscopy
- D. Three month course of a standard-dose proton pump inhibitor
- ✓ E. One month course of a full-dose proton pump inhibitor

This question highlights the NICE guidelines for the management of dyspepsia.

There is no evidence currently to suggest whether a one month course of a PPI or 'test and treat' strategy should be adopted first line. Many clinicians prefer to test for H pylori first as this cannot be done within 2 weeks of acid-suppression therapy, as false-negative results may occur

Given the options available, only the answer is in line with current NICE guidelines

Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')

This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month*
- 4. 'Test and treat' using carbon-13 urea breath test

*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Question 6 of 142

A patient with upper gastrointestinal symptoms tests positive for *Helicobacter pylori* following a urea breath test. Which one of the following conditions is most strongly associated *Helicobacter pylori* infection?

- A. Gastric adenocarcinoma
- B. Gastro-oesophageal reflux disease
- C. Oesophageal cancer
- D. Duodenal ulceration
- E. Atrophic gastritis

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- ✓ D. Duodenal ulceration
- E. Atrophic gastritis

Helicobacter pylori infection is also associated with both gastric adenocarcinoma and atrophic gastritis but the strongest association is with duodenal ulceration.

Helicobacter pylori

Helicobacter pylori is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

Associations
- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of
- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

Question 7 of 142

Which one of the following is most suggestive of Wilson's disease?

- A. Reduced hepatic copper concentration
- B. Reduced 24hr urinary copper excretion
- C. Increased skin pigmentation
- D. Reduced serum caeruloplasmin
- E. Reduced serum copper

Question 7 of 142

Which one of the following is most suggestive of Wilson's disease?

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- B. Reduced 24hr urinary copper excretion
- C. Increased skin pigmentation
- ✓ D. Reduced serum caeruloplasmin
- E. Reduced serum copper

Wilson's disease - serum caeruloplasmin is **decreased**

Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Question 8 of 142

A 22-year-old male blood donor is noted to have the following blood results:

Bilirubin	41 µmol/L
ALP	84 U/L
ALT	23 U/L
Albumin	41 g/L

Dipstick urinalysis No bilirubinuria

He has recently complained of coryzal symptoms and a non-productive cough. What is the most likely diagnosis?

- A. Gilbert's syndrome
- B. Dubin-Johnson syndrome
- C. Rotor syndrome
- D. Hepatitis C infection
- E. Infectious mononucleosi

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An isolated hyperbilirubinaemia in a 22-year-old male is likely to be secondary to Gilbert's syndrome. The normal dipstix urinalysis excludes Dubin-Johnson and Rotor syndrome as these both produce a conjugated bilirubinaemia. Viral infections are common triggers for a rise in the bilirubin in patients with Gilbert's

Gilbert's syndrome

Gilbert's syndrome is an autosomal recessive* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

Features

- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

Investigation and management

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

*the exact mode of inheritance is still a matter of debate

Question 9 of 142

A 49-year-old female is referred to the gastroenterology out-patient clinic with a 3 month history of epigastric pain and diarrhoea. Her GP initially prescribed lansoprazole 30mg od but this didn't alleviate her symptoms. The only past medical history of note is hyperparathyroidism.

Endoscopy revealed multiple duodenal ulcerations. What is the likely diagnosis?

- A. Multiple endocrine neoplasia type II a
- B. Coeliac disease
- C. Multiple endocrine neoplasia type I
- D. Autoimmune polyendocrinopathy syndrome
- E. Crohn's disease

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Zollinger-Ellison syndrome: epigastric pain and diarrhoea

Zollinger-Ellison syndrome typically presents with multiple gastroduodenal ulcers causing abdominal pain and diarrhoea. High-dose proton pump inhibitors are needed to control the symptoms. Around a third of patients may have multiple endocrine neoplasia type I (MEN-I), explaining the hyperparathyroidism in this patient.

MEN-I
- parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia
- pituitary (70%)
- pancreas (50%, e.g. Insulinoma, gastrinoma)
- also: adrenal and thyroid

Zollinger-Ellison syndrome

Zollinger-Ellison syndrome is condition characterised by excessive levels of gastrin, usually from a gastrin secreting tumour usually of the duodenum or pancreas. Around 30% occur as part of MEN type I syndrome

Features
- multiple gastroduodenal ulcers
- diarrhoea
- malabsorption

Diagnosis
- fasting gastrin levels: the single best screen test
- secretin stimulation test

Question 10 of 142

A 31-year-old man with a known history of alcoholic liver disease is reviewed following a suspected oesophageal variceal haemorrhage. He has been resuscitated and intravenous terlipressin has been given. His blood pressure is now 104/60 mmHg and his pulse is 84/min. What is the most appropriate intervention?

- A. Transjugular Intrahepatic Portosystemic Shunt
- B. Surgical referral
- C. Endoscopic variceal band ligation
- D. Sengstaken-Blakemore tube
- E. Endoscopic sclerotherapy

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Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 11 of 142

Which one of the following is the most likely presentation of *Staphylococcus aureus* food poisoning?

- A. Tenesmus
- B. Watery diarrhoea
- C. Dysentery
- D. Severe vomiting
- E. Presentation 24-48 hours after eating affected food

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Severe nausea and vomiting are caused by enterotoxins A-E

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 12 of 142

A 43-year-old man presents with diarrhoea and rectal bleeding for the past ten days. On examination he has brown pigmented lesions on his lips and palms but abdominal and rectal examination is unremarkable. What is the most likely cause for this presentation?

- A. Intussusception
- B. Angiodysplasia
- C. Meckel's Diverticulum
- D. Colon cancer
- E. Diverticular abscess

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- B. Angiodysplasia
- C. Meckel's Diverticulum
- ✓ D. Colon cancer
- E. Diverticular abscess

This patient has Peutz-Jeghers syndrome. Intussusception would not normally cause rectal bleeding at this age. Colon cancer is the most common type of gastrointestinal cancer that patients with Peutz-Jeghers syndrome develop.

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 13 of 142

A 46-year-old man is being investigated for indigestion. Jejunal biopsy shows deposition of macrophages containing PAS-positive granules. What is the most likely diagnosis?

- A. Bacterial overgrowth
- B. Coeliac disease
- C. Tropical sprue
- D. Whipple's disease
- E. Small bowel lymphoma

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- C. Tropical sprue
- ✓ D. Whipple's disease
- E. Small bowel lymphoma

Whipple's disease: jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

Whipple's disease

Whipple's disease is a rare multi-system disorder caused by Tropheryma whippelii infection. It is more common in those who are HLA-B27 positive and in middle-aged men

\Features
- malabsorption: diarrhoea, weight loss
- large-joint arthralgia
- lymphadenopathy
- skin: hyperpigmentation and photosensitivity
- pleurisy, pericarditis
- neurological symptoms (rare): ophthalmoplegia, dementia, seizures, ataxia, myoclonus

Investigation
- jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

Management
- varies e.g. IV penicillin then oral co-trimoxazole for a year

Question 14 of 142

Of the following, which one is the most useful prognostic marker in paracetamol overdose?

- A. ALT
- B. Prothrombin time
- C. Paracetamol levels at presentation
- D. Paracetamol levels at 12 hours
- E. Paracetamol levels at 24 hours

Question 14 of 142

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- ✓ B. Prothrombin time
- C. Paracetamol levels at presentation
- D. Paracetamol levels at 12 hours
- E. Paracetamol levels at 24 hours

An elevated prothrombin time signifies liver failure in paracetamol overdose and is a marker of poor prognosis. However, arterial pH, creatinine and encephalopathy are also markers of a need for liver transplantation \

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300 µmol/l
- grade III or IV encephalopathy

Question 15 of 142

A 54-year-old female presents with a 3 month history of dysphagia affecting both food and liquids from the start, along with occasional symptoms of heartburn. What is the most likely underlying diagnosis?

- A. Pharyngeal pouch
- B. Gastric adenocarcinoma
- C. Benign stricture
- D. Oesophageal cancer
- E. Achalasia

Question 15 of 142

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- B. Gastric adenocarcinoma
- C. Benign stricture
- D. Oesophageal cancer
- ✓ E. Achalasia

Dysphagia affecting both solids and liquids from the start - think achalasia

This is a classic history of achalasia with dysphagia affecting both solids and liquids from the start.

Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is more common in women

Clinical features
- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

Investigations
- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

Treatment
- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Question 16 of 142

A 25-year-old man presents with lethargy and increased skin pigmentation. Blood test reveal deranged liver function tests and impaired glucose tolerance. Given the likely diagnosis of haemochromatosis, what is the most appropriate initial investigation strategy?

- A. Transferrin saturation + ferritin
- B. Haematocrit + ferritin
- C. Liver biopsy with Perl's stain
- D. Serum iron + ferritin
- E. Serum iron + haematocrit

Question 16 of 142

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- E. Serum iron + haematocrit

Screening for haemochromatosis
- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

The British Committee for Standards in Haematology (BCSH) guidelines recommend measuring the transferrin saturation first as this is the most specific and sensitive test for iron accumulation. They also recommend that serum ferritin is measured but this marker is not usually abnormal in the early stages of iron accumulation

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:
- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

Diagnostic tests
- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis
- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection
- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 17 of 142

Crohn's disease is associated with each one of the following findings, except:

- A. Inflammation confined to the mucosa and submucosa
- B. Non-caseating granulomas
- C. Rose-thorn ulcers
- D. Cobblestone pattern
- E. Fistulas

Question 17 of 142

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IBD: histology

This histological differences between ulcerative colitis and Crohn's are summarised below:

Ulcerative colitis

- inflammation in mucosa and submucosa only (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

Crohn's

- inflammation occurs in all layers, down to the serosa. This predisposes to strictures, fistulas and adhesions
- oedema of mucosa and submucosa, combined with deep fissured ulcers ('rose-thorn') leads to a 'cobblestone' pattern
- lymphoid aggregates
- non-caseating granulomas

Question 18 of 142

A 34-year-old female with a history of alcoholic liver disease is admitted with frank haematemesis. She was discharged three months ago following treatment for bleeding oesophageal varices. Following resuscitation, what is the most appropriate treatment whilst awaiting endoscopy?

- A. Octreotide
- B. Omeprazole
- C. Propranolol
- D. Tranexamic acid
- E. Terlipressin

Question 18 of 142

A 34-year-old female with a history of alcoholic liver disease is admitted with frank haematemesis. She was discharged three months ago following treatment for bleeding oesophageal varices. Following resuscitation, what is the most appropriate treatment whilst awaiting endoscopy?

- A. Octreotide
- B. Omeprazole
- C. Propranolol
- D. Tranexamic acid
- ✓ E. Terlipressin

Terlipressin is the only licensed vasoactive agent for variceal haemorrhage in the UK

Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
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Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 19 of 142

A 25-year-old man with a history of Crohn's disease is reviewed in clinic. Over the past week he has developed painful perianal ulcers. On examination numerous shallow ulcers can be seen with a small number of skin tags. What is the most appropriate first-line treatment?

- A. Topical mesalazine
- B. Oral metronidazole
- C. Barrier creams + laxatives
- D. Oral prednisolone
- E. Oral mesalazine

Question 19 of 142

A 25-year-old man with a history of Crohn's disease is reviewed in clinic. Over the past week he has developed painful perianal ulcers. On examination numerous shallow ulcers can be seen with a small number of skin tags. What is the most appropriate first-line treatment?

- A. Topical mesalazine
- ✓ B. Oral metronidazole
- C. Barrier creams + laxatives
- D. Oral prednisolone
- E. Oral mesalazine

Please see the British Society of Gastroenterology guidelines for more details.

Crohn's disease: management

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

General points
- patients should be strongly advised to stop smoking
- some studies suggest an increased risk of relapse secondary to NSAIDs and the combined oral contraceptive pill but the evidence is patchy

Active disease
- mesalazine: whilst evidence base is limited widely used in active disease
- steroids (oral, topical or intravenous)
- azathioprine is used as a second-line treatment in active disease
- methotrexate is used in patients intolerant of azathioprine or refractory disease. Usually given intramuscularly
- infliximab is useful in refractory disease and fistulating Crohn's. Patients typically continue on azathioprine or methotrexate

Perianal disease
- metronidazole is first-line

Enteral feeding with an elemental diet
- may be used in addition to or instead of other measures to induce remission

Surgery
- around 80% of patients with Crohn's disease will eventually have surgery

Question 20 of 142

A 44-year-old man is diagnosed with a duodenal ulcer. CLO testing performed during the gastroscopy is positive for *Helicobacter pylori*. What is the most appropriate management to eradicate *Helicobacter pylori*?

- A. Lansoprazole + clindamycin + metronidazole
- B. Lansoprazole + amoxicillin + clindamycin
- C. Lansoprazole + amoxicillin + clarithromycin
- D. Omeprazole + amoxicillin + clindamycin
- E. Omeprazole + penicillin + metronidazole

Question 20 of 142

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- D. Omeprazole + amoxicillin + clindamycin
- E. Omeprazole + penicillin + metronidazole

H. pylori eradication:
- PPI + amoxicillin + clarithromycin, or
- PPI + metronidazole + clarithromycin

The BNF recommends a regimen containing amoxicillin and clarithromycin as first-line therapy

Helicobacter pylori

Helicobacter pylori is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

Associations
- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of
- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

Question 21 of 142

Which one of the following is true regarding bacterial exotoxins?

- A. They are mainly produced by Gram positive bacteria
- B. Cholera toxin inhibits cAMP release in intestinal cells
- C. Diphtheria toxin necrosis is limited to the pharynx, nasopharynx and tonsils
- D. *Staph. aureus* exotoxins are not known to cause gastroenteritis
- E. 'Lockjaw' seen in tetanus is secondary to blockade of the neuromuscular junction by Botulinus toxin

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Exotoxins

Exotoxins are generally released by Gram positive bacteria with the notable exceptions of Vibrio cholerae and some strains of *E. coli*

Diphtheria toxin commonly causes a 'diphtheric membrane' on tonsils caused by necrotic mucosal cells. Systemic distribution may produce necrosis of myocardial, neural and renal tissue.

Staph. aureus exotoxins lead to acute gastroenteritis, toxic shock syndrome and Staphylococcal scalded skin syndrome

Lockjaw is caused by *Clostridium tetani* neurotoxin (tetanospasmin)

Cholera toxin causes activation of adenylate cyclase leading to increases in cAMP levels, which in turn leads to increased chloride secretion.

Question 22 of 142

A 54-year-old female with a history of scleroderma presents with chronic diarrhoea and bloating. Blood tests show a mild macrocytic anaemia. A diagnosis of small bowel bacterial overgrowth is suspected. Which one of the following tests is most likely to confirm the diagnosis?

- A. Jejunal biopsy
- B. Small bowel aspiration and culture
- C. 14C-xylose breath test
- D. Small bowel meal
- E. 14C-glycocholate breath test

Question 22 of 142

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- C. 14C-xylose breath test
- D. Small bowel meal
- E. 14C-glycocholate breath test

Whilst small bowel aspiration and culture is the gold standard investigation in this situation, its use is often limited due to resource limitations. Please see the British Society of Gastroenterology guidelines

The hydrogen breath test is another option. It has low sensitivity but high specificity

Bacterial overgrowth: investigation

The gold standard investigation of bacterial overgrowth is small bowel aspiration and culture

Other possible investigations include:

- hydrogen breath test
- 14C-xylose breath test
- 14C-glycocholate breath test: used increasingly less due to low specificity

In practice many clinicians give an empirical course of antibiotics as a trial

Question 23 of 142

A 38-year-old female with a long history of alcohol excess presents with abdominal pain, weight loss and bulky stools. What is the most suitable investigation to confirm the diagnosis?

- A. Endoscopic ultrasound
- B. Endoscopic retrograde cholangiopancreatography
- C. Ultrasound abdomen
- D. CT abdomen
- E. Endoscopy with D2 biopsy

Question 23 of 142

A 38-year-old female with a long history of alcohol excess presents with abdominal pain, weight loss and bulky stools. What is the most suitable investigation to confirm the diagnosis?

- A. Endoscopic ultrasound
- B. Endoscopic retrograde cholangiopancreatography
- C. Ultrasound abdomen
- ✓ D. CT abdomen
- E. Endoscopy with D2 biopsy

This patient has chronic pancreatitis. CT is the most sensitive method to detect the characteristic pancreatic calcification which is associated with the condition

Chronic pancreatitis

Chronic pancreatitis is an inflammatory condition which can ultimately affect both the exocrine and endocrine functions of the pancreas. Around 80% of cases are due to alcohol excess with up to 20% of cases being unexplained

Features

- pain is typically worse 15 to 30 minutes following a meal
- steatorrhoea: symptoms of pancreatic insufficiency usually develop between 5 and 25 years after the onset of pain
- diabetes mellitus develops in the majority of patients. It typically occurs more than 20 years after symptom begin

Investigation

- abdominal x-ray shows pancreatic calcification in 30% of cases
- CT is more sensitive at detecting pancreatic calcification
- functional tests: pancreolauryl and Lundh tests may be used to assess exocrine function if imaging inconclusive

Management

- pancreatic enzyme supplements
- analgesia
- antioxidants: limited evidence base - one study suggests benefit in early disease

Question 24 of 142

A 31-year-old female is admitted to the Emergency Department following a paracetamol overdose. The paracetamol level comes back as elevated but the doctor is unsure which treatment line to use. Which one of the following features in the medical history would classify the patient as high risk?

- A. Hypothyroidism
- B. Anorexia nervosa
- C. Previous paracetamol overdose
- D. Combined overdose with codeine
- E. Long-term sodium valproate use

Question 24 of 142

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- C. Previous paracetamol overdose
- D. Combined overdose with codeine
- E. Long-term sodium valproate use

Paracetamol overdose - high risk if chronic alcohol, HIV, anorexia or P450 inducers

Paracetamol overdose: risk factors

The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose:

- chronic alcohol excess
- patients on P450 enzyme inducers (rifampicin, phenytoin, carbamazepine)
- anorexia nervosa: decreased glutathione stores
- HIV

Question 25 of 142

A 54-year-old man is investigated for dyspepsia. An endoscopy shows a gastric ulcer and a CLO test done during the procedure demonstrates *H. pylori* infection. A course of *H. pylori* eradication therapy is given. What is the most appropriate test to confirm eradication?

- A. Culture of gastric biopsy
- B. *H. pylori* serology
- C. Hydrogen breath test
- D. Urea breath test
- E. Stool culture

Question 25 of 142

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- B. *H. pylori* serology
- C. Hydrogen breath test
- ✓ D. Urea breath test
- E. Stool culture

It is important to remember that *H. pylori* serology remains positive following eradication

***Helicobacter pylori*: tests**

Urea breath test
- patients consume a drink containing carbon isotope 13 (13C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of 13C CO2
- sensitivity 95-98%, specificity 97-98%

Rapid urease test (e.g. CLO test)
- biopsy sample is mixed with urea and pH indicator
- colour change if H pylori urease activity
- sensitivity 90-95%, specificity 95-98%

Serum antibody
- remains positive after eradication
- sensitivity 85%, specificity 80%

Culture of gastric biopsy
- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

Gastric biopsy
- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

Stool antigen test
- sensitivity 90%, specificity 95%

Question 26 of 142

A 25-year-old woman develops deranged liver function tests following the introduction of a new drug. Alb 40, Bilirubin 46, ALT 576, ALP 95, yGT 150. Which of the following drugs is the most likely cause?

- A. Oral contraceptive pill
- B. Sodium valproate
- C. Flucloxacillin
- D. Chlorpromazine
- E. Tetracycline

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- C. Flucloxacillin
- D. Chlorpromazine
- E. Tetracycline

The liver function tests suggest a hepatitis rather than cholestasis. Sodium valproate may be associated with such a picture

Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 27 of 142

Primary sclerosing cholangitis is most associated with:

- A. Primary biliary cirrhosis
- B. Crohn's disease
- C. Hepatitis C infection
- D. Ulcerative colitis
- E. Coeliac disease

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Primary sclerosing cholangitis

Primary sclerosing cholangitis is a biliary disease of unknown aetiology characterised by inflammation and fibrosis of intra and extra-hepatic bile ducts

Associations
- ulcerative colitis: 4% of patients with UC have PSC, 80% of patients with PSC have UC
- Crohn's (much less common association than UC)
- HIV

Features
- cholestasis

Investigation
- ERCP is the standard diagnostic tool, showing multiple biliary strictures giving a 'beaded' appearance
- ANCA may be positive
- there is a limited role for liver biopsy, which may show fibrous, obliterative cholangitis often described as 'onion skin'

Complications
- cholangiocarcinoma (in 10%)
- increased risk of colorectal cancer

Question 28 of 142

A patient presents with gastrointestinal symptoms. Which one of the following features in the history would be least consistent with making a diagnosis of irritable bowel syndrome?

- A. Past medical history of epilepsy
- B. Symptoms made worse by eating
- C. 62-year-old female
- D. Passage of mucous with stool
- E. Bladder symptoms

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- B. Symptoms made worse by eating
- ✓ C. 62-year-old female
- D. Passage of mucous with stool
- E. Bladder symptoms

Onset after 60 years of age is considered a red flag in the new NICE guidelines. A history of epilepsy has no bearing on whether a patient is diagnosed with irritable bowel syndrome

Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Question 29 of 142

A 26-year-old woman who is known to have type 1 diabetes mellitus presents with a three-month history of diarrhoea, fatigue and weight loss. She has tried excluding gluten from her diet for the past 4 weeks and feels much better. She requests to be tested so that a diagnosis of coeliac disease is confirmed. What is the most appropriate next step?

- A. Check her HbA1c
- B. No need for further investigation as the clinical response is diagnostic
- C. Check anti-endomysial antibodies
- D. Arrange a jejunal biopsy
- E. Ask her to reintroduce gluten for the next 6 weeks before further testing

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- D. Arrange a jejunal biopsy
- ✓ E. Ask her to reintroduce gluten for the next 6 weeks before further testing

Serological tests and jejunal biopsy may be negative if the patient is following a gluten-free diet. The patient should eat some gluten in more than one meal every day for at least 6 weeks before further testing.

Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

Immunology
- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

Jejunal biopsy
- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

Question 30 of 142

A 52-year-old woman is diagnosed with non-alcoholic steatohepatitis following a liver biopsy. What is the single most important step to help prevent the progression of her disease?

- A. Stop smoking
- B. Start statin therapy
- C. Eat more omega-3 fatty acids
- D. Start sulfonylurea therapy
- E. Weight loss

Question 30 of 142

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- D. Start sulfonylurea therapy
- ✓ E. Weight loss

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and though to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

Question 31 of 142

Which of the following statements is true regarding the genetics of colon cancer?

- A. Hereditary non-polyposis colorectal carcinoma is a autosomal recessive condition
- B. The adenomatous polyposis coli gene is located on chromosome 12
- C. Around 50% of patients with familial adenomatous polyposis develop colon cancer
- D. Both hereditary and non-hereditary colon cancers typically present at 60-70 yrs of age
- E. Non-inherited colon cancer often involves mutation of the adenomatous polyposis coli gene

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Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:
- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are often poorly differentiated and highly aggressive. Currently four gene mutations have been identified (including in the hMLH1 and hMSH2 genes). The Amsterdam criteria are sometimes used to aid diagnosis:

Amsterdam criteria for HNPCC
- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Question 32 of 142

A 23-year-old man develops watery diarrhoea 5 days after arriving in Mexico. Which one of the following is the most likely responsible organism?

- A. *Salmonella*
- B. *Shigella*
- C. *Campylobacter*
- D. *Escherichia coli*
- E. *Bacillus cereus*

Question 32 of 142

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- C. *Campylobacter*
- ✓ D. *Escherichia coli*
- E. *Bacillus cereus*

E. coli is the most common cause of travellers' diarrhoea

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 33 of 142

Each one of the following is a risk factor for gastric cancer, except:

- A. Smoking
- B. Blood group O
- C. Nitrates in diet
- D. Pernicious anaemia
- E. *H. pylori* infection

Question 33 of 142

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Gastric cancer

Epidemiology
- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Colombia than the West
- more common in males, 2:1

Associations
- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

Investigation
- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Question 34 of 142

Which one of the following is most associated with the development of acute pancreatitis?

- A. Hyperchylomicronaemia
- B. Amyloidosis
- C. Hypogammaglobulinaemia
- D. Hypercholesterolaemia
- E. Hypotriglyceridaemia

Question 34 of 142

Which one of the following is most associated with the development of acute pancreatitis?

- ✓ A. Hyperchylomicronaemia
- B. Amyloidosis
- C. Hypogammaglobulinaemia
- D. Hypercholesterolaemia
- E. Hypotriglyceridaemia

Hyperchylomicronaemia may be caused by hereditary lipoprotein lipase deficiency and apolipoprotein CII deficiency. It predisposes to recurrent attacks of acute pancreatitis

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 35 of 142

A 25-year-old female currently under investigation for secondary amenorrhoea presents with jaundiced sclera. On examination spider naevi are present along with tender hepatomegaly. Blood tests show:

Hb	11.6 g/dl
Plt	145 * 10^9/l
WCC	6.4 * 10^9/l
Albumin	33 g/l
Bilirubin	78 µmol/l
ALT	245 iu/l

What is the most likely diagnosis?

- A. Haemochromatosis
- B. Wilson's disease
- C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Primary sclerosing cholangitis

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ALT 245 iu/l

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- B. Wilson's disease
- C. Primary biliary cirrhosis
- ✓ D. Autoimmune hepatitis
- E. Primary sclerosing cholangitis

The combination of deranged LFTs combined with secondary amenorrhoea in a young female strongly suggest autoimmune hepatitis

Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	**Type II**	**Type III**
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA) Affects both adults and children	Anti-liver/kidney microsomal type 1 antibodies (LKM1) Affects children only	Soluble liver-kidney antigen Affects adults in middle-age

Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Question 36 of 142

What is the most common cause of hepatocellular carcinoma in the United Kingdom?

- A. Haemochromatosis
- B. Hepatitis B
- C. Alcohol excess
- D. Aflatoxin
- E. Hepatitis C

Question 36 of 142

What is the most common cause of hepatocellular carcinoma in the United Kingdom?

- A. Haemochromatosis
- B. Hepatitis B
- C. Alcohol excess
- D. Aflatoxin
- ✓ E. Hepatitis C

Hepatocellular carcinoma
• hepatitis B most common cause worldwide • hepatitis C most common cause in Europe

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

*Wilson's disease is an exception

Question 37 of 142

A 34-year-old HIV positive man is referred to gastroenterology due to jaundiced sclera. Liver function tests are as follows:

Albumin 34 g/l

ALP 540 iu/l

Bilirubin 67 µmol/l

ALT 45 iu/l

What is the most likely diagnosis?

- A. Hepatic abscess
- B. Fungal obstruction of the bile duct
- C. Duodenal adenoma
- D. Primary biliary cirrhosis
- E. Sclerosing cholangitis

Question 37 of 142

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What is the most likely diagnosis?

- A. Hepatic abscess
- B. Fungal obstruction of the bile duct
- C. Duodenal adenoma
- D. Primary biliary cirrhosis
- ✓ E. Sclerosing cholangitis

The LFTs clearly show a cholestatic picture. Given the background of HIV the most likely cause is sclerosing cholangitis

HIV: biliary and pancreatic disease

The most common cause of biliary disease in patients with HIV is sclerosing cholangitis due to infections such as CMV, Cryptosporidium and Microsporidia

Pancreatitis in the context of HIV infection may be secondary to anti-retroviral treatment (especially didanosine) or by opportunistic infections e.g. CMV

Question 38 of 142

A 65-year-old man with a history of dyspepsia is found to have a gastric MALT lymphoma on biopsy. What treatment should be offered?

- A. Gastrectomy
- B. Laser ablation
- C. None
- D. CHOP chemotherapy
- E. *H. pylori* eradication

Question 38 of 142

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- B. Laser ablation
- C. None
- D. CHOP chemotherapy
- ✓ E. *H. pylori* eradication

Gastric MALT lymphoma

Overview
- associated with *H. pylori* infection in 95% of cases
- good prognosis
- if low grade then 80% respond to *H. pylori* eradication

Features
- paraproteinaemia may be present

Question 39 of 142

A 42-year-old dentist is reviewed in the medical clinic complaining of persistent lethargy. Routine bloods show abnormal liver function tests so a hepatitis screen is sent. The results are shown below:

Anti-HAV IgG	negative
HBsAg	negative
Anti-HBs	positive
Anti-HBc	negative
Anti-HCV	positive

What do these results most likely demonstrate?

- A. Hepatitis B infection
- B. Hepatitis C infection
- C. Previous vaccination to hepatitis B and C
- D. Hepatitis C infection with previous hepatitis B vaccination
- E. Hepatitis B and C infection

Question 39 of 142

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Anti-HBs	positive
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Anti-HCV	positive

What do these results most likely demonstrate?

- A. Hepatitis B infection
- B. Hepatitis C infection
- C. Previous vaccination to hepatitis B and C
- ✓ D. Hepatitis C infection with previous hepatitis B vaccination
- E. Hepatitis B and C infection

Given the deranged liver function tests these results most likely indicate previous hepatitis B vaccination with active hepatitis C infection. However, around 15% of patients exposed to the hepatitis C virus clear the infection. It would therefore be necessary to perform a HCV PCR to see if the virus is still present

There is currently no vaccination for hepatitis C

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 40 of 142

You wish to screen a patient for hepatitis B infection. Which one of the following is the most suitable test to perform?

- A. HBcAg
- B. HBsAg
- C. Hepatitis B viral load
- D. anti-HBs
- E. HBeAg

Question 40 of 142

You wish to screen a patient for hepatitis B infection. Which one of the following is the most suitable test to perform?

- A. HBcAg
- ✓ B. HBsAg
- C. Hepatitis B viral load
- D. anti-HBs
- E. HBeAg

A positive anti-HBs would imply immunity through either previous immunisation or disease. A positive HBsAg implies either acute or chronic hepatitis B.

Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Question 41 of 142

A 76-year-old woman with a history of atrial fibrillation presents with abdominal pain and bloody diarrhoea. On examination her temperature is 37.8ºC, pulse 102 / min and respiratory rate 30 / min. Her abdomen is tender with generalised guarding. Blood tests reveal the following:

Hb	10.9 g/dl
MCV	76 fl
Plt	348 * 10^9/l
WBC	23.4 * 10^9/l
Na^+	141 mmol/l
K^+	5.0 mmol/l
Bicarbonate	14 mmol/l
Urea	8.0 mmol/l
Creatinine	118 µmol/l

What is the most likely diagnosis?

- A. Diverticulitis
- B. Mesenteric ischaemia
- C. *Campylobacter* infection
- D. Ruptured abdominal aortic aneurysm
- E. Ulcerative colitis

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- C. *Campylobacter* infection
- D. Ruptured abdominal aortic aneurysm
- E. Ulcerative colitis

The low bicarbonate points to a metabolic acidosis - highly suggestive of mesenteric ischaemia.

Mesenteric ischaemia

Mesenteric ischaemia is primarily caused by arterial embolism resulting in infarction of the colon. It is more likely to occur in areas such as the splenic flexure that are located at the borders of the territory supplied by the superior and inferior mesenteric arteries.

Predisposing factors

- increasing age
- atrial fibrillation
- other causes of emboli: endocarditis
- cardiovascular disease risk factors: smoking, hypertension, diabetes

Features

- abdominal pain
- rectal bleeding
- diarrhoea
- fever
- bloods typically show an elevated WBC associated with acidosis

Management

- supportive care
- laparotomy and bowel resection

Question 42 of 142

Which one of the following medications is least associated with dyspepsia?

- A. Isosorbide mononitrate
- B. Prednisolone
- C. Aminophylline
- D. Atenolol
- E. Amlodipine

Question 42 of 142

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Drugs causing dyspepsia

Causes
- NSAIDs
- bisphosphonates
- steroids

The following drugs may cause reflux by reducing lower oesophageal sphincter (LOS) pressure
- calcium channel blockers*
- nitrates*
- theophyllines

*calcium channel blockers and nitrates are occasionally used in the management of achalasia, itself a cause of dyspepsia, because of their effect on the LOS.

Question 43 of 142

A 31-year-old man with ulcerative colitis presents with a worsening of his symptoms. He is passing around four loose stools a day which do not contain blood. He has also experienced some urgency and tenesmus but is otherwise systemically well. What is the most appropriate management?

- A. Rectal mesalazine
- B. Oral metronidazole
- C. Rectal corticoteroids
- D. Observe with review in 7 days time
- E. Oral loperamide

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- E. Oral loperamide

Ulcerative colitis: management

Treatment can be divided into inducing and maintaining remission

Inducing remission

- treatment depends on the extent and severity of disease
- rectal aminosalicylates or steroids: for distal colitis rectal mesalazine has been shown to be superior to rectal steroids
- oral aminosalicylates or steroids
- severe colitis should be referred to hospital

Maintaining remission

- oral aminosalicylates e.g. Mesalazine
- azathioprine and mercaptopurine
- methotrexate is not recommended for the management of ulcerative colitis (in contrast to Crohn's disease)
- there is some evidence that probiotics may prevent relapse in patients with mild to moderate disease

Question 44 of 142

A 23-year-old nurse is reviewed in occupational health following a needle stick injury from a man known to be a carrier of hepatitis B. Which one of the following would appear first during acute hepatitis B infection?

- A. HBsAg
- B. HBeAg
- C. anti-HBg
- D. anti-HBs
- E. HBcAg

Question 44 of 142

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Question 45 of 142

The increased risk of oesophageal malignancy in patients with Barrett's oesophagus is approximately:

- A. No increased risk
- B. Twice risk
- C. 5 times risk
- D. 50 - 100 times risk
- E. 500 - 1,000 times risk

Question 45 of 142

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Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

Question 46 of 142

A 59-year-old woman presents with dysphagia. There is no history of heartburn, weight loss or change in bowel habit. During endoscopy there is some difficulty passing through the lower oesophageal sphincter but no other abnormality is noted. Which one of the following tests is most likely to reveal the diagnosis?

- A. Oesophageal biopsy
- B. Oesophageal manometry
- C. Plain chest x-ray
- D. Endoscopy ultrasound
- E. CT thorax

Question 46 of 142

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- ✓ B. Oesophageal manometry
- C. Plain chest x-ray
- D. Endoscopy ultrasound
- E. CT thorax

The gold standard test for achalasia is oesophageal manometry

Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is more common in women

Clinical features
- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

Investigations
- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

Treatment
- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Question 47 of 142

The most common type of inherited colorectal cancer:

- A. Familial adenomatous polyposis
- B. Li-Fraumeni syndrome
- C. Hereditary non-polyposis colorectal carcinoma
- D. Fanconi syndrome
- E. Peutz-Jeghers syndrome

Question 47 of 142

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Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are often poorly differentiated and highly aggressive. Currently four gene mutations have been identified (including in the hMLH1 and hMSH2 genes). The Amsterdam criteria are sometimes used to aid diagnosis:

Amsterdam criteria for HNPCC

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Question 48 of 142

Which one of the following statements best describes the prevention and treatment of hepatitis C?

- A. No vaccine is available and treatment is only successful in around 10-15% of patients
- B. No vaccine and no treatment is available
- C. A vaccine is available and treatment is successful in around 50% of patients
- D. A vaccine is available but no treatment has been shown to be effective
- E. No vaccine is available but treatment is successful in around 50% of patients

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Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 49 of 142

A 36-year-old man is reviewed in clinic. He has recently been started on mesalazine 400mg tds for ulcerative colitis. Which one of the following adverse effects is least likely to be attributable to mesalazine?

- A. Interstitial nephritis
- B. Headaches
- C. Acute pancreatitis
- D. Agranulocytosis
- E. Infertility

Question 49 of 142

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- B. Headaches
- C. Acute pancreatitis
- D. Agranulocytosis
- ✓ E. Infertility

Oligospermia is seen in patients taking sulphasalazine due to the sulphapyridine moiety, which is not present in mesalazine

Aminosalicylate drugs

5-aminosalicyclic acid (5-ASA) is released in the colon and is not absorbed. It acts locally as an anti-inflammatory. The mechanism of action is not fully understood but 5-ASA may inhibit prostaglandin synthesis

Sulphasalazine
- a combination of sulphapyridine (a sulphonamide) and 5-ASA
- many side-effects are due to the sulphapyridine moiety: rashes, oligospermia, headache, Heinz body anaemia
- other side-effects are common to 5-ASA drugs (see mesalazine)

Mesalazine
- a delayed release form of 5-ASA
- sulphapyridine side-effects seen in patients taking sulphasalazine are avoided
- mesalazine is still however associated with side-effects such as GI upset, headache, agranulocytosis, pancreatitis*, interstitial nephritis

Olsalazine
- two molecules of 5-ASA linked by a diazo bond, which is broken by colonic bacteria

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 50 of 142

A 59-year-old female presents with a two month history of indigestion. She is otherwise well, has not had a similar episode before and takes no regular medication. Of note there is no recent weight loss or vomiting and abdominal examination is unremarkable. What is the most appropriate initial management?

- A. Long-term course of a H2 receptor antagonist
- B. Lifestyle advice with follow-up appointment in one month
- C. Urgent referral for endoscopy
- D. One month course of a full-dose proton pump inhibitor
- E. Urea breath testing and treat for H pylori if positive

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- ✓ C. Urgent referral for endoscopy
- D. One month course of a full-dose proton pump inhibitor
- E. Urea breath testing and treat for H pylori if positive

This patient meets the criteria for urgent referral for endoscopy as she is older than 55 years, has recent onset, persistent and unexplained symptoms

Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')
This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month*
- 4. 'Test and treat' using carbon-13 urea breath test

*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Question 51 of 142

A 27-year-old man with multiple pigmented freckles on his lips and face is investigated for iron-deficiency anaemia. A diagnosis of Peutz-Jeghers syndrome is suspected. What is the mode of inheritance?

- A. Autosomal recessive
- B. Mitochondrial inheritance
- C. X-linked dominant
- D. Autosomal dominant
- E. X-linked recessive

Question 51 of 142

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- ✓ D. Autosomal dominant
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Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 52 of 142

Where do the majority of VIPomas arise from?

- A. Small intestine
- B. Pituitary
- C. Pancreas
- D. Antrum of stomach
- E. Pylorus of stomach

Question 52 of 142

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VIPoma

VIP (vasoactive intestinal peptide)
- source: small intestine, pancreas
- stimulation: neural
- actions: stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion

VIPoma
- 90% arise from pancreas
- large volume diarrhoea
- weight loss
- dehydration
- hypokalaemia, hypochlorhydia

Question 53 of 142

A 34-year-old male is admitted with central abdominal pain radiating through to the back and vomiting. The following results are obtained:

Amylase 1,245 u/dl

Which one of the following medications is most likely to be responsible?

- A. Phenytoin
- B. Sodium valproate
- C. Metoclopramide
- D. Sumatriptan
- E. Pizotifen

Question 53 of 142

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- C. Metoclopramide
- D. Sumatriptan
- E. Pizotifen

Sodium valproate induced pancreatitis is more common in young adults and tends to occur within the first few months of treatment. Asymptomatic elevation of the amylase level is seen in up to 10% of patients

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 54 of 142

Which one of the following investigations is considered the gold standard for the diagnosis of gastro-oesophageal reflux disease?

- A. Endoscopy
- B. 24hr oesophageal pH monitoring
- C. Oesophageal manometry
- D. Barium swallow
- E. CT thorax

Question 54 of 142

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- A. Endoscopy
- ✓ B. 24hr oesophageal pH monitoring
- C. Oesophageal manometry
- D. Barium swallow
- E. CT thorax

24hr oesophageal pH monitoring is gold standard investigation in GORD

GORD: investigation

Overview
- poor correlation between symptoms and endoscopy appearance

Indications for upper GI endoscopy:
- age > 55 years
- symptoms > 4 weeks or persistent symptoms despite treatment
- dysphagia
- relapsing symptoms
- weight loss

If endoscopy is negative consider 24-hr oesophageal pH monitoring (the gold standard test for diagnosis)

Question 55 of 142

A 30-year-old woman presents with a three month history of indigestion. There is no history of weight less, anorexia, dysphagia, vomiting or change in bowel habit and abdominal examination is unremarkable. Which one of the following may decrease the accuracy of a 13C-urea breath test?

- A. Use of Gaviscon around 10 days ago
- B. Use of ranitidine stopping 4 weeks ago
- C. Course of amoxicillin stopping 3 weeks ago
- D. Use of lansoprazole stopping 6 weeks ago
- E. Current use of the combined oral contraceptive pill

Question 55 of 142

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- D. Use of lansoprazole stopping 6 weeks ago
- E. Current use of the combined oral contraceptive pill

Urea breath test - no antibiotics in past 4 weeks, no antisecretory drugs (e.g. PPI) in past 2 weeks

***Helicobacter pylori*: tests**

Urea breath test
- patients consume a drink containing carbon isotope 13 (13C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of 13C CO2
- sensitivity 95-98%, specificity 97-98%

Rapid urease test (e.g. CLO test)
- biopsy sample is mixed with urea and pH indicator
- colour change if H pylori urease activity
- sensitivity 90-95%, specificity 95-98%

Serum antibody
- remains positive after eradication
- sensitivity 85%, specificity 80%

Culture of gastric biopsy
- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

Gastric biopsy
- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

Stool antigen test
- sensitivity 90%, specificity 95%

Question 56 of 142

A 40-year-old man is investigated for abnormal liver function tests. It is decided to perform a liver biopsy. Which one of the following is a contraindication to liver biopsy?

- A. ALT of 2,212 iu/l
- B. Aspirin therapy
- C. Platelet count of 100 * 10^9/l
- D. Body mass index of 33 kg/m^2
- E. Bile duct dilatation

Question 56 of 142

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- B. Aspirin therapy
- C. Platelet count of 100 * 10^9/l
- D. Body mass index of 33 kg/m^2
- ✓ E. Bile duct dilatation

With modern techniques such as ERCP and MRI cholangiography the risks of liver biopsy when there is extra-hepatic biliary obstruction are rarely justified.

Liver biopsy

Contraindications to percutaneous liver biopsy

- deranged clotting (e.g. INR > 1.4)
- low platelets (e.g. < 60 * 10^9/l)
- anaemia
- bile duct obstruction
- hydatid cyst
- haemoangioma
- uncooperative patient
- ascites

Question 57 of 142

A 45-year-old man with a history of alcohol excess is diagnosed as having grade 3 oesophageal varices during an outpatient endoscopy. Of the following options, what is the most appropriate management to prevent variceal bleeding?

- A. Propranolol
- B. Isosorbide mononitrate
- C. Endoscopic sclerotherapy
- D. Terlipressin
- E. Lansoprazole

Question 57 of 142

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- B. Isosorbide mononitrate
- C. Endoscopic sclerotherapy
- D. Terlipressin
- E. Lansoprazole

Endoscopic sclerotherapy now has little role in the prophylaxis of variceal haemorrhage.

Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 58 of 142

A 27-year-old female is referred to the medical outpatient clinic due to a long history of fatigue and joint pains. An autoimmune screen is done which is positive for smooth muscle antibodies. What is the most appropriate next investigation?

- A. Liver function tests
- B. Thyroid function tests
- C. Creatine kinase
- D. Serum glucose
- E. Electrocardiogram

Question 58 of 142

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- ✓ A. Liver function tests
- B. Thyroid function tests
- C. Creatine kinase
- D. Serum glucose
- E. Electrocardiogram

Smooth muscle antibodies are associated with autoimmune hepatitis. Presentation is usually insidious and extrahepatic clinical features are common

Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	**Type II**	**Type III**
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA) Affects both adults and children	Anti-liver/kidney microsomal type 1 antibodies (LKM1) Affects children only	Soluble liver-kidney antigen Affects adults in middle-age

Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Question 59 of 142

Which one of the following statements is incorrect regarding Dubin-Johnson syndrome?

- A. Runs a benign course
- B. Due to a defect in the canillicular multispecific organic anion transporter
- C. Causes defective hepatic bilirubin excretion
- D. It is an autosomal recessive disorder
- E. Results in an unconjugated hyperbilirubinaem

Question 59 of 142

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- C. Causes defective hepatic bilirubin excretion
- D. It is an autosomal recessive disorder
- ✓ E. Results in an unconjugated hyperbilirubinaemia

Dubin-Johnson syndrome

Dubin-Johnson syndrome is a benign autosomal recessive disorder resulting in hyperbilirubinaemia (conjugated, therefore present in urine). It is due to a defect in the canillicular multispecific organic anion transporter (cMOAT) protein. This causes defective hepatic bilirubin excretion

Question 60 of 142

Which one of the following is least likely to cause malabsorption?

- A. Systemic sclerosis
- B. Cystic fibrosis
- C. Primary biliary cirrhosis
- D. Whipple's disease
- E. Haemochromatosis

Question 60 of 142

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- ✓ E. Haemochromatosis

Malabsorption

Malabsorption is characterised by diarrhoea, steatorrhoea and weight loss. Causes may be broadly divided into intestinal (e.g. villous atrophy), pancreatic (deficiency of pancreatic enzyme production or secretion) and biliary (deficiency of bile-salts needed for emulsification of fats)

Intestinal causes of malabsorption
- coeliac disease
- Crohn's disease
- tropical sprue
- Whipple's disease
- Giardiasis
- brush border enzyme deficiencies (e.g. lactase insufficiency)

Pancreatic causes of malabsorption
- chronic pancreatitis
- cystic fibrosis
- pancreatic cancer

Biliary causes of malabsorption
- biliary obstruction
- primary biliary cirrhosis

Other causes
- bacterial overgrowth (e.g. systemic sclerosis, diverticulae, blind loop)
- short bowel syndrome
- lymphoma

Question 61 of 142

A 27-year-old woman with a history of depression presents to the Emergency Department. She reports taking 50 paracetamol tablets yesterday. Bloods are taken on admission. Which one of the following would most strongly indicate the need for a liver transplant?

- A. Blood glucose 2.2 mmol/l
- B. ALT 2364 iu/l
- C. INR 4.1
- D. Creatinine 230 µmol/l
- E. Arterial pH 7.27

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- C. INR 4.1
- D. Creatinine 230 µmol/l
- ✓ E. Arterial pH 7.27

The arterial pH is the single most important factor according to the King's College Hospital criteria for liver transplantation.

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300 µmol/l
- grade III or IV encephalopathy

Question 62 of 142

According to recent NICE guidelines, which one of the following may have a role in the management of irritable bowel syndrome?

- A. Reflexology
- B. Acupuncture
- C. Aloe vera
- D. Homeopathy
- E. Hypnotherapy

Question 62 of 142

A 64-year-old female with a history of COPD and hypertension presents with pain on swallowing. Current medication includes a salbutamol and becotide inhaler, bendrofluazide and amlodipine. What is the most likely cause of the presentation?

- A. Myasthenia gravis precipitated by bendrofluazide
- B. Oesophageal web
- C. Achalasia secondary to amlodipine
- ✓ D. Oesophageal candidiasis
- E. Oesophageal cancer

Pain on swallowing (odynophagia) is a typical of oesophageal candidiasis, a well documented complication of inhaled steroid therapy

Dysphagia

The table below gives characteristic exam question features for conditions causing dysphagia:

Oesophageal cancer	Dysphagia may be associated with weight loss, anorexia or vomiting during eating Past history may include Barrett's oesophagus, GORD, excessive smoking or alcohol use
Oesophagitis	May be history of heartburn Odynophagia but no weight loss and systemically well
Oesophageal candidiasis	There may be a history of HIV or other risk factors such as steroid inhaler use
Achalasia	Dysphagia of both liquids and solids from the start Heartburn Regurgitation of food - may lead to cough, aspiration pneumonia etc
Pharyngeal pouch	More common in older men Represents a posteromedial herniation between thyropharyngeus and cricopharyngeus muscles Usually not seen but if large then a midline lump in the neck that gurgles on palpation Typical symptoms are dysphagia, regurgitation, aspiration and chronic cough. Halitosis may occasionally be seen
Systemic sclerosis	Other features of CREST syndrome may be present, namely Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia
Myasthenia gravis	Other symptoms may include extraocular muscle weakness or ptosis Dysphagia with liquids as well as solids
Globus hystericus	May be history of anxiety Symptoms are often intermittent

Question 63 of 142

A 45-year-old man is admitted to the Emergency Department with severe abdominal pain. He smokes 20 cigarettes a day and drinks approximately 50 units of alcohol per week. He also complains of sudden deterioration in vision. Fundoscopy reveals shows multiple micro infarcts (cotton wool spots). Which investigation would best confirm the most likely diagnosis?

- A. Gastroscopy
- B. Serum glucose
- C. Amylase
- D. Biliary USS
- E. ECG

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- A. Gastroscopy
- B. Serum glucose
- ✓ C. Amylase
- D. Biliary USS
- E. ECG

The cotton wool spots seen on fundoscopy represents Purtscher retinopathy. This condition may be seen following head trauma and in conditions such as acute pancreatitis, fat embolisation, amniotic fluid embolisation, and vasculitic diseases

Acute pancreatitis: features

Rare features associated with pancreatitis include:

- ischaemic (Purtscher) retinopathy - may cause temporary or permanent blindness

Question 64 of 142

Which of the following is not a recognised complication of coeliac disease?

- A. Hypersplenism
- B. Osteoporosis
- C. Lactose intolerance
- D. Oesophageal cancer
- E. Subfertility

Question 64 of 142

Which of the following is not a recognised complication of coeliac disease?

- ✓ A. Hypersplenism
- B. Osteoporosis
- C. Lactose intolerance
- D. Oesophageal cancer
- E. Subfertility

Hypo-, not hypersplenism is seen in coeliac disease

Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
? Chronic or intermittent diarrhoea ? Failure to thrive or faltering growth (in children) ? Persistent or unexplained gastrointestinal symptoms including nausea and vomiting ? Prolonged fatigue ('tired all the time') ? Recurrent abdominal pain, cramping or distension ? Sudden or unexpected weight loss ? Unexplained iron-deficiency anaemia, or other unspecified anaemia	? Autoimmune thyroid disease ? Dermatitis herpetiformis ? Irritable bowel syndrome ? Type 1 diabetes ? First-degree relatives (parents, siblings or children) with coeliac disease

Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

Question 65 of 142

A 19-year-old man is referred to the general medical clinic. For the past six months his family have noted increasing behavioural and speech problems. He himself has noticed that he is more clumsy than normal and reports excessive salivation. His older brother died of liver disease. Given the likely underlying condition what is the most appropriate therapy?

- A. Vitamin B6 supplements
- B. Venesection
- C. Ribavirin + interferon alpha
- D. Pulsed methylprednisolone
- E. Penicillamine

Question 65 of 142

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- A. Vitamin B6 supplements
- B. Venesection
- C. Ribavirin + interferon alpha
- D. Pulsed methylprednisolone
- ✓ E. Penicillamine

This man is likely to have Wilson's disease.

Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Question 66 of 142

Which one of the following is not associated with villous atrophy on jejunal biopsy?

- A. Tropical sprue
- B. Coeliac disease
- C. Hypogammaglobulinaemia
- D. Familial Mediterranean Fever
- E. Whipple's disease

Question 66 of 142

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- A. Tropical sprue
- B. Coeliac disease
- C. Hypogammaglobulinaemia
- ✓ D. Familial Mediterranean Fever
- E. Whipple's disease

Causes of villous atrophy (other than coeliacs): tropical sprue, Whipple's, lymphoma, hypogammaglobulinaemia

Jejunal villous atrophy

Whilst coeliac disease is the classic cause of jejunal villous atrophy there are a number of other causes you need to be aware of

Causes

- coeliac disease
- tropical sprue
- hypogammaglobulinaemia
- gastrointestinal lymphoma
- Whipple's disease
- cow's milk intolerance

Question 67 of 142

A 45-year-old man is noted to have non-tender, smooth hepatomegaly associated Dupuytren's contracture and parotid enlargement. He recently returned from a holiday in Thailand. What is the likely diagnosis?

- A. Primary hepatoma
- B. Hydatid disease
- C. Alcoholic liver disease
- D. Viral hepatitis
- E. Tricuspid regurgitation

Question 67 of 142

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- ✓ C. Alcoholic liver disease
- D. Viral hepatitis
- E. Tricuspid regurgitation

Both Dupuytren's contracture and parotitis are associated with alcoholic liver disease. Whilst a history of alcohol excess would normally be volunteered it should be remembered many patients will lie about their alcohol intake.

The recent holiday in Thailand is a distractor.

Hepatomegaly

Common causes of hepatomegaly

- Cirrhosis: if early disease, later liver decreases in size. Associated with a non-tender, firm liver
- Malignancy: metastatic spread or primary hepatoma. Associated with a hard, irregular. liver edge
- Right heart failure: firm, smooth, tender liver edge. May be pulsatile

Other causes

- viral hepatitis
- glandular fever
- malaria
- abscess: pyogenic, amoebic
- hydatid disease
- haematological malignancies
- haemochromatosis
- primary biliary cirrhosis
- sarcoidosis, amyloidosis

Question 68 of 142

A 42-year-old woman is investigated for lethargy and diarrhoea. Investigations reveal positive anti-endomysial antibodies. Each of the following food stuffs should be avoided, except:

- A. Beer
- B. Rye
- C. Maize
- D. Bread
- E. Pasta

Question 68 of 142

A 42-year-old woman is investigated for lethargy and diarrhoea. Investigations reveal positive anti-endomysial antibodies. Each of the following food stuffs should be avoided, except:

- A. Beer
- B. Rye
- ✓ C. Maize
- D. Bread
- E. Pasta

Coeliac disease: management

The management of coeliac disease involves a gluten-free diet. Gluten containing cereals include:

- wheat: bread, pasta, pastry
- barley*: beer
- rye
- oats**

Some notable foods which are gluten-free include:

- rice
- potatoes
- corn (maize)

*whisky is made using malted barley. Proteins such as gluten are however removed during the distillation process making it safe to drink for patients with coeliac disease

**some patients with coeliac disease appear able to tolerate oats

Question 69 of 142

A 17-year-old girl presents with a 6 week history of nausea and abdominal discomfort. Routine blood tests reveal the following.

Hb	10.9 g/dl
WBC	6.7 *10^9/l
Platelets	346 *10^9/l
Calcium	2.33 mmol/l
Bilirubin	7 µmol/l
ALP	262 u/l
ALT	35 u/l

What is the most likely diagnosis?

- A. Alcoholic liver disease
- B. Cholangiocarcinoma
- C. Pregnancy
- D. Gallstones
- E. Primary biliary cirrhosis

Question 69 of 142

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What is the most likely diagnosis?

- A. Alcoholic liver disease
- B. Cholangiocarcinoma
- ✓ C. Pregnancy
- D. Gallstones
- E. Primary biliary cirrhosis

Alkaline phosphatase is significantly elevated in pregnancy. This would also explain the borderline anaemia

Alkaline phosphatase

Causes of raised alkaline phosphatase (ALP)

- liver: cholestasis, hepatitis, fatty liver, neoplasia
- Paget's
- osteomalacia
- bone metastases
- hyperparathyroidism
- renal failure
- physiological: pregnancy, growing children, healing fractures

The table below splits the causes according to the calcium level

Raised ALP and raised calcium	Raised ALP and low calcium
• Bone metastases • Hyperparathyroidism	• Osteomalacia • Renal failure

Question 70 of 142

Which one of the following statements regarding hepatitis C is correct?

- A. Cannot be transmitted vertically from mother to child
- B. Interferon-alpha and ribavirin are the treatments of choice
- C. It is more infectious than hepatitis B following a needle stick injury
- D. Breast feeding is contraindicated in mothers with hepatitis C
- E. HCV RNA is the initial investigation of choice for at-risk groups

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Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 71 of 142

Which one of the following is not associated with oesophageal cancer?

- A. Achalasia
- B. Smoking
- C. Gastro-oesophageal reflux disease
- D. *Helicobacter pylori*
- E. Alcohol

Question 71 of 142

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- A. Achalasia
- B. Smoking
- C. Gastro-oesophageal reflux disease
- ✓ D. *Helicobacter pylori*
- E. Alcohol

Helicobacter pylori may actually be protective against oesophageal cancer

Oesophageal cancer

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

Risk factors

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

Question 72 of 142

A 43-year-old man with type 2 diabetes mellitus presents with lethargy. His current medications include metformin and gliclazide, although the gliclazide may soon be stopped due to his obesity. A number of blood tests are ordered which reveal the following:

HbA1c 8.2%

Ferritin 204 ng/ml

Bilirubin 23 µmol/l

ALP 162 u/l

ALT 120 u/l

AST 109 u/l

On discussing these results he states that he does not drink alcohol. What is the most likely cause of these abnormal results?

- A. Metformin-induced steatohepatitis
- B. Haemochromatosis
- C. Acute hepatitis secondary to gliclazide
- D. Cryptogenic cirrhosis
- E. Non-alcoholic fatty liver disease

Question 72 of 142

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Obese T2DM with abnormal LFTs - ? non-alcoholic fatty liver disease

By far the most likely diagnosis in an obese type 2 diabetic is non-alcoholic fatty liver disease. This patient will require a liver screen, ultrasound and liver biopsy to confirm the diagnosis.

A normal ferritin makes a diagnosis of haemochromatosis unlikely, although it should always be considered in patients with both abnormal LFTs and diabetes.

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and though to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

Question 73 of 142

Which one of the following conditions is least likely to develop following hepatitis B infection?

- A. Glomerulonephritis
- B. Hepatocellular carcinoma
- C. Acute pancreatitis
- D. Chronic infection
- E. Polyarteritis nodosa

Question 73 of 142

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- A. Glomerulonephritis
- B. Hepatocellular carcinoma
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- D. Chronic infection
- E. Polyarteritis nodosa

Deterioration in patient with hepatitis B - ? hepatocellular carcinoma

Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	**Response**
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for past or previous infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in d dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

Question 74 of 142

Which one of the following patients is most likely to require screening for hepatocellular carcinoma?

- A. A 45-year-old man with liver cirrhosis secondary to hepatitis C
- B. A 33-year-old man with HIV. He is taking antiretroviral therapy
- C. A 22-year-old man with alpha-1 antitrypsin deficiency. He has no evidence of current liver disease
- D. A 52-year-old woman with alcohol-related liver cirrhosis who is still drinking
- E. A 75-year-old man who drinks 100 units / week. He has no current signs of liver disease

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- E. A 75-year-old man who drinks 100 units / week. He has no current signs of liver disease

Patients with liver cirrhosis secondary to hepatitis C have a 3-5% annual incidence of hepatocellular carcinoma.

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

*Wilson's disease is an exception

Question 75 of 142

Which one the following disorders is most strongly associated with primary biliary cirrhosis?

- A. Systemic sclerosis
- B. Thyroid disease
- C. Sjogren's syndrome
- D. Rheumatoid arthritis
- E. Systemic lupus erythematous

Question 75 of 142

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- A. Systemic sclerosis
- B. Thyroid disease
- ✓ C. Sjogren's syndrome
- D. Rheumatoid arthritis
- E. Systemic lupus erythematous

All of the above conditions are associated with primary biliary cirrhosis but Sjogren's syndrome is the most common, being seen in up to 80% of patients

Primary biliary cirrhosis

Primary biliary cirrhosis is a chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

Associations
- Sjogren's syndrome (seen in up to 80% of patients)
- rheumatoid arthritis
- systemic sclerosis
- thyroid disease

Diagnosis
- anti-mitochondrial antibodies (AMA) M2 subtype are present in 98% of patients and are highly specific
- smooth muscle antibodies in 30% of patients
- raised serum IgM

Management
- pruritus: cholestyramine
- fat-soluble vitamin supplementation
- ursodeoxycholic acid
- liver transplantation e.g. if bilirubin > 100 (PBC is a major indication) - recurrence in graft can occur but is not usually a problem

Question 76 of 142

A 27-year-old woman with chronic left iliac fossa pain and alternating bowel habit is diagnosed with irritable bowel syndrome. Initial treatment is tried with a combination of antispasmodics, laxatives and anti-motility agents. Unfortunately after 6 months there has been no significant improvement in her symptoms. According to recent NICE guidelines, what is the most appropriate next step?

- A. Low-dose tricyclic antidepressant
- B. Cognitive behavioural therapy
- C. Refer for sigmoidoscopy
- D. Trial of probiotics
- E. Selective serotonin reuptake inhibitor

Question 76 of 142

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- E. Selective serotonin reuptake inhibitor

NICE recommend considering psychological interventions after 12 months. Tricyclic antidepressants should be used in preference to selective serotonin reuptake inhibitors

Irritable bowel syndrome: management

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom
- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment
- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options
- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

General dietary advice
- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

Question 77 of 142

A 78-year-old woman is admitted with a productive cough and pyrexia to hospital. Chest x-ray shows a pneumonia and she is commenced on intravenous ceftriaxone. Four days following admission a stool sample is sent because of diarrhoea. This confirms the suspected diagnosis of *Clostridium difficile* diarrhoea and a 10-day course of oral metronidazole is started. After 10 days her diarrhoea is ongoing but she remains clinically stable. What is the most appropriate treatment?

- A. Oral vancomycin for 14 days
- B. IV vancomycin for 3 days
- C. Oral rifampicin for 7 days
- D. Oral clindamycin for 7 days
- E. Oral metronidazole for a further 7 days

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The Health Protection Agency suggests switching to oral vancomycin in this scenario.

Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

Question 78 of 142

A 29-year-old female is noted to have an elevated bilirubin during a viral illness. Gilbert's syndrome is suspected. Which one of the following tests may confirm the diagnosis?

- A. Bromsulphthalein excretion test
- B. Ammonium chloride acidification test
- C. Urine analysis
- D. Nicotinic acid test
- E. Faecal fat excretion

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Gilbert's syndrome

Gilbert's syndrome is an autosomal recessive* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

Features
- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

Investigation and management
- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

*the exact mode of inheritance is still a matter of debate

Question 79 of 142

A 43-year-old man is reviewed in the gastroenterology clinic. He has had troublesome dyspepsia for the past six months which has not settled with proton pump inhibitor therapy. During the review of systems he also reports passing 6-7 watery stools per day. An OGD 3 weeks ago showed gastric erosions and ulcers. Which one of the following investigations is most likely to be diagnostic?

- A. Serum amylase
- B. Urea breath test for *Helicobacter pylori*
- C. Fasting gastrin
- D. 14C-xylose breath test
- E. CT abdomen

Question 79 of 142

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- D. 14C-xylose breath test
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CT abdomen has a sensitivity of only 50% for primary tumours in Zollinger-Ellison syndrome (ZES). Normal levels of fasting gastrin in untreated ZES are extremely rare

Zollinger-Ellison syndrome

Zollinger-Ellison syndrome is condition characterised by excessive levels of gastrin, usually from a gastrin secreting tumour usually of the duodenum or pancreas. Around 30% occur as part of MEN type I syndrome

Features
- multiple gastroduodenal ulcers
- diarrhoea
- malabsorption

Diagnosis
- fasting gastrin levels: the single best screen test
- secretin stimulation test

Question 80 of 142

A 71-year-old man presents with two year history of intermittent problems with swallowing. His wife has also noticed he has halitosis and is coughing at night. He has a past medical history of type 2 diabetes mellitus but states he is otherwise well. Of note his weight is stable and he has a good appetite. Clinical examination is unremarkable. What is the most likely diagnosis?

- A. Oesophageal cancer
- B. Hiatus hernia
- C. Pharyngeal pouch
- D. Oesophageal candidiasis
- E. Benign oesophageal stricture

Question 80 of 142

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- ✓ C. Pharyngeal pouch
- D. Oesophageal candidiasis
- E. Benign oesophageal stricture

Given the two year history and good health oesophageal cancer is much less likely

Pharyngeal pouch

A pharyngeal pouch is a posteromedial diverticulum through Killian's dehiscence. Killian's dehiscence is a triangular area in the wall of the pharynx between the thyropharyngeus and cricopharyngeus muscles. It is more common in older patients and is 5 times more common in men

Features

- dysphagia
- regurgitation
- aspiration
- neck swelling which gurgles on palpation
- halitosis

Question 81 of 142

A 54-year-old female is diagnosed with primary biliary cirrhosis. What is her increased risk of developing hepatocellular cancer, compared to a standard population?

- A. 50% increased risk
- B. 3-fold increased risk
- C. 5-fold increased risk
- D. 10-fold increased risk
- E. 20-fold increased risk

Question 81 of 142

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- A. 50% increased risk
- B. 3-fold increased risk
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Primary biliary cirrhosis: features

Primary biliary cirrhosis is chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis, which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

Clinical features

- early: may be asymptomatic (e.g. raised ALP on routine LFTs) or fatigue, pruritus
- cholestatic jaundice
- hyperpigmentation, especially over pressure points
- xanthelasmas, xanthomata
- also: clubbing, hepatosplenomegaly
- late: may progress to liver failure

Complications

- malabsorption: osteomalacia, coagulopathy
- sicca syndrome occurs in 70% of cases
- portal hypertension: ascites, variceal haemorrhage
- hepatocellular cancer (20-fold increased risk)

Question 82 of 142

What percentage of patients with Peutz-Jeghers syndrome will have died from a related cancer by the age of 60 years?

- A. 2-3%
- B. 50%
- C. 5-7%
- D. >95%
- E. 10-20%

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Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 83 of 142

A 44-year-old obese female is noted to have gallstones during an abdominal ultrasound, which was requested due to repeated urinary tract infections. Apart from the repeated UTIs she is otherwise well. What is the most appropriate management of the gallstones?

- A. Ursodeoxycholic acid
- B. Extracorporeal Short Wave Lithotripsy
- C. List for laparoscopic cholecystectomy when 50 years old
- D. Observation
- E. List now for laparoscopic cholecystectomy

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- E. List now for laparoscopic cholecystectomy

Gallstones

Asymptomatic gallstones are common and do not require treatment

Question 84 of 142

Each one of the following is associated with pancreatic cancer, except:

- A. Chronic pancreatitis
- B. Smoking
- C. Blood group O
- D. Diabetes
- E. BRCA2 gene

Question 84 of 142

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Pancreatic cancer

Associations
- smoking
- diabetes
- chronic pancreatitis
- hereditary pancreatitis
- hereditary non-polyposis colorectal carcinoma
- multiple endocrine neoplasia
- Peutz-Jeghers syndrome
- BRCA2
- dysplastic naevus syndrome

Management
- less than 20% are suitable for surgery at diagnosis
- radio and chemotherapy are ineffective

Question 85 of 142

A 25-year-old intravenous drug user with chronic hepatitis C becomes pregnant. Approximately what is the chance of the virus being transmitted to her child?

- A. <10%
- B. 10-20%
- C. 20-30%
- D. 30-40%
- E. 40-50%

Question 85 of 142

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- C. 20-30%
- D. 30-40%
- E. 40-50%

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 86 of 142

A 31-year-old woman is reviewed in clinic. She has been referred by her GP with an 8 month history of abdominal discomfort associated with bloating. Which one of the following tests is it least useful to perform before making a positive diagnosis of irritable bowel syndrome?

- A. Erythrocyte sedimentation rate
- B. Thyroid function tests
- C. Full blood count
- D. C-reactive protein
- E. Tissue transglutaminase antibodies

Question 86 of 142

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NICE recommends that thyroid function tests are not necessary prior to making a positive diagnosis of IBS. Erythrocyte sedimentation rate and C-reactive protein may help exclude inflammatory bowel disease.

Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Question 87 of 142

A 31-year-old woman presents with symptoms consistent with coeliac disease. Which one of the following tests should be used first-line when screening patients for coeliac disease?

- A. Anti-casein antibodies
- B. Tissue transglutaminase antibodies
- C. Anti-gliadin antibodies
- D. Xylose absorption test
- E. Anti-endomyseal antibodies

Question 87 of 142

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Coeliac disease - tissue transglutaminase antibodies first-line test

Tissue transglutaminase antibodies are recommended as the first-line serological test according to NICE.

Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

Immunology

- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

Jejunal biopsy

- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

Question 88 of 142

A 36-year-old man presents with dyspepsia. No alarm symptoms are present. This is his first episode and he has no significant medical history of note. A test-and-treat strategy is agreed upon. What is the most appropriate investigation to test for *Helicobacter pylori*?

- A. Gastric biopsy
- B. CLO test (rapid urease test)
- C. Stool culture
- D. Hydrogen breath test
- E. 13C-urea breath test

Question 88 of 142

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- B. CLO test (rapid urease test)
- C. Stool culture
- D. Hydrogen breath test
- ✓ E. 13C-urea breath test

The urea breath test is highly sensitive, specific and non-invasive. There is no indication for an endoscopy. Stool antigen, rather than culture, is an alternative.

***Helicobacter pylori*: tests**

Urea breath test
- patients consume a drink containing carbon isotope 13 (13C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of 13C CO2
- sensitivity 95-98%, specificity 97-98%

Rapid urease test (e.g. CLO test)
- biopsy sample is mixed with urea and pH indicator
- colour change if H pylori urease activity
- sensitivity 90-95%, specificity 95-98%

Serum antibody
- remains positive after eradication
- sensitivity 85%, specificity 80%

Culture of gastric biopsy
- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

Gastric biopsy
- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

Stool antigen test
- sensitivity 90%, specificity 95%

Question 89 of 142

A 34-year-old woman with a history of alcohol excess is admitted with abdominal swelling to the Acute Medical Unit. A diagnosis of ascites secondary to liver cirrhosis is made and paracentesis is performed. The serum creatinine on admission is 95 µmol/l. Ten days after admission urine output decreases significantly and blood tests reveal:

Na^+	129 mmol/l
K^+	3.7 mmol/l
Urea	14.2 mmol/l
Creatinine	221 µmol/l

Albumin is given to correct suspected hypovolaemia. What is the most appropriate further management?

- A. Octreotide
- B. Propranolol
- C. Terlipressin
- D. Acetylcysteine
- E. Dopamine

Question 89 of 142

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- B. Propranolol
- ✓ C. Terlipressin
- D. Acetylcysteine
- E. Dopamine

This patient has developed hepatorenal syndrome

Hepatorenal syndrome: management

The management of hepatorenal syndrome (HRS) is notoriously difficult. The ideal treatment is liver transplantation but patients are often too unwell to have surgery and there is a shortage of donors

Hepatorenal syndrome has been categorized into two types:

Type 1 HRS	Type 2 HRS
• Rapidly progressive • Doubling of serum creatinine to > 221 µmol/L or a halving of the creatinine clearance to less than 20 ml/min over a period of less than 2 weeks • Very poor prognosis	• Slowly progressive • Prognosis poor, but patients may live for longer

Management options

- vasopressin analogues, for example terlipressin, have a growing evidence base supporting their use. They work by causing vasoconstriction of the splanchnic circulation
- volume expansion with 20% albumin
- transjugular intrahepatic portosystemic shunt

Question 90 of 142

Which one of the following is least useful in assessing the severity of a patient with liver cirrhosis?

- A. ALT
- B. Prothrombin time
- C. Bilirubin
- D. The presence of ascites
- E. The presence of encephalopathy

Question 90 of 142

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- E. The presence of encephalopathy

Child-Pugh classification of liver cirrhosis

The Child-Pugh classification is a scoring system to assess the severity of liver cirrhosis

Score	**1**	**2**	**3**
Bilirubin (µmol/l)	<34	34-50	>50
Albumin (g/l)	>35	28-35	<28
Prothrombin time, prolonged by (s)	<4	4-6	>6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

Summation of the scores allows the severity to be graded either A, B or C:

- < 7 = A
- 7-9 = B
- > 9 = C

Question 91 of 142

Which one of the following is least associated with hepatosplenomegaly?

- A. Glandular fever
- B. Chronic myeloid leukaemia
- C. Alcoholic liver disease
- D. Amyloidosis
- E. Infective endocarditis

Question 91 of 142

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- B. Chronic myeloid leukaemia
- C. Alcoholic liver disease
- D. Amyloidosis
- ✓ E. Infective endocarditis

Infective endocarditis normally causes an isolated splenomegaly. Theoretically severe infective endocarditis may cause right heart failure and hence hepatomegaly but this would be unusual

Hepatosplenomegaly

Causes of hepatosplenomegaly

- chronic liver disease* with portal hypertension
- infections: glandular fever, malaria, hepatitis
- lymphoproliferative disorders
- myeloproliferative disorders e.g. CML
- amyloidosis

*the latter stages of cirrhosis are associated with a small liver

Question 92 of 142

Which of the following conditions is least associated with *Helicobacter pylori*?

- A. Gastric carcinoma
- B. B cell lymphoma of MALT tissue
- C. Gastro-oesophageal reflux disease
- D. Atrophic gastritis
- E. Peptic ulcer disease

Question 92 of 142

Which of the following conditions is least associated with *Helicobacter pylori*?

- A. Gastric carcinoma
- B. B cell lymphoma of MALT tissue
- ✓ C. Gastro-oesophageal reflux disease
- D. Atrophic gastritis
- E. Peptic ulcer disease

Helicobacter pylori

Helicobacter pylori is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

Associations
- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of
- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

Question 93 of 142

Which one of the following is least associated with the development of colorectal cancer in patients with ulcerative colitis?

- A. Unremitting disease
- B. Disease duration > 10 years
- C. Onset before 15 years old
- D. Poor compliance to treatment
- E. Disease confined to the rectum

Question 93 of 142

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Ulcerative colitis: colorectal cancer

Overview
- risk of colorectal cancer is 10-20 times that of general population
- the increased risk mainly related to chronic infection
- worse prognosis than patients without ulcerative colitis (partly due to delayed diagnosis)
- lesions may be multifocal

Factors increasing risk of cancer
- disease duration > 10 years
- patients with pancolitis
- onset before 15 years old
- unremitting disease
- poor compliance to treatment

Question 94 of 142

A 39-year-old man with a history of alcohol excess presents to the Emergency Department with a 2 day history of severe epigastric pain. His amylase is found to be 1260. What is the best marker of severity?

- A. CRP
- B. Amylase (on admission)
- C. Pain scores
- D. Lipase (on admission)
- E. Number of similar previous admissions

Question 94 of 142

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- D. Lipase (on admission)
- E. Number of similar previous admissions

CRP is now a widely used marker of severity in acute pancreatitis. Other methods which have to correlate with prognosis include the Ranson criteria and APACHE II score (Acute Physiology And Chronic Health Evaluation)

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 95 of 142

A 45-year-old man with a history of alcoholic liver disease presents with abdominal distension. Examination reveals tense ascites which is drained. What is the appropriate type of diuretic to help prevent reaccumulation of ascites?

- A. Aldosterone antagonist
- B. Loop diuretic
- C. Thiazide diuretic
- D. Osmotic diuretic
- E. Carbonic anhydrase inhibitor

Question 95 of 142

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- C. Thiazide diuretic
- D. Osmotic diuretic
- E. Carbonic anhydrase inhibitor

Aldosterone antagonists such as spironolactone are used in high doses to help prevent the formation of ascites in patients with chronic liver disease. A loop diuretic may need to be added in patients who don't respond

Spironolactone

Spironolactone is an aldosterone antagonist which acts act in the distal convoluted tubule

Indications
- ascites: patients with cirrhosis develop a secondary hyperaldosteronism. Relatively large doses such as 100 or 200mg are often used
- heart failure (see RALES study below)
- nephrotic syndrome
- Conn's syndrome

Adverse effects
- hyperkalaemia
- gynaecomastia

RALES
- NYHA III + IV, patients already taking ACE inhibitor
- low dose spironolactone reduces all cause mortality

Question 96 of 142

A 54-year-old man who is known to have gastric cancer is reviewed in clinic. He asks you about a rash he has developed. Which of the following skin disorders is most associated with gastric cancer?

- A. Erythema gyratum repens
- B. Necrolytic migratory erythema
- C. Sweet's syndrome
- D. Acquired ichthyosis
- E. Acanthosis nigricans

Question 96 of 142

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- ✓ E. Acanthosis nigricans

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 97 of 142

A 59-year-old woman is admitted to the Emergency Department with a productive cough and pyrexia. She is usually fit and well but is undergoing investigation for dysphagia. This has been present for the past 3 months and affects both food and drink. A chest x-ray shows an air-fluid level behind a normal-sized heart. What is the most likely diagnosis?

- A. Massive pericardial effusion
- B. Tuberculosis
- C. Achalasia
- D. Pharyngeal pouch
- E. Hiatus hernia

Question 97 of 142

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- ✓ C. Achalasia
- D. Pharyngeal pouch
- E. Hiatus hernia

A retrocardiac air-fluid level is sometimes seen in patients with achalasia

Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is more common in women

Clinical features
- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

Investigations
- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

Treatment
- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Question 98 of 142

A 29-year-old man presents with a nine day history of watery diarrhoea that developed one week after returning from India. He had travelled around northern India for two months. On examination he is apyrexial and his abdomen is soft and non-tender. What is the most likely causative organism?

- A. Amoebiasis
- B. Giardiasis
- C. *Campylobacter*
- D. *Shigella*
- E. *Salmonella*

Question 98 of 142

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- D. *Shigella*
- E. *Salmonella*

The incubation period and prolonged, non-bloody diarrhoea point towards giardiasis

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 99 of 142

A 59-year-old female with a history of hypothyroidism presents with fatigue. Blood tests reveal the following:

Hb 9.4 g/dl

MCV 121 fl

Plt 156 * 10^9/l

WBC 4.3 * 10^9/l

What is the most appropriate investigation to perform next?

- A. Antral biopsy
- B. Bone marrow biopsy
- C. Lactate dehydrogenase
- D. Intrinsic factor antibodies
- E. Barium enema

Question 99 of 142

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- C. Lactate dehydrogenase
- ✓ D. Intrinsic factor antibodies
- E. Barium enema

Macrocytic anaemia in a patient with a history of hypothyroidism points towards a diagnosis of pernicious anaemia

Pernicious anaemia: investigation

Investigation
- anti gastric parietal cell antibodies in 90% (but low specificity)
- anti intrinsic factor antibodies in 50% (specific for pernicious anaemia)
- macrocytic anaemia
- low WCC and platelets
- LDH may be raised due to ineffective erythropoiesis
- also low serum B12, hypersegmented polymorphs on film, megaloblasts in marrow
- Schilling test

Schilling test
- radiolabelled B12 given on two occasions
- first on its own
- second with oral IF
- urine B12 levels measured

Question 100 of 142

You are asked to review a 24-year-old man who has been admitted with an exacerbation of Crohn's disease. Despite prednisolone and mesalazine therapy for the past 3 weeks he is still passing 6-7 watery stools per day. He has lost a considerable amount of weight during this period. On examination he is apyrexial, haemodynamically stable and his abdomen is soft and non-tender. What is the most appropriate next step?

- A. Metronidazole
- B. Infliximab
- C. Methotrexate
- D. Azathioprine
- E. Surgery

Question 100 of 142

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- ✓ D. Azathioprine
- E. Surgery

Crohn's disease: management

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

General points
- patients should be strongly advised to stop smoking
- some studies suggest an increased risk of relapse secondary to NSAIDs and the combined oral contraceptive pill but the evidence is patchy

Active disease
- mesalazine: whilst evidence base is limited widely used in active disease
- steroids (oral, topical or intravenous)
- azathioprine is used as a second-line treatment in active disease
- methotrexate is used in patients intolerant of azathioprine or refractory disease. Usually given intramuscularly
- infliximab is useful in refractory disease and fistulating Crohn's. Patients typically continue on azathioprine or methotrexate

Perianal disease
- metronidazole is first-line

Enteral feeding with an elemental diet
- may be used in addition to or instead of other measures to induce remission

Surgery
- around 80% of patients with Crohn's disease will eventually have surgery

Question 101 of 142

A 22-year-old man is investigated for weight loss and diarrhoea. A rectal biopsy is taken and reported as follows:

Deep inflammatory infiltrate from the mucosa to the lamina propria
Numerous granulomata noted

What is the most likely diagnosis?

- A. Crohn's disease
- B. Rectal carcinoma-in-situ
- C. Tuberculosis
- D. Laxative abuse
- E. Ulcerative colitis

Question 101 of 142

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- B. Rectal carcinoma-in-situ
- C. Tuberculosis
- D. Laxative abuse
- E. Ulcerative colitis

Inflammation in ulcerative colitis is usually limited to the mucosa and submucosa.

Crohn's disease: investigation

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

Bloods
- C-reactive protein correlates well with disease activity

Endoscopy
- colonoscopy is the investigation of choice
- features suggest of Crohn's include deep ulcers, skip lesions

Histology
- inflammation in all layers from mucosa to serosa
- goblet cells
- granulomas

Small bowel enema
- high sensitivity and specificity for examination of the terminal ileum
- strictures: 'Kantor's string sign'
- proximal bowel dilation
- 'rose thorn' ulcers
- fistulae

Question 102 of 142

A 54-year-old man develops central abdominal pain a few hours after having an Endoscopic Retrograde Cholangiopancreatography (ERCP) performed. Investigations reveal the following:

Amylase 545 u/dl

Erect chest x-ray Normal heart and lungs. No free air noted

What is the most appropriate management?

- A. Repeat ERCP + analgesia
- B. Reassure normal + analgesia
- C. Intravenous ciprofloxacin + analgesia
- D. Surgical opinion + analgesia
- E. Intravenous fluids + analgesia

Question 102 of 142

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- D. Surgical opinion + analgesia
- ✓ E. Intravenous fluids + analgesia

This patient has developed acute pancreatitis following ERCP and should be treated with intravenous fluids and analgesia.

Quinolones have not been shown to be beneficial in acute pancreatitis.

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 103 of 142

A patient who was an intravenous drug user in the 1990s asks for a hepatitis C test. What is the most appropriate action?

- A. Refer him for pre-test counselling to discuss the pros and cons of testing
- B. Advise him that no accurate test is currently available but that he should undertake normal precautions
- C. Arrange an anti-HCV antibody test
- D. Arrange a HCV RNA test
- E. Refer him to gastroenterology for a liver biopsy

Question 103 of 142

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- ✓ C. Arrange an anti-HCV antibody test
- D. Arrange a HCV RNA test
- E. Refer him to gastroenterology for a liver biopsy

HCV RNA tests are normally only ordered following a positive antibody test.

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 104 of 142

A 30-year-old woman presents with abdominal pain that is associated with alternating diarrhoea and constipation. Which one of the following symptoms is least consistent with a diagnosis of irritable bowel syndrome?

- A. Feeling of incomplete stool evacuation
- B. Waking at night due to the pain
- C. Abdominal bloating
- D. Faecal urgency
- E. Passage of mucous with stool

Question 104 of 142

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✓ B. Waking at night due to the pain

C. Abdominal bloating

D. Faecal urgency

E. Passage of mucous with stool

Pain which wakes a patient at night is not a feature that would be expected in irritable bowel syndrome.

Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Question 105 of 142

A 23-year-old female with a history of diarrhoea and weight loss has a colonoscopy to investigate her symptoms. A biopsy is taken and reported as follows:

Pigment laden macrophages

What is the most likely diagnosis?

- A. Intestinal melanoma
- B. Haemochromatosis
- C. Ulcerative colitis
- D. Laxative abuse
- E. Colorectal cancer

Question 105 of 142

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- C. Ulcerative colitis
- ✓ D. Laxative abuse
- E. Colorectal cancer

Diarrhoea - biospy shows pigment laden macrophages = laxative abuse

Melanosis coli

Melanosis coli is a disorder of pigmentation of the bowel wall. Histology demonstrates pigment-laden macrophages

It is associated with laxative abuse, especially anthraquinone compounds such as senna

Question 106 of 142

Which one of the following is not associated with non-alcoholic steatohepatitis?

- A. Hyperlipidaemia
- B. Obesity
- C. Sudden weight loss or starvation
- D. Jejunoileal bypass
- E. Type 1 diabetes mellitus

Question 106 of 142

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- A. Hyperlipidaemia
- B. Obesity
- C. Sudden weight loss or starvation
- D. Jejunoileal bypass
- ✓ E. Type 1 diabetes mellitus

Obese T2DM with abnormal LFTs - ? non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and though to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

Question 107 of 142

A 25-year-old man presents with bloating and alteration in his bowel habit. He has been keeping a food diary and feels his symptoms may be secondary to a food allergy. Blood tests show a normal full blood count, ESR and thyroid function tests. Anti-endomysial antibodies are negative. What is the most suitable test to investigate possible food allergy?

- A. Total IgE levels
- B. Hair analysis
- C. Skin patch testing
- D. Skin prick test
- E. Jejunal biopsy

Question 107 of 142

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- C. Skin patch testing
- ✓ D. Skin prick test
- E. Jejunal biopsy

Skin prick testing would be first-line here as it is inexpensive and a large number of allergens can be investigated

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours

Question 108 of 142

A 31-year-old woman who initially presented with abdominal pain and constipation is diagnosed with irritable bowel syndrome. Which one of the following bits of dietary advice is it least suitable to give?

- A. Avoid missing meals
- B. Restrict tea and coffee to 3 cups per day
- C. Increase the intake of fibre such as bran and wholemeal bread
- D. Reduce intake of alcohol
- E. Drink at least 8 cups of fluid per day

Question 108 of 142

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- B. Restrict tea and coffee to 3 cups per day
- ✓ C. Increase the intake of fibre such as bran and wholemeal bread
- D. Reduce intake of alcohol
- E. Drink at least 8 cups of fluid per day

Insoluble sources of fibre such as bran and wholemeal should be avoided in IBS

Irritable bowel syndrome: management

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom
- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment
- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options
- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

General dietary advice
- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

Question 109 of 142

What percentage of cases of chronic pancreatitis in the UK are due to alcohol excess?

- A. 35%
- B. 50%
- C. 65%
- D. 80%
- E. 95%

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Chronic pancreatitis

Chronic pancreatitis is an inflammatory condition which can ultimately affect both the exocrine and endocrine functions of the pancreas. Around 80% of cases are due to alcohol excess with up to 20% of cases being unexplained

Features

- pain is typically worse 15 to 30 minutes following a meal
- steatorrhoea: symptoms of pancreatic insufficiency usually develop between 5 and 25 years after the onset of pain
- diabetes mellitus develops in the majority of patients. It typically occurs more than 20 years after symptom begin

Investigation

- abdominal x-ray shows pancreatic calcification in 30% of cases
- CT is more sensitive at detecting pancreatic calcification
- functional tests: pancreolauryl and Lundh tests may be used to assess exocrine function if imaging inconclusive

Management

- pancreatic enzyme supplements
- analgesia
- antioxidants: limited evidence base - one study suggests benefit in early disease

Question 110 of 142

Autoimmune hepatitis is most characteristically associated with elevated levels of which one of the following immunoglobulins?

- A. IgE
- B. IgA
- C. IgD
- D. IgM
- E. IgG

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Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	**Type II**	**Type III**
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA) Affects both adults and children	Anti-liver/kidney microsomal type 1 antibodies (LKM1) Affects children only	Soluble liver-kidney antigen Affects adults in middle-age

Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Question 111 of 142

Which one of the following features is least associated with ulcerative colitis?

- A. Inflammatory cell infiltrate in the lamina propria
- B. Pseudopolyps
- C. Non-caseating granulomas
- D. Depletion of goblet cells
- E. Inflammation confined to the mucosa and submucosa

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IBD: histology

This histological differences between ulcerative colitis and Crohn's are summarised below:

Ulcerative colitis

- inflammation in mucosa and submucosa only (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

Crohn's

- inflammation occurs in all layers, down to the serosa. This predisposes to strictures, fistulas and adhesions
- oedema of mucosa and submucosa, combined with deep fissured ulcers ('rose-thorn') leads to a 'cobblestone' pattern
- lymphoid aggregates
- non-caseating granulomas

Question 112 of 142

A 70-year-old man who is known to have atrial fibrillation presents with abdominal pain and rectal bleeding. A diagnosis of ischaemic colitis is suspected. Which part of the colon is most likely to be affected?

- A. Hepatic flexure
- B. Descending colon
- C. Splenic flexure
- D. Ascending colon
- E. Rectum

Question 112 of 142

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- D. Ascending colon
- E. Rectum

Mesenteric ischaemia

Mesenteric ischaemia is primarily caused by arterial embolism resulting in infarction of the colon. It is more likely to occur in areas such as the splenic flexure that are located at the borders of the territory supplied by the superior and inferior mesenteric arteries.

Predisposing factors
- increasing age
- atrial fibrillation
- other causes of emboli: endocarditis
- cardiovascular disease risk factors: smoking, hypertension, diabetes

Features
- abdominal pain
- rectal bleeding
- diarrhoea
- fever
- bloods typically show an elevated WBC associated with acidosis

Management
- supportive care
- laparotomy and bowel resection

Question 113 of 142

A 23-year-old who is 10 weeks pregnant is reviewed by the midwife at the booking visit. This is her first pregnancy and she is well apart from some sickness which is worse in the morning and a generalised pruritus. Bloods tests including the full blood count, hepatitis B, C and HIV serology are normal. A slight yellow tinge of her sclera is noticed and liver function tests are ordered:

Bilirubin 42 µmol/L

ALP 160 U/L

ALT 25 U/L

Albumin 34 g/L

What is the most likely diagnosis?

- A. Gilbert's syndrome
- B. Gallstones
- C. Acute fatty liver
- D. Intrahepatic cholestasis of pregnancy
- E. Primary biliary cirrhosis

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Morning sickness and pruritus are common in pregnant women. Intrahepatic cholestasis of pregnancy would not occur in the first trimester. An ALP of 160 U/l is normal in a pregnant woman leaving the only abnormal result being the raised bilirubin (which usually falls in pregnancy). The most likely diagnosis is therefore Gilbert's syndrome.

Gilbert's syndrome

Gilbert's syndrome is an autosomal recessive* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

Features

- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

Investigation and management

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

*the exact mode of inheritance is still a matter of debate

Question 114 of 142

Which one of the following patients would it be most suitable to offer a screening test for coeliac disease to?

- A. A patient who is 'tired all the time'
- B. A patient with rheumatoid arthritis
- C. A patient who has a family history of inflammatory bowel disease
- D. A patient with type 2 diabetes mellitus
- E. A patient who develops erythema nodosum

Question 114 of 142

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Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
? Chronic or intermittent diarrhoea ? Failure to thrive or faltering growth (in children) ? Persistent or unexplained gastrointestinal symptoms including nausea and vomiting ? Prolonged fatigue ('tired all the time') ? Recurrent abdominal pain, cramping or distension ? Sudden or unexpected weight loss ? Unexplained iron-deficiency anaemia, or other unspecified anaemia	? Autoimmune thyroid disease ? Dermatitis herpetiformis ? Irritable bowel syndrome ? Type 1 diabetes ? First-degree relatives (parents, siblings or children) with coeliac disease

Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

Question 115 of 142

A 44-year-old man with alcoholic liver disease is admitted with pyrexia. He has been unwell for the past three days and has multiple previous admissions before with variceal bleeding. Examination shows multiple stigmata of chronic liver disease, ascites and jaundice. Paracentesis is performed with the following results:

Neutrophils 487 cells/ul

What is the most appropriate treatment?

- A. Therapeutic abdominal washout
- B. Intravenous vancomycin + metronidazole
- C. Intravenous cefotaxime
- D. Insert an ascitic drain
- E. Intravenous ciprofloxacin

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Spontaneous bacterial peritonitis - intravenous cefotaxime

Please see the British Society of Gastroenterology guidelines for more details.

Spontaneous bacterial peritonitis

Spontaneous bacterial peritonitis (SBP) is a form of peritonitis usually seen in patients with ascites secondary to liver cirrhosis.

Diagnosis
- paracentesis: neutrophil count > 250 cells/ul

Management
- intravenous cefotaxime is usually given
- patients who have had an episode of SBP should be on prophylactic antibiotics

Alcoholic liver disease is a marker of poor prognosis in SBP.

Question 116 of 142

A 26-year-old man with a history of speech and behavioural problems presents with lethargy. On examination he is noted to have jaundiced sclera. What is the most likely diagnosis?

- A. Wiskott-Aldrich syndrome
- B. Haemochromatosis
- C. Friedreich's ataxia
- D. Wilson's disease
- E. Acute intermittent porphyria

Question 116 of 142

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Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Question 117 of 142

The action of which one of the following brush border enzymes results in the formation of glucose and galactose?

- A. Dipeptidase
- B. A-dextrinase
- C. Maltase
- D. Lactase
- E. Sucrase

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Brush border enzymes:
- maltase: glucose + glucose
- sucrase: glucose + fructose
- lactase: glucose + galactose

Gastrointestinal physiology: enzymes

Amylase is present in saliva and pancreatic secretions. It breaks starch down into sugar

The following brush border enzymes are involved in the breakdown of carbohydrates:
- maltase: cleaves disaccharide maltose to glucose + glucose
- sucrase: cleaves sucrose to fructose and glucose
- lactase: cleaves disaccharide lactose to glucose + galactose

Question 118 of 142

A 18-year-old male is admitted following after deliberately ingesting 40 grams of paracetamol. Twenty-four hours after admission he is reassessed with a view to liver transplantation. Of the following, which one would most strongly indicate the need for a liver transplant?

- A. CRP 306
- B. Arterial pH 7.25
- C. Creatinine 267 µmol/l
- D. Grade IV encephalopathy
- E. INR 5.7

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The arterial pH is the single most important factor. The creatinine, encephalopathy grade and INR must all be grossly abnormal otherwise

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300 µmol/l
- grade III or IV encephalopathy

Question 119 of 142

A 39-year-old man with a history of liver cirrhosis secondary to alcohol excess is admitted with an upper gastrointestinal haemorrhage. He is treated with terlipressin and has an endoscopy with variceal band ligation 6 hours following admission. Which further intervention has been shown to reduce mortality during the acute admission?

- A. IV labetalol to induce hypotension for the first 3 days
- B. Low-molecular weight heparin prophylaxis
- C. Nasogastric tube feeding for the first 3 days
- D. Antibiotic prophylaxis
- E. High-dose proton pump inhibitor therapy

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Antibiotic prophylaxis reduces mortality in cirrhotic patients with gastrointestinal bleeding

Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 120 of 142

A 54-year-old female is admitted one week following a cholecystectomy with profuse diarrhoea. What is the most likely diagnosis?

- A. *Campylobacter*
- B. *E. coli*
- C. *Clostridium difficile*
- D. *Salmonella*
- E. *Staphylococcus aureus*

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Clostridium difficile is the most likely cause as the patient would have been given broad-spectrum antibiotics at the time of the operation

Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

Question 121 of 142

A 28-year-old woman is diagnosed with constipation predominant irritable bowel syndrome. She occasionally experiences spasms of pain in the left iliac fossa. Which one of the following is least likely to help her symptoms?

- A. Mebeverine
- B. Ispaghula
- C. Methylcellulose
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NICE recommend avoiding lactulose in the management of IBS

Irritable bowel syndrome: management

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First-line pharmacological treatment - according to predominant symptom
- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

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Other management options
- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

General dietary advice
- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
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- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

Question 122 of 142

What percentage of patients with ulcerative colitis have primary sclerosing cholangitis?

- A. 0.5%
- B. 1%
- C. 2%
- D. 4%
- E. 10%

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4% of patients with UC have PSC, 80% of patients with PSC have UC

Primary sclerosing cholangitis

Primary sclerosing cholangitis is a biliary disease of unknown aetiology characterised by inflammation and fibrosis of intra and extra-hepatic bile ducts

Associations
- ulcerative colitis: 4% of patients with UC have PSC, 80% of patients with PSC have UC
- Crohn's (much less common association than UC)
- HIV

Features
- cholestasis

Investigation
- ERCP is the standard diagnostic tool, showing multiple biliary strictures giving a 'beaded' appearance
- ANCA may be positive
- there is a limited role for liver biopsy, which may show fibrous, obliterative cholangitis often described as 'onion skin'

Complications
- cholangiocarcinoma (in 10%)
- increased risk of colorectal cancer

Question 123 of 142

A 31-year-old man returns for review. He was diagnosed with an anal fissure around 7 weeks ago and has tried dietary modification, laxatives and topical anaesthetic with little benefit. What is the most appropriate next step?

- A. Oral bisacodyl
- B. Oral calcium channel blocker
- C. Topical steroid
- D. Buccal glyceryl trinitrate prior to defecation
- E. Topical glyceryl trinitrate

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Anal fissure - topical glyceryl trinitrate

Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks)

- dietary advice: high-fibre diet with high fluid intake
- bulk-forming laxatives are first line - if not tolerated then lactulose should be tried
- lubricants such as petroleum jelly may be tried before defecation
- topical anaesthetics
- sitz baths: hip baths in hot water for 2–5 minutes followed by cold water for 1 minute
- topical steroids do not provide significant relief

Management of a chronic anal fissure (> 6 weeks)

- the above techniques should be continued
- topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure
- if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

Question 124 of 142

What percentage of patients who contract the hepatitis C virus will become chronically infected?

- A. 30-35%
- B. 80-85%
- C. 65-70%
- D. 5-10%
- E. 15-20%

Question 124 of 142

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- C. 65-70%
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Hepatitis C - 80-85% become chronically infected

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 125 of 142

Which one of the following is least associated with Crohn's disease?

- A. Fistulae
- B. Kantor's string sign
- C. 'Cobblestone' pattern of mucosa
- D. Crypt abscesses
- E. Involvement of all layers of bowel wall

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- C. 'Cobblestone' pattern of mucosa
- ✓ D. Crypt abscesses
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Crypt abscesses are sometimes seen in Crohn's disease but they are more commonly associated with ulcerative colitis

Crohn's disease: investigation

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

Bloods
- C-reactive protein correlates well with disease activity

Endoscopy
- colonoscopy is the investigation of choice
- features suggest of Crohn's include deep ulcers, skip lesions

Histology
- inflammation in all layers from mucosa to serosa
- goblet cells
- granulomas

Small bowel enema
- high sensitivity and specificity for examination of the terminal ileum
- strictures: 'Kantor's string sign'
- proximal bowel dilation
- 'rose thorn' ulcers
- fistulae

Question 126 of 142

Which one of the following conditions is most associated with angiodysplasia?

- A. Aortic regurgitation
- B. Ventricular septal defect
- C. Aortic stenosis
- D. Hypertrophic obstructive cardiomyopathy
- E. Mitral regurgitation

Question 126 of 142

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- D. Hypertrophic obstructive cardiomyopathy
- E. Mitral regurgitation

Angiodysplasia is associated with aortic stenosis

The association between angiodysplasia and aortic stenosis is thought to be caused by von Willebrand factor (vWF) being proteolysed in the turbulent blood flow around the aortic valve

vWF is most active in vascular beds with high shear stress, such as angiodysplasia, and deficiency of vWF increases the bleeding risk from such lesions

Angiodysplasia

Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia. There is thought to be an association with aortic stenosis, although this is debated.

Diagnosis
- colonoscopy
- mesenteric angiography if acutely bleeding

Management
- endoscopic cautery or argon plasma coagulation
- antifibrinolytics e.g. Tranexamic acid
- oestrogens may also be used

Question 127 of 142

A 29-year-old woman who is 30 weeks pregnant is admitted to the Emergency Department with central abdominal pain. Initial blood tests show the following:
Amylase 1,438 u/dl

What is the most likely cause of this presentation?

- A. Gestational diabetes
- B. HELLP syndrome
- C. Gallstones
- D. Hypertriglyceridaemia-induced pancreatitis
- E. Pre-eclampsia

Question 127 of 142

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- D. Hypertriglyceridaemia-induced pancreatitis
- E. Pre-eclampsia

Pancreatitis occurs in around 1 in 2,000 pregnancies. Most cases of pancreatitis in pregnancy are gallstone related.

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 128 of 142

Which one of the following factors is most responsible for the increased rate of colorectal cancer in patients with ulcerative colitis?

- A. Shared mutation in the HNPCC gene
- B. Chronic inflammation
- C. Increased surveillance with colonoscopy
- D. Increased susceptibility to bacterial gastroenteritis
- E. Prolonged immunosuppression

Question 128 of 142

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- C. Increased surveillance with colonoscopy
- D. Increased susceptibility to bacterial gastroenteritis
- E. Prolonged immunosuppression

Chronic inflammation is an important factor in the development of a number of cancers. An example is hepatocellular carcinoma secondary to viral hepatitis.

Ulcerative colitis: colorectal cancer

Overview
- risk of colorectal cancer is 10-20 times that of general population
- the increased risk mainly related to chronic infection
- worse prognosis than patients without ulcerative colitis (partly due to delayed diagnosis)
- lesions may be multifocal

Factors increasing risk of cancer
- disease duration > 10 years
- patients with pancolitis
- onset before 15 years old
- unremitting disease
- poor compliance to treatment

Question 129 of 142

Which one of the following adverse effects is least associated with sulfasalazine?

- A. Male infertility
- B. Skin rashes
- C. Visual disturbance
- D. Diarrhoea
- E. Agranulocytosis

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Aminosalicylate drugs

5-aminosalicyclic acid (5-ASA) is released in the colon and is not absorbed. It acts locally as an anti-inflammatory. The mechanism of action is not fully understood but 5-ASA may inhibit prostaglandin synthesis

Sulphasalazine
- a combination of sulphapyridine (a sulphonamide) and 5-ASA
- many side-effects are due to the sulphapyridine moiety: rashes, oligospermia, headache, Heinz body anaemia
- other side-effects are common to 5-ASA drugs (see mesalazine)

Mesalazine
- a delayed release form of 5-ASA
- sulphapyridine side-effects seen in patients taking sulphasalazine are avoided
- mesalazine is still however associated with side-effects such as GI upset, headache, agranulocytosis, pancreatitis*, interstitial nephritis

Olsalazine
- two molecules of 5-ASA linked by a diazo bond, which is broken by colonic bacteria

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 130 of 142

What percentage of patients with chronic hepatitis C will develop liver cirrhosis over a 20-30 year period?

- A. 5-10%
- B. 10-20%
- C. 20-30%
- D. 40-50%
- E. 60-70%

Question 130 of 142

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- A. 5-10%
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- ✓ C. 20-30%
- D. 40-50%
- E. 60-70%

Liver cirrhosis will develop in around 20-30% of patients over 20-30 years

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 131 of 142

A 27-year-old female presents with alternating loose and hard stools associated with abdominal discomfort and bloating. Which one of the following is it most important to do before making a positive diagnosis of irritable bowel syndrome?

- A. Arrange ultrasound abdomen
- B. Flexible sigmoidoscopy
- C. Ask about family history of ovarian cancer
- D. Use a standardised screening tool for depression
- E. Perform thyroid function tests

Question 131 of 142

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- E. Perform thyroid function tests

Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Question 132 of 142

A 72-year-old female is admitted with diarrhoea to the acute medical unit. A sigmoidoscopy is performed which shows multiple white plaques adhered to the gastrointestinal mucosa. What is the most likely diagnosis?

- A. Crohn's disease
- B. Ulcerative colitis
- C. Ischaemic colitis
- D. Pseudomembranous colitis
- E. Colorectal cancer

Question 132 of 142

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- C. Ischaemic colitis
- ✓ D. Pseudomembranous colitis
- E. Colorectal cancer

Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

Features
- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management
- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

Question 133 of 142

A 68-year-old woman comes back to rheumatology clinic for review. Two weeks ago she was referred with pain in her left knee and the clinical impression at the time was osteoarthritis. As her pain was not responding to paracetamol she was commenced on diclofenac 50mg tds and lansoprazole 30mg od. Shortly afterwards she developed some indigestion which seems to resolve if she skips the diclofenac dose. She is otherwise asymptomatic and got good pain relief from diclofenac. Clinical examination is normal. What is the most appropriate action?

- A. 13C-urea breath test
- B. Stop diclofenac, continue lansoprazole + review in 1 week
- C. Switch diclofenac to ibuprofen, continue lansoprazole
- D. Urgent endoscopy
- E. Admit

Question 133 of 142

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- E. Admit

When NICE first published their dyspepsia guidelines there was a policy of referral for any older patients with new onset dyspepsia. This led to a deluge of referrals and amended guidelines were published in 2004. This modified approach seems to be supported by a large trial demonstrating a minimal effect on mortality of routine referral.

This question gives an example of a scenario where NICE would recommend not initially referring a patient when there is an obvious trigger (NSAID use).

Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')

This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month*
- 4. 'Test and treat' using carbon-13 urea breath test

*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Question 134 of 142

Which one of the following is most associated with oesophageal cancer?

- A. Coeliac disease
- B. Hypothyroidism
- C. Crohn's disease
- D. Addison's disease
- E. Ulcerative colitis

Question 134 of 142

Which one of the following is most associated with oesophageal cancer?

- ✓ A. Coeliac disease
- B. Hypothyroidism
- C. Crohn's disease
- D. Addison's disease
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Oesophageal cancer

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

Risk factors

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

Question 135 of 142

Which one of the following statements regarding hepatocellular carcinoma is correct?

- A. Diabetes mellitus is a risk factor
- B. Screening has not been shown to be effective
- C. Bevacizumab may be used for advanced cases
- D. The incidence is significantly higher in women
- E. Alcohol excess is the most common underlying cause worldwide

Question 135 of 142

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Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

*Wilson's disease is an exception

Question 136 of 142

Which one of the following is not a contraindication to performing a percutaneous liver biopsy?

- A. INR 2.6
- B. Viral hepatitis
- C. Hydatid cyst
- D. Uncooperative patient
- E. Haemoangioma

Question 136 of 142

Which one of the following is not a contraindication to performing a percutaneous liver biopsy?

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- ✓ B. Viral hepatitis
- C. Hydatid cyst
- D. Uncooperative patient
- E. Haemoangioma

Liver biopsy

Contraindications to percutaneous liver biopsy

- deranged clotting (e.g. INR > 1.4)
- low platelets (e.g. < 60 * 10^9/l)
- anaemia
- bile duct obstruction
- hydatid cyst
- haemoangioma
- uncooperative patient
- ascites

Question 137 of 142

Which one of the following statements regarding hepatitis B and pregnancy is correct?

- A. Without intervention the vertical transmission rate is around 3%
- B. Only at risk groups should be screened for hepatitis B during pregnancy
- C. Around 30% of mothers with hepatitis B develop pre-eclampsia
- D. It is safe for a mother with hepatitis B to breastfeed her newborn
- E. All pregnant women with hepatitis B should take oral ribavirin in the last trimester of pregnancy

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- E. All pregnant women with hepatitis B should take oral ribavirin in the last trimester of pregnancy

Without intervention the vertical transmission rate is around 20%, which increases to 90% if the woman is positive for HBeAg.

Hepatitis B and pregnancy

Basics

- all pregnant women are offered screening for hepatitis B
- babies born to mothers who are chronically infected with hepatitis B or to mothers who've had acute hepatitis B during pregnancy should receive a complete course of vaccination + hepatitis B immunoglobulin
- studies are currently evaluating the role of oral antiviral treatment (e.g. Lamivudine) in the latter part of pregnancy
- there is little evidence to suggest caesarean section reduces vertical transmission rates
- hepatitis B cannot be transmitted via breastfeeding (in contrast to HIV)

Question 138 of 142

Which one of the following is characteristic of Crohn's disease? (in comparison to ulcerative colitis)

- A. Loss of haustrations on barium enema
- B. Increased goblet cells
- C. Crypt abscesses
- D. Abdominal pain in the left lower quadrant
- E. Primary sclerosing cholangitis

Question 138 of 142

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Inflammatory bowel disease: key differences

The two main types of inflammatory bowel disease are Crohn's disease and Ulcerative colitis. They have many similarities in terms of presenting symptoms, investigation findings and management options. There are however some key differences which are highlighted in table below:

	Crohn's disease (CD)	**Ulcerative colitis (UC)**
Features	Diarrhoea usually non-bloody Weight loss more prominent Upper gastrointestinal symptoms, mouth ulcers, perianal disease Abdominal mass palpable in the right iliac fossa	Bloody diarrhoea more common Abdominal pain in the left lower quadrant Tenesmus
Extra-intestinal		Primary sclerosing cholangitis more common
Complications	Obstruction, fistula, colorectal cancer	Risk of colorectal cancer high in UC than CD
Pathology	Lesions may be seen anywhere from the mouth to anus Skip lesions may be present	Inflammation always starts at rectum and never spreads beyond ileocaecal valve Continuous disease
Histology	Inflammation in all layers from mucosa to serosa • increased goblet cells • granulomas	No inflammation beyond submucosa (unless fulminant disease) - inflammatory cell infiltrate in lamina propria • neutrophils migrate through the walls of glands to form crypt abscesses • depletion of goblet cells and mucin from gland epithelium • granulomas are infrequent
Endoscopy	Deep ulcers, skip lesions	Widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
Radiology	Small bowel enema • high sensitivity and specificity for examination of the terminal ileum • strictures: 'Kantor's string sign' • proximal bowel dilation • 'rose thorn' ulcers • fistulae	Barium enema • loss of haustrations • superficial ulceration, 'pseudopolyps' • long standing disease: colon is narrow and short -'drainpipe colon'

Question 139 of 142

What are the most common type of antibodies seen in pernicious anaemia?

- A. Vitamin B12 receptor antibodies
- B. Gastric parietal cell antibodies
- C. Jejunal mucosa antibodies
- D. Intrinsic factor antibodies
- E. Vitamin B12 antibodies

Question 139 of 142

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- D. Intrinsic factor antibodies
- E. Vitamin B12 antibodies

Pernicious anaemia: investigation

Investigation
- anti gastric parietal cell antibodies in 90% (but low specificity)
- anti intrinsic factor antibodies in 50% (specific for pernicious anaemia)
- macrocytic anaemia
- low WCC and platelets
- LDH may be raised due to ineffective erythropoiesis
- also low serum B12, hypersegmented polymorphs on film, megaloblasts in marrow
- Schilling test

Schilling test
- radiolabelled B12 given on two occasions
- first on its own
- second with oral IF
- urine B12 levels measured

Question 140 of 142

Which one of the following is least associated with primary biliary cirrhosis?

- A. Ulcerative colitis
- B. Systemic sclerosis
- C. Thyroid disease
- D. Sjogren's syndrome
- E. Rheumatoid arthritis

Question 140 of 142

Which one of the following is least associated with primary biliary cirrhosis?

- ✓ A. Ulcerative colitis
- B. Systemic sclerosis
- C. Thyroid disease
- D. Sjogren's syndrome
- E. Rheumatoid arthritis

Whilst ulcerative colitis is associated with primary biliary cirrhosis this is less common than the other four options

Primary sclerosing cholangitis is strongly associated with ulcerative colitis

Primary biliary cirrhosis

Primary biliary cirrhosis is a chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

Associations

- Sjogren's syndrome (seen in up to 80% of patients)
- rheumatoid arthritis
- systemic sclerosis
- thyroid disease

Diagnosis

- anti-mitochondrial antibodies (AMA) M2 subtype are present in 98% of patients and are highly specific
- smooth muscle antibodies in 30% of patients
- raised serum IgM

Management

- pruritus: cholestyramine
- fat-soluble vitamin supplementation
- ursodeoxycholic acid
- liver transplantation e.g. if bilirubin > 100 (PBC is a major indication) - recurrence in graft can occur but is not usually a problem

Question 141 of 142

Which one of the following is not a feature of Peutz-Jeghers syndrome?

- A. Intestinal obstruction
- B. Pigmented lesions on palms
- C. More than 10-fold increased risk of gastrointestinal malignancy
- D. Osteomas
- E. Iron-deficiency anaemia

Question 141 of 142

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- ✓ D. Osteomas
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Osteomas are a feature of Gardner's syndrome, a variant of familial adenomatous polyposis

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 142 of 142

Which one of the following is most strongly associated with coeliac disease?

- A. HLA A5
- B. HLA-DQ2
- C. HLA-DR2
- D. HLA-DR4
- E. HLA-B27

Question 142 of 142

Which one of the following is most strongly associated with coeliac disease?

- A. HLA A5
- ✓ B. HLA-DQ2
- C. HLA-DR2
- D. HLA-DR4
- E. HLA-B27

Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms

? Chronic or intermittent diarrhoea
? Failure to thrive or faltering growth (in children)
? Persistent or unexplained gastrointestinal symptoms including nausea and vomiting
? Prolonged fatigue ('tired all the time')
? Recurrent abdominal pain, cramping or distension
? Sudden or unexpected weight loss
? Unexplained iron-deficiency anaemia, or other unspecified anaemia

Conditions

? Autoimmune thyroid disease
? Dermatitis herpetiformis
? Irritable bowel syndrome
? Type 1 diabetes
? First-degree relatives (parents, siblings or children) with coeliac disease

Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

Question 1

A 45-year-old female with nephrotic syndrome develops renal vein thrombosis. What changes in patients with nephrotic syndrome predispose to the development of venous thromboembolism?

A. Reduced excretion of protein S
B. Loss of antithrombin III
C. Reduced excretion of protein C
D. Loss of fibrinogen
E. Reduced metabolism of vitamin K

Question 1

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D. Loss of fibrinogen
E. Reduced metabolism of vitamin K

Nephrotic syndrome

Triad of
1. Proteinuria (> 3g/24hr) causing
2. Hypoalbuminaemia (< 30g/L) and
3. Oedema

Loss of antithrombin-III, proteins C and S and a associated rise in fibrinogen levels predispose to thrombosis. Loss of TBG lowers total, but not free thyroxine levels

Question 2

A 24-year-old woman is diagnosed as having nephrotic syndrome after being investigated for proteinuria. A diagnosis of minimal change glomerulonephritis is made. What is the most appropriate initial treatment to reduce proteinuria?

A. Protein restriction in diet
B. No treatment shown to effective
C. Angiotensin-converting-enzyme inhibitor
D. Diuretic
E. Prednisolone

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B. No treatment shown to effective
C. Angiotensin-converting-enzyme inhibitor
D. Diuretic
E. Prednisolone

Minimal change glomerulonephritis - prednisolone

Angiotensin-converting-enzyme inhibitors may be used to reduce proteinuria in patients with heavy proteinuria or who have a slow response to prednisolone

Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:
- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

Features
- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria*
- renal biopsy: electron microscopy shows fusion of podocytes

Management
- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:
- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Question 3

A 25-year-old man has a renal biopsy due to worsening renal function. This reveals linear IgG deposits along the basement membrane. What is the most likely diagnosis?

A. Systemic lupus erythematous
B. IgA nephropathy
C. Minimal change disease
D. Post-streptococcal glomerulonephritis
E. Goodpasture's syndrome

Question 3

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B. IgA nephropathy
C. Minimal change disease
D. Post-streptococcal glomerulonephritis
E. Goodpasture's syndrome

Goodpasture's syndrome
- Ig**G** deposits on renal biopsy
- anti-**G**BM antibodies

These changes are characteristic of Goodpasture's syndrome.

Goodpasture's syndrome

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

Features
- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

Factors which increase likelihood of pulmonary haemorrhage
- young males
- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons

Investigations
- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

Management
- plasma exchange
- steroids
- cyclophosphamide

Question 4

A 64-year-old female is brought to the Emergency Department by her family, who are concerned about her increasing confusion over the past 2 days. On examination she is found to be pyrexial at 38ºC. Blood tests reveal:

Hb	9.6 g/dl
Platelets	65 * 10^9/l
WCC	11.1 * 10^9/l
Urea	23.1 mmol/l
Creatinine	366 µmol/l

What is the most likely diagnosis?

A. Wegener's granulomatosis
B. Thrombotic thrombocytopenic purpura
C. Haemolytic uraemic syndrome
D. Idiopathic thrombocytopenic purpura
E. Rapidly progressive glomerulonephritis

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HUS or TTP? Neuro signs and purpura point towards TTP

The combination of neurological features, renal failure, pyrexia and thrombocytopaenia point towards a diagnosis of thrombotic thrombocytopenic purpura

Thrombotic thrombocytopenic purpura

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia
- renal failure

Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV

Question 5

A 54-year-old woman with a history membranous glomerulonephritis secondary to systemic lupus erythematous is admitted to hospital. Her previous stable renal function has deteriorated rapidly. The following blood tests were obtained:

Na^+	139 mmol/l
K^+	5.8 mmol/l
Urea	44 mmol/l
Creatinine	867 µmol/l
Albumin	17 g/l
ESR	49 mm/hr
Urinary protein	14 g/24 hours
Urine dipstick	protein +++ blood ++

What has likely caused the sudden deterioration in renal function?

A. Exacerbation of SLE
B. Renal vein thrombosis
C. Bilateral hydronephrosis
D. Acute interstitial nephritis
E. Analgesic nephropathy

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- E. Analgesic nephropathy

Nephrotic syndrome predisposes to thrombotic episodes, possibly due to loss of antithrombin III. These commonly occur in the renal veins and may be bilateral. Common symptoms include loin pain and haematuria.

A greater rise in the ESR would be expected if the renal failure was due to an exacerbation of SLE.

Nephrotic syndrome: complications

Complications

- increased risk of infection due to urinary immunoglobulin loss
- increased risk of thromboembolism related to loss of antithrombin III and plasminogen in the urine
- hyperlipidaemia
- hypocalcaemia (vitamin D and binding protein lost in urine)
- acute renal failure

Question 6

A 29-year-old woman who is 28 weeks pregnant is reviewed. She has developed pre-eclampsia with her current blood pressure being 156/104 mmHg and the urine dipstick reported as follows:

Protein	+
Leucocytes	negative
Blood	negative

There is no oedema and the patient is otherwise asymptomatic. Of the following drugs, which one is least suitable to use?

A. Labetalol
B. Nifedipine
C. Losartan
D. Methyldopa
E. Hydralazine

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ACE inhibitors and angiotensin-2 receptor blockers should be avoided as they are teratogenic. Most clinicians would either use methyldopa or labetalol first-line in this situation

Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m^2
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count < 100 * 10^6/l, abnormal liver enzymes or HELLP syndrome

Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral methyldopa is often used first-line with oral labetalol, nifedipine and hydralazine also being used
- for severe hypertension IV labetalol and IV hydralazine are used in addition to the above

delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Question 7

A 65-year-old female with a 20 year history of rheumatoid arthritis is referred to the acute medical unit with bilateral leg oedema. The following results are obtained:

Urea	11.2 mmol/l
Creatinine	205 µmol/l
Albumin	26 g/l
Bilirubin	12 mmol/l
ALP	120 IU/l
Urine protein	6.2 g/24 hours

Which investigation is most likely to lead to the correct diagnosis?

A. CT abdomen
B. Plasma magnesium
C. Intravenous urogram
D. Rectal biopsy
E. Renal angiogram

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This rather odd question fooled most *Candida*tes when it appeared. The chronic inflammatory process (rheumatoid) predisposes to amyloidosis which in turn can cause nephrotic syndrome. Rectal biopsy is an (infrequent) test done to look for amyloidosis.

Rheumatoid drugs such as gold may cause nephrotic syndrome but none of the other options point to this as an answer

Amyloidosis: types

AL amyloid
- L for immunoglobulin Light chain fragment
- due to myeloma, Waldenstrom's, MGUS
- features include: cardiac and neurological involvement, macroglossia, periorbital eccymoses

AA amyloid
- A for precursor serum amyloid A protein, an acute phase reactant
- seen in chronic infection/inflammation
- e.g. TB, bronchiectasis, rheumatoid arthritis
- features: renal involvement most common feature

Beta-2 microglobulin amyloidosis
- precursor protein is beta-2 microglobulin, part of the major histocompatibility complex
- associated with patients on renal dialysis

Question 8

Which one of the following types of glomerulonephritis is most characteristically associated with partial lipodystrophy?

A. Minimal change disease
B. Diffuse proliferative glomerulonephritis
C. Mesangiocapillary glomerulonephritis
D. Membranous glomerulonephritis
E. Rapidly progressive glomerulonephritis

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D. Membranous glomerulonephritis
E. Rapidly progressive glomerulonephritis

Mesangiocapillary glomerulonephritis (membranoproliferative)
- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Type 2 mesangiocapillary glomerulonephritis is associated with partial lipodystrophy. Type 1 is seen in association with hepatitis C and cryoglobulinaemia

Mesangiocapillary glomerulonephritis is sometimes referred to as membranoproliferative glomerulonephritis

Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis
- presentation: proteinuria / nephrotic syndrome / CRF
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop CRF

IgA nephropathy - aka Berger's disease, mesangioproliferative GN
- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis
- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / ARF
- most common form of renal disease in SLE

Minimal change disease
- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

Focal segmental glomerulosclerosis
- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / CRF

Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis
- rapid onset, often presenting as ARF
- causes include Goodpasture's, ANCA positive vasculitis

Mesangiocapillary glomerulonephritis (membranoproliferative)
- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Question 9

A 5-year-old boy is seen in the Emergency Department due to lethargy and pallor. There is no recent history of diarrhoea. The following results are obtained:

Hb	8.4 g/dl
Platelets	30 * 10^9/l
Urea	24 mmol/l
Creatinine	164 µmol/l

Urinalysis reveals proteinuria and haematuria. What is the most appropriate management?

A. IV cyclophosphamide
B. Ciprofloxacin
C. Oral prednisolone
D. IV methylprednisolone followed by oral prednisolone
E. Plasma exchange

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E. Plasma exchange

There is no role for antibiotics, steroids or immunosuppressants in haemolytic uraemic syndrome (HUS). Plasma exchange may be indicated, particularly in severe cases of HUS not associated with diarrhoea

Haemolytic uraemic syndrome

Haemolytic uraemic syndrome is generally seen in young children and produces a triad of:

- acute renal failure
- microangiopathic haemolytic anaemia
- thrombocytopenia

Causes

- post-dysentery - classically E coli 0157:H7 ('verotoxigenic', 'enterohaemorrhagic')
- tumours
- pregnancy
- ciclosporin, the Pill
- systemic lupus erythematosus
- HIV

Management

- treatment is supportive e.g. fluids, blood transfusion and dialysis if required
- there is no role for antibiotics, despite the preceding diarrhoeal illness in many patients
- the indications for plasma exchange in HUS are complicated. As a general rule plasma exchange is reserved for severe cases of HUS not associated with diarrhoea

Question 10

Which one of the following statements regarding the assessment of proteinuria in patients with chronic kidney disease is incorrect?

A. Albumin:creatinine ratio (ACR) is more sensitive than protein:creatinine ratio (PCR)
B. An ACR of 30 mg/mmol is approximately equal to a PCR of 50 mg/mmol
C. An ACR sample is collected over 24 hours
D. Women typically have higher ACR values
E. An ACR of 3.1 mg/mmol in a diabetic man is clinically significant

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Chronic kidney disease: proteinuria

Proteinuria is an important marker of chronic kidney disease, especially for diabetic nephropathy. NICE recommend using the albumin:creatinine ratio (ACR) in preference to the protein:creatinine ratio (PCR) when identifying patients with proteinuria as it has greater sensitivity. For quantification and monitoring of proteinuria, PCR can be used as an alternative, although ACR is recommended in diabetics. Urine reagent strips are not recommended unless they express the result as an ACR

Approximate equivalent values

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24 h)
30	50	0.5
70	100	1

Collecting an ACR sample

- by collecting a 'spot' sample it avoids the need to collect urine over a 24 hour period in order to detect or quantify proteinuria
- should be a first-pass morning urine specimen
- if the initial ACR is greater than 30 mg/mmol and less than 70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is greater than 70 mg/mmol a repeat sample need not be tested

Interpreting the ACR results

- in non-diabetics an ACR greater than 30 mg/mmol is considered clinically significant proteinuria
- in diabetics microalbuminuria (ACR greater than 2.5 mg/mmol in men and ACR greater than 3.5 mg/mmol in women) is considered clinically significant

Question 11

Each one of the following is a recognised side-effect of erythropoietin, except:

A. Urticaria
B. Hypertension
C. Bone aches
D. Long bone fractures
E. Pure red cell aplasia

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Erythropoietin

Erythropoietin is a haematopoietic growth factor that stimulates the production of erythrocytes. The main uses of erythropoietin are to treat the anaemia associated with chronic renal failure and that associated with cytotoxic therapy

Side-effects of erythropoietin

- accelerated hypertension potentially leading to encephalopathy and seizures (blood pressure increases in 25% of patients)
- bone aches
- flu-like symptoms
- skin rashes, urticaria
- pure red cell aplasia* (due to antibodies against erythropoietin)
- raised PCV increases risk of thrombosis (e.g. fistula)
- iron deficiency 2nd to increased erythropoiesis

There are a number of reasons why patients may failure to respond to erythropoietin therapy

- iron deficiency
- inadequate dose
- concurrent infection/inflammation
- hyperparathyroid bone disease
- aluminium toxicity

*the risk is greatly reduced with darbepoetin

Question 12

A 27-year-old man is diagnosed with Goodpasture's syndrome. Which one of the following does not increase the likelihood of a pulmonary haemorrhage?

A. Smoking
B. Inhalation of hydrocarbons
C. Male gender
D. Dehydration
E. Lower respiratory tract infection

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A 27-year-old man is diagnosed with Goodpasture's syndrome. Which one of the following does not increase the likelihood of a pulmonary haemorrhage?

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B. Inhalation of hydrocarbons
C. Male gender
D. Dehydration
E. Lower respiratory tract infection

Dehydration may decrease the likelihood of a pulmonary haemorrhage. Pulmonary oedema is associated with an increased risk

Goodpasture's syndrome

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

Features
- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

Factors which increase likelihood of pulmonary haemorrhage
- young males
- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons

Investigations
- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

Management
- plasma exchange
- steroids
- cyclophosphamide

Question 13

Which one of the following is least recognised as a cause of membranous glomerulonephritis?

A. Malaria
B. Lymphoma
C. Hepatitis B
D. Cryoglobulinaemia
E. Gold

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Membranous glomerulonephritis

Membranous glomerulonephritis is the commonest type of glomerulonephritis in adults and is the third most common cause of end-stage renal failure (ESRF). It usually presents as nephrotic syndrome or proteinuria

Renal biopsy demonstrates:
- sub-epithelial immune complex (mainly IgG and C3) deposition in the glomerulus
- electron microscopy: the basement membrane is thickened with sub-epithelial electron dense deposits

Causes
- idiopathic
- infections: hepatitis B, malaria
- malignancy: lung cancer, lymphoma, leukaemia
- drugs: gold, penicillamine, NSAIDs
- systemic lupus erythematosus (class V disease)

Prognosis - rule of thirds
- one-third: spontaneous remission
- one-third: remain proteinuric
- one-third: develop ESRF

Management
- immunosuppression: steroids, chlorambucil e.g. Ponticelli regime
- BP control
- consider anticoagulation

Question 14

A 62-year-old man with chronic kidney disease secondary to diabetes mellitus is reviewed. When assessing his estimated glomerular filtration rate (eGFR), which one of the following variables is not required by the Modification of Diet in Renal Disease (MDRD) equation?

A. Age
B. Serum creatinine
C. Ethnicity
D. Gender
E. Serum urea

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B. Serum creatinine
C. Ethnicity
D. Gender
E. Serum urea

Chronic kidney disease: eGFR and classification

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were develop to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

CKD may be classified according to GFR:

CKD stage	**GFR range**
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

*i.e. normal U&Es and no proteinuria

Question 15

A 73-year-old with a history of alcohol excess is admitted following a fall at home. On admission the following blood results are obtained:

Urea	3.5 mmol/l
Creatinine	110 µmol/l
Creatine kinase	180 u/l

Three days later the blood results are as follows:

Urea	14.5 mmol/l
Creatinine	248 µmol/l
Creatine kinase	4,400 u/l

Which one of the following would have been most likely to prevent the deterioration in renal function?

A. Low dose dopamine
B. Urinary acidification
C. Intravenous fluids
D. Frusemide
E. Mannitol

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Collapse + ARF --> rhabdomyolysis - treat with IV fluids

Intravenous fluids are the most important management step in the prevent of rhabdomyolysis in such patients

Rhabdomyolysis

Rhabdomyolysis will typically feature in the exam as a patient who has had a fall or prolonged epileptic seizure and is found to have acute renal failure on admission

Features
- acute renal failure with disproportionately raised creatinine
- elevated CK
- myoglobinuria
- hypocalcaemia (myoglobin binds calcium)
- elevated phosphate (released from myocytes)

Causes
- seizure
- collapse/coma (e.g. elderly patients collapses at home, found 8 hours later)
- ecstasy
- crush injury
- McArdle's syndrome
- drugs: statins

Management
- IV fluids to maintain good urine output
- urinary alkalinization is sometimes used

Question 16

Which one of the following causes of glomerulonephritis is associated with normal complement levels?

A. Post-streptococcal glomerulonephritis
B. Mesangiocapillary glomerulonephritis
C. Subacute bacterial endocarditis
D. Goodpasture's syndrome
E. Systemic lupus erythematous

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Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Complement levels are normal

Glomerulonephritis and low complement

Disorders associated with glomerulonephritis and low serum complement levels

- post-streptococcal glomerulonephritis
- subacute bacterial endocarditis
- systemic lupus erythematosus
- mesangiocapillary glomerulonephritis

Question 17

An 18-year-old girl who is deaf and has a history of renal impairment is reviewed in clinic. She has previously been diagnosed with Alport's syndrome but is thinking about having children and asks about the risks of passing the condition on. What is the mode of inheritance of Alport's syndrome in the majority of cases?

A. X-linked dominant
B. Mitochondrial
C. Autosomal recessive
D. Autosomal dominant
E. X-linked recessive

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D. Autosomal dominant
E. X-linked recessive

Alport's syndrome - X-linked dominant (in the majority)

Around 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants also existing

Alport's syndrome

Alport's syndrome is usually inherited in an X-linked dominant pattern*. It is due to a defect in the gene which codes for type IV collagen resulting in an abnormal glomerular-basement membrane (GBM). The disease is more severe in males with females rarely developing renal failure

A favourite question in the MRCP is an Alport's patient with a failing renal transplant. This may be caused by the presence of anti-GBM antibodies leading to a Goodpasture's syndrome like picture

Alport's syndrome usually presents in childhood. The following features may be seen:

- microscopic haematuria
- progressive renal failure
- bilateral sensorineural deafness
- lenticonus: protrusion of the lens surface into the anterior chamber
- retinitis pigmentosa

*in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing

Question 18

A patient with type 1 diabetes mellitus is reviewed in the nephrology outpatient clinic. He is known to have stage 1 diabetic nephropathy. Which of the following best describes his degree of renal involvement?

A. Latent phase
B. Hyperfiltration
C. End-stage renal failure
D. Overt nephropathy
E. Microalbuminuria

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For the purposes of the MRCP, increase in the glomerular filtration rate (GFR) is most characteristic of stage 1 diabetic nephropathy. It is however known that elevation of the GFR usually persists into stage 2

Diabetic nephropathy: stages

Diabetic nephropathy may be classified as occurring in five stages*:

Stage 1
- hyperfiltration: increase in GFR
- may be reversible

Stage 2 (silent or latent phase)
- most patients do not develop microalbuminuria for 10 years
- GFR remains elevated

Stage 3 (incipient nephropathy)
- microalbuminuria (albumin excretion of 30 - 300 mg/day, dipstick negative)

Stage 4 (overt nephropathy)
- persistent proteinuria (albumin excretion > 300 mg/day, dipstick positive)
- hypertension is present in most patients
- histology shows diffuse glomerulosclerosis and focal glomerulosclerosis (Kimmelstiel-Wilson nodules)

Stage 5
- end-stage renal disease, GFR typically < 10ml/min
- renal replacement therapy needed

The timeline given here is for type 1 diabetics. Patients with type 2 diabetes mellitus (T2DM) progress through similar stages but in a different timescale - some T2DM patients may progress quickly to the later stages

Question 19

Which one of the following may be useful in the prevention of calcium renal stones?

A. Pyridoxine
B. Allopurinol
C. Lithium
D. Ferrous sulphate
E. Thiazide diuretics

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C. Lithium
D. Ferrous sulphate
E. Thiazide diuretics

The fact that thiazide diuretics cause hypercalcaemia is sometimes confused with their role in preventing calcium renal stones - the hypercalcaemia seen is secondary to increased distal tubular calcium resorption and hence lower calcium concentration in the urine

Renal stones: management

Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic*. A second dose can be given after 30 minutes if necessary

Prevention of renal stones

Calcium stones
- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

Oxalate stones
- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

Uric acid stones
- allopurinol
- urinary alkalinization e.g. oral bicarbonate

*PR diclofenac is an alternative

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E. Mannitol

Question 20

A 73-year-old with a history of alcohol excess is admitted following a fall at home. On admission the following blood results are obtained:

Urea	3.5 mmol/l
Creatinine	110 µmol/l
Creatine kinase	180 u/l

Three days later the blood results are as follows:

Urea	14.5 mmol/l
Creatinine	248 µmol/l
Creatine kinase	4,400 u/l

Which one of the following would have been most likely to prevent the deterioration in renal function?

A. Low dose dopamine
B. Urinary acidification
C. Intravenous fluids
D. Frusemide
E. Mannitol

Collapse + ARF --> rhabdomyolysis - treat with IV fluids

Intravenous fluids are the most important management step in the prevent of rhabdomyolysis in such patients

Rhabdomyolysis

Rhabdomyolysis will typically feature in the exam as a patient who has had a fall or prolonged epileptic seizure and is found to have acute renal failure on admission

Features

- acute renal failure with disproportionately raised creatinine
- elevated CK
- myoglobinuria
- hypocalcaemia (myoglobin binds calcium)
- elevated phosphate (released from myocytes)

Causes

- seizure
- collapse/coma (e.g. elderly patients collapses at home, found 8 hours later)
- ecstasy
- crush injury
- McArdle's syndrome
- drugs: statins

Management

- IV fluids to maintain good urine output
- urinary alkalinization is sometimes used

Question 21

Which one of the following causes of glomerulonephritis is associated with normal complement levels?

A. Post-streptococcal glomerulonephritis
B. Mesangiocapillary glomerulonephritis
C. Subacute bacterial endocarditis
D. Goodpasture's syndrome
E. Systemic lupus erythematous

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B. Mesangiocapillary glomerulonephritis
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D. Goodpasture's syndrome
E. Systemic lupus erythematous

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Complement levels are normal

Glomerulonephritis and low complement

Disorders associated with glomerulonephritis and low serum complement levels

- post-streptococcal glomerulonephritis
- subacute bacterial endocarditis
- systemic lupus erythematosus
- mesangiocapillary glomerulonephritis

Question 22

An 18-year-old girl who is deaf and has a history of renal impairment is reviewed in clinic. She has previously been diagnosed with Alport's syndrome but is thinking about having children and asks about the risks of passing the condition on. What is the mode of inheritance of Alport's syndrome in the majority of cases?

A. X-linked dominant
B. Mitochondrial
C. Autosomal recessive
D. Autosomal dominant
E. X-linked recessive

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A. X-linked dominant
B. Mitochondrial
C. Autosomal recessive
D. Autosomal dominant
E. X-linked recessive

Alport's syndrome - X-linked dominant (in the majority)

Around 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants also existing

Alport's syndrome

Alport's syndrome is usually inherited in an X-linked dominant pattern*. It is due to a defect in the gene which codes for type IV collagen resulting in an abnormal glomerular-basement membrane (GBM). The disease is more severe in males with females rarely developing renal failure

A favourite question in the MRCP is an Alport's patient with a failing renal transplant. This may be caused by the presence of anti-GBM antibodies leading to a Goodpasture's syndrome like picture

Alport's syndrome usually presents in childhood. The following features may be seen:

- microscopic haematuria
- progressive renal failure
- bilateral sensorineural deafness
- lenticonus: protrusion of the lens surface into the anterior chamber
- retinitis pigmentosa

*in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing

Question 23

A patient with type 1 diabetes mellitus is reviewed in the nephrology outpatient clinic. He is known to have stage 1 diabetic nephropathy. Which of the following best describes his degree of renal involvement?

A. Latent phase
B. Hyperfiltration
C. End-stage renal failure
D. Overt nephropathy
E. Microalbuminuria

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B. Hyperfiltration
C. End-stage renal failure
D. Overt nephropathy
E. Microalbuminuria

For the purposes of the MRCP, increase in the glomerular filtration rate (GFR) is most characteristic of stage 1 diabetic nephropathy. It is however known that elevation of the GFR usually persists into stage 2

Diabetic nephropathy: stages

Diabetic nephropathy may be classified as occurring in five stages*:

Stage 1
- hyperfiltration: increase in GFR
- may be reversible

Stage 2 (silent or latent phase)
- most patients do not develop microalbuminuria for 10 years
- GFR remains elevated

Stage 3 (incipient nephropathy)
- microalbuminuria (albumin excretion of 30 - 300 mg/day, dipstick negative)

Stage 4 (overt nephropathy)
- persistent proteinuria (albumin excretion > 300 mg/day, dipstick positive)
- hypertension is present in most patients
- histology shows diffuse glomerulosclerosis and focal glomerulosclerosis (Kimmelstiel-Wilson nodules)

Stage 5
- end-stage renal disease, GFR typically < 10ml/min
- renal replacement therapy needed

The timeline given here is for type 1 diabetics. Patients with type 2 diabetes mellitus (T2DM) progress through similar stages but in a different timescale - some T2DM patients may progress quickly to the later stages

Question 24

Which one of the following may be useful in the prevention of calcium renal stones?

A. Pyridoxine
B. Allopurinol
C. Lithium
D. Ferrous sulphate
E. Thiazide diuretics

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C. Lithium
D. Ferrous sulphate
E. Thiazide diuretics

The fact that thiazide diuretics cause hypercalcaemia is sometimes confused with their role in preventing calcium renal stones - the hypercalcaemia seen is secondary to increased distal tubular calcium resorption and hence lower calcium concentration in the urine

Renal stones: management

Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic*. A second dose can be given after 30 minutes if necessary

Prevention of renal stones

Calcium stones
- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

Oxalate stones
- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

Uric acid stones
- allopurinol
- urinary alkalinization e.g. oral bicarbonate

*PR diclofenac is an alternative

Question 25

A 47-year-old woman presents with loin pain and haematuria. Urine dipstick demonstrates:

Blood	++++
Nitrites	POS
Leucocytes	+++
Protein	++

Urine culture shows a Proteus infection. An x-ray demonstrates a stag-horn calculus in the left renal pelvis. What is the most likely composition of the renal stone?

A. Xanthine
B. Calcium oxalate
C. Struvite
D. Cystine
E. Urate

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Leucocytes +++

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A. Xanthine
B. Calcium oxalate
C. Struvite
D. Cystine
E. Urate

Stag-horn calculi are composed of struvite and form in alkaline urine (ammonia producing bacteria therefore predispose)

Renal stones: imaging

The table below summarises the appearance of different types of renal stone on x-ray

Type	Frequency	Radiograph appearance
Calcium oxalate	40%	Opaque
Mixed calcium oxalate/phosphate stones	25%	Opaque
Triple phosphate stones*	10%	Opaque
Calcium phosphate	10%	Opaque
Urate stones	5-10%	Radio-lucent
Cystine stones	1%	Semi-opaque, 'ground-glass' appearance
Xanthine stones	<1%	Radio-lucent

*stag-horn calculi involve the renal pelvis and extend into at least 2 calyces. They develop in alkaline urine and are composed of struvite (ammonium magnesium phosphate, triple phosphate). Ureaplasma urealyticum and Proteus infections predispose to their formation

Question 26

Which one of the following types of glomerulonephritis is most characteristically associated with Goodpasture's syndrome?

- A. Diffuse proliferative glomerulonephritis
- B. Mesangiocapillary glomerulonephritis
- C. Membranous glomerulonephritis
- D. Rapidly progressive glomerulonephritis
- E. Focal segmental glomerulosclerosis

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- D. Rapidly progressive glomerulonephritis
- E. Focal segmental glomerulosclerosis

Rapidly progressive glomerulonephritis, causes:
- Goodpasture's
- ANCA positive vasculitis

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen

Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis
- presentation: proteinuria / nephrotic syndrome / CRF
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop CRF

IgA nephropathy - aka Berger's disease, mesangioproliferative GN
- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis
- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / ARF
- most common form of renal disease in SLE

Minimal change disease
- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

Focal segmental glomerulosclerosis
- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / CRF

Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis
- rapid onset, often presenting as ARF
- causes include Goodpasture's, ANCA positive vasculitis

Mesangiocapillary glomerulonephritis (membranoproliferative)
- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Question 27

A 35-year-old female is admitted to hospital with hypovolaemic shock. CT abdomen reveals a haemorrhagic lesion in the right kidney. Following surgery and biopsy this is shown to be an angiomyolipomata. What is the most likely underlying diagnosis?

A. Neurofibromatosis
B. Budd-Chiari syndrome
C. Hereditary haemorrhagic telangiectasia
D. Von Hippel-Lindau syndrome
E. Tuberous sclerosis

Question 27

A 35-year-old female is admitted to hospital with hypovolaemic shock. CT abdomen reveals a haemorrhagic lesion in the right kidney. Following surgery and biopsy this is shown to be an angiomyolipomata. What is the most likely underlying diagnosis?

A. Neurofibromatosis
B. Budd-Chiari syndrome
C. Hereditary haemorrhagic telangiectasia
D. Von Hippel-Lindau syndrome
E. Tuberous sclerosis

Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

Cutaneous features
- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots* may be seen

Neurological features
- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

Also
- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Question 28

Autosomal dominant polycystic kidney disease type 1 is associated with a gene defect in:

A. Chromosome 4
B. Chromosome 8
C. Chromosome 12
D. Chromosome 16
E. Chromosome 20

Question 28

Autosomal dominant polycystic kidney disease type 1 is associated with a gene defect in:

A. Chromosome 4
B. Chromosome 8
C. Chromosome 12
D. Chromosome 16
E. Chromosome 20

ADPKD type 1 = chromosome 16 = 85% of cases

ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	**ADPKD type 2**
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Question 29

A 43-year-old man has a work-up for hypertension. He has found to have blood + on a urine dipstick of a freshly voided sample. Which one of the following may account for this finding?

A. Smoking
B. Exercise
C. Obesity
D. Eating red meat the previous day
E. Use of ramipril

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E. Use of ramipril

Haematuria

The management of patients with haematuria is often difficult due to the absence of widely followed guidelines. It is sometimes unclear whether patients are best managed in primary care, by urologists or by nephrologists.

The terminology surrounding haematuria is changing. Microscopic or dipstick positive haematuria is increasingly termed non-visible haematuria whilst macroscopic haematuria is termed visible haematuria.

Causes of transient or spurious non-visible haematuria
- urinary tract infection
- menstruation
- vigorous exercise
- sexual intercourse

Causes of persistent non-visible haematuria
- cancer (bladder, renal, prostate)
- stones
- benign prostatic hyperplasia
- prostatitis
- urethritis e.g. *Chlamydia*
- renal causes: IgA nephropathy, thin basement membrane disease

Management

Current evidence does not support screening for haematuria. The incidence of non-visible haematuria is similar in patients taking aspirin/warfarin to the general population hence these patients should also be investigated.

Testing
- urine dipstick is the test of choice for detecting haematuria
- urine microscopy may be used but time to analysis significantly affects the number of red blood cells detected

NICE urgent cancer referral guidelines
- of any age with painless macroscopic haematuria
- aged 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria
- aged 50 years and older who are found to have unexplained microscopic haematuria

Question 30

A 10-year-old boy is taken to see the GP by his mother. For the past two days he has had a sore throat associated with blood in his urine. There is no significant past medical history. The GP suspects glomerulonephritis and refers the patient to hospital. What would a renal biopsy most likely show?

A. Proliferation of endothelial cells
B. No change
C. Mesangial hypercellularity
D. Basement membrane thickening
E. Capillary wall necrosis

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B. No change
C. Mesangial hypercellularity
D. Basement membrane thickening
E. Capillary wall necrosis

This boy is likely to have IgA nephropathy. Histological features include mesangial hypercellularity and positive immunofluorescence for IgA & C3

IgA nephropathy

Basics
- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis
- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

Presentations
- young male, recurrent episodes of macroscopic haematuria
- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

Associated conditions
- alcoholic cirrhosis
- coeliac disease/dermatitis herpetiformis

Management
- steroids/immunosuppressants not be shown to be useful

Prognosis
- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD

Question 31

A 67-year-old woman presents for review due to ankle swelling. She has a history of rheumatoid arthritis which was diagnosed when she was 24 years old and a 8 year history of type 2 diabetes mellitus. Her current medication includes metformin and methotrexate. On examination she has bilateral pitting lower limb oedema. A 24 hour urine collection is reported as follows:

24 hr urinary protein 4.8g

What is the most likely cause of her leg oedema?

A. Diabetic nephropathy
B. Nephrotic syndrome secondary to methotrexate
C. Dilated cardiomyopathy secondary to methotrexate
D. Amyloidosis
E. Protein-losing enteropathy secondary to metformin

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C. Dilated cardiomyopathy secondary to methotrexate
D. Amyloidosis
E. Protein-losing enteropathy secondary to metformin

This patient has developed nephrotic syndrome secondary to amyloidosis, a recognised complication of inflammatory conditions such as rheumatoid arthritis. Methotrexate is not a common cause of nephrotic syndrome.

Nephrotic syndrome: causes

Glomerulonephritis (GN, c. 80%)
- minimal change GN (causes 80% in children, 30% in adults)
- membranous GN
- focal segmental glomerulosclerosis

Systemic disease (c. 20%)
- amyloidosis
- SLE

Drugs
- gold (sodium aurothiomalate), penicillamine

Others
- congenital
- neoplasia: carcinoma, lymphoma, leukaemia, myeloma
- infection: bacterial endocarditis, hepatitis B, malaria
- renal vein thrombosis

Question 32

An sample of tissue from a renal biopsy is viewed using an electron microscope. Podocyte fusion is seen. Which one of the following types of glomerulonephritis is most associated with this finding?

A. Membranous glomerulonephritis
B. IgA nephropathy
C. Focal segmental glomerulosclerosis
D. Mesangiocapillary glomerulonephritis
E. Minimal change glomerulonephritis

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B. IgA nephropathy
C. Focal segmental glomerulosclerosis
D. Mesangiocapillary glomerulonephritis
E. Minimal change glomerulonephritis

Podocyte fusion is seen in minimal change glomerulonephritis but may occasionally be a feature of focal segmental glomerulosclerosis as well. Minimal change glomerulonephritis however is far more common

Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:
- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

Features
- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria*
- renal biopsy: electron microscopy shows fusion of podocytes

Management
- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:
- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Question 33

Each of the following is a risk factor for renal stone formation, except:

A. Renal tubular acidosis
B. Cadmium
C. Hyperparathyroidism
D. Dehydration
E. Cystinosis

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B. Cadmium
C. Hyperparathyroidism
D. Dehydration
E. Cystinosis

Cystinuria, not cystinosis, is a risk factor for renal stone formation

Renal stones: risk factors

Risk factors
- dehydration
- hypercalciuria, hyperparathyroidism, hypercalcaemia
- cystinuria
- high dietary oxalate
- renal tubular acidosis
- medullary sponge kidney, polycystic kidney disease
- beryllium or cadmium exposure

Risk factors for urate stones
- gout
- ileostomy: loss of bicarbonate and fluid results in acidic urine, causing the precipitation of uric acid

Drug causes
- drugs that promote calcium stones: loop diuretics, steroids, acetazolamide, theophylline
- thiazides can prevent calcium stones (increase distal tubular calcium resorption)

Question 34

Which one of the following is least associated with focal segmental glomerulosclerosis?

A. Alport's syndrome
B. Heroin
C. Sickle-cell anaemia
D. Bleomycin
E. HIV infection

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Focal segmental glomerulosclerosis

Causes
- idiopathic
- secondary to other renal pathology e.g. IgA nephropathy, reflux nephropathy
- HIV
- heroin
- Alport's syndrome
- sickle-cell

Presentations
- nephrotic syndrome

Focal segmental glomerulosclerosis is noted for having a high recurrence rate in renal transplants

Question 35

A 34-year-old man presents to the Emergency Department with abdominal pain. This started earlier on in the day and is getting progressively worse. The pain is located on his left flank and radiates down into his groin. He has had not had a similar pain before and is normally fit and well. Examination reveals a man who is flushed and sweaty but is otherwise unremarkable. What is the most suitable initial management?

A. Oral ciprofloxacin
B. IM diclofenac 75 mg
C. Immediate abdominal ultrasound
D. IM morphine 5 mg
E. IM diclofenac 75 mg + start bendroflumethiazide to prevent further episodes

Question 35

A 34-year-old man presents to the Emergency Department with abdominal pain. This started earlier on in the day and is getting progressively worse. The pain is located on his left flank and radiates down into his groin. He has had not had a similar pain before and is normally fit and well. Examination reveals a man who is flushed and sweaty but is otherwise unremarkable. What is the most suitable initial management?

A. Oral ciprofloxacin
B. IM diclofenac 75 mg
C. Immediate abdominal ultrasound
D. IM morphine 5 mg
E. IM diclofenac 75 mg + start bendroflumethiazide to prevent further episodes

This man may need to be referred acutely to the surgeons for pain relief and investigations to exclude obstruction. It would not be suitable to start bendroflumethiazide in the initial phase of the first episode. An immediate abdominal ultrasound is not necessary as neither his age nor symptoms point to a diagnosis of abdominal aneurysm.

Renal stones: management

Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic*. A second dose can be given after 30 minutes if necessary

Prevention of renal stones

Calcium stones
- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

Oxalate stones
- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

Uric acid stones
- allopurinol
- urinary alkalinization e.g. oral bicarbonate

*PR diclofenac is an alternative

Question 36

A 26-year-old man with loin pain and haematuria is found to have autosomal dominant polycystic kidney disease. A defect in which one of the following genes is likely to be responsible?

A. Fibrillin-2 gene
B. Polycystin gene
C. Fibrillin-1 gene
D. Von Hippel-Lindau gene
E. PKD1 gene

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B. Polycystin gene
C. Fibrillin-1 gene
D. Von Hippel-Lindau gene
E. PKD1 gene

Most cases of autosomal dominant polycystic kidney disease (ADPKD) are due to a mutation in the PKD1 gene. The PKD1 gene encodes for a polycystin-1, a large cell-surface glycoprotein of unknown function

ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	**ADPKD type 2**
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Question 37

Which one of the following types of glomerulonephritis is most characteristically associated with streptococcal infection in children?

A. Focal segmental glomerulosclerosis
B. Diffuse proliferative glomerulonephritis
C. Membranous glomerulonephritis
D. Mesangiocapillary glomerulonephritis
E. Rapidly progressive glomerulonephritis

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E. Rapidly progressive glomerulonephritis

Diffuse proliferative glomerulonephritis, causes:
- post-streptococcal
- SLE

Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis
- presentation: proteinuria / nephrotic syndrome / CRF
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop CRF

IgA nephropathy - aka Berger's disease, mesangioproliferative GN
- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis
- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / ARF
- most common form of renal disease in SLE

Minimal change disease
- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

Focal segmental glomerulosclerosis
- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / CRF

Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis
- rapid onset, often presenting as ARF
- causes include Goodpasture's, ANCA positive vasculitis

Mesangiocapillary glomerulonephritis (membranoproliferative)
- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Question 38

Each one of the following is associated with papillary necrosis, except:

A. Acute pyelonephritis
B. Tuberculosis
C. Chronic analgesia use
D. Syphilis
E. Sickle cell disease

Papillary necrosis

Causes
- chronic analgesia use
- sickle cell disease
- TB
- acute pyelonephritis
- diabetes mellitus

Features
- fever, loin pain, haematuria
- IVU - papillary necrosis with renal scarring - 'cup & spill'

Question 38

Each one of the following is associated with papillary necrosis, except:

A. Acute pyelonephritis
B. Tuberculosis
C. Chronic analgesia use
D. Syphilis
E. Sickle cell disease

Papillary necrosis

Causes
- chronic analgesia use
- sickle cell disease
- TB
- acute pyelonephritis
- diabetes mellitus

Features
- fever, loin pain, haematuria
- IVU - papillary necrosis with renal scarring - 'cup & spill'

Question 39

A 45-year-old woman with nephrotic syndrome is noted to have marked loss of subcutaneous tissue from the face. What is the most likely underlying cause of her renal disease?

A. Mesangiocapillary glomerulonephritis type II
B. Focal segmental glomerulosclerosis
C. Minimal change glomerulonephritis
D. Renal vein thrombosis
E. Membranous glomerulonephritis

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E. Membranous glomerulonephritis

Mesangiocapillary glomerulonephritis (membranoproliferative) • type 1: cryoglobulinaemia, hepatitis C • type 2: partial lipodystrophy

This patient has partial lipodystrophy which is associated with mesangiocapillary glomerulonephritis type II

Mesangiocapillary glomerulonephritis

Overview
- aka membranoproliferative glomerulonephritis
- may present as nephrotic syndrome, haematuria or proteinuria
- poor prognosis

Type 1
- subendothelial immune deposits
- cause: cryoglobulinaemia, hepatitis C

Type 2 - 'dense deposit disease'
- intramembranous deposits of electron dense material
- causes: partial lipodystrophy, factor H deficiency
- reduced serum complement
- C3b nephritic factor (an antibody against C3bBb) found in 70%

Type 3
- causes: hepatitis B and C

Management
- steroids may be effective

Question 40

Which one of the following is least associated with retroperitoneal fibrosis?

A. Riedel's thyroiditis
B. Previous radiotherapy
C. Inflammatory abdominal aortic aneurysm
D. Methysergide
E. Sulphonamides

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Retroperitoneal fibrosis

Lower back pain is the most common presenting feature

Associations

- Riedel's thyroiditis
- previous radiotherapy
- sarcoidosis
- inflammatory abdominal aortic aneurysm
- drugs: methysergide

Question 41

Which one of the following is most characteristic of type 1 renal tubular acidosis?

A. Hyperkalaemia
B. Osteomalacia
C. Decreased bicarbonate reabsorption in the proximal tubule
D. Raised anion gap metabolic acidosis
E. Renal stones

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D. Raised anion gap metabolic acidosis
E. Renal stones

Osteomalacia is more commonly seen in type 2 renal tubular acidosis

Renal tubular acidosis

All three types of renal tubular acidosis (RTA) are associated with hyperchloraemic metabolic acidosis (normal anion gap)

Type 1 RTA (distal)
- inability to generate acid urine (secrete H+) in distal tubule
- causes hypokalaemia
- complications include nephrocalcinosis and renal stones
- causes include idiopathic, RA, SLE, Sjogren's

Type 2 RTA (proximal)
- decreased HCO3- reabsorption in proximal tubule
- causes hypokalaemia
- complications include osteomalacia
- causes include idiopathic, as part of Fanconi syndrome, Wilson's disease, cystinosis, outdated tetracyclines

Type 4 RTA (hyperkalaemic)
- causes hyperkalaemia
- causes include hypoaldosteronism, diabetes

Question 42

A 62-year-old man is diagnosed with renal cell cancer. Which one of the following hormones is least likely to be present in excessive levels?

A. Erythropoietin
B. Parathyroid hormone
C. Growth hormone
D. ACTH
E. Renin

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B. Parathyroid hormone
C. Growth hormone
D. ACTH
E. Renin

Renal cell cancer

Renal cell cancer is also known as hypernephroma and accounts for 85% of primary renal neoplasms. It arises from proximal renal tubular epithelium

Associations*
- more common in middle-aged men
- smoking
- von Hippel-Lindau syndrome
- tuberous sclerosis

Features
- classical triad: haematuria, loin pain, abdominal mass
- pyrexia of unknown origin
- left varicocele (due to occlusion of left testicular vein)
- endocrine effects: may secrete erythropoietin (polycythaemia), parathyroid hormone (hypercalcaemia), renin, ACTH
- 25% have metastases at presentation

Management
- radical nephrectomy for confined disease
- alpha-interferon and interleukin-2 have been used to reduce tumour size and also treat patients with metatases
- receptor tyrosine kinase inhibitors (e.g. sorafenib, sunitinib) have been shown to have superior efficacy compared to interferon-alpha

*incidence of renal cell cancer is only slightly increased in patients with autosomal dominant polycystic kidney disease

Question 43

Which one of the following is least recognised as an indication for plasma exchange?

A. Guillain-Barre syndrome
B. Churg-Strauss syndrome
C. Myasthenia gravis
D. Cerebral malaria
E. Goodpasture's syndrome

Question 43

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B. Churg-Strauss syndrome
C. Myasthenia gravis
D. Cerebral malaria
E. Goodpasture's syndrome

Cerebral malaria is not a standard indication for plasma exchange. Exchange transfusions have been tried but it is generally only justified when peripheral parasitemia is greater than 10% of circulating erythrocytes. The role of blood transfusions remains controversial, as they are both expensive and potentially dangerous in many malaria areas

Plasma exchange

Indications for plasma exchange

- Guillain-Barre syndrome
- myasthenia gravis
- Goodpasture's syndrome
- ANCA positive vasculitis e.g. Wegener's, Churg-Strauss
- TTP/HUS
- cryoglobulinaemia
- hyperviscosity syndrome e.g. secondary to myeloma

Question 44

Which one of the following features is least likely to be seen in Henoch-Schonlein purpura?

A. Abdominal pain
B. Renal failure
C. Polyarthritis
D. Thrombocytopenia
E. Purpuric rash over buttocks

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C. Polyarthritis
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Henoch-Schonlein purpura

Henoch-Schonlein purpura (HSP) is an IgA mediated small vessel vasculitis. There is a degree of overlap with IgA nephropathy (Berger's disease). HSP is usually seen in children following an infection

Features

- palpable purpuric rash (with localized oedema) over buttocks and extensor surfaces of arms and legs
- abdominal pain
- polyarthritis
- features of IgA nephropathy may occur e.g. haematuria, renal failure

Question 45

Which of the following factors would suggest that a patient has established acute tubular necrosis rather than pre-renal uraemia?

A. Urine sodium = 10 mmol/L
B. Fractional urea excretion = 20%
C. Increase in urine output following fluid challenge
D. Specific gravity = 1025
E. Fractional sodium excretion = 1.5%

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C. Increase in urine output following fluid challenge
D. Specific gravity = 1025
E. Fractional sodium excretion = 1.5%

ATN or prerenal uraemia? In prerenal uraemia think of the kidneys holding on to sodium to preserve volume

ARF: ATN vs. prerenal uraemia

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	Pre-renal uraemia	**Acute tubular necrosis**
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	>35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

*fractional sodium excretion = (urine sodium/plasma sodium) / (urine creatinine/plasma creatinine) x 100

**fractional urea excretion = (urine urea /blood urea) / (urine creatinine/plasma creatinine) x 100

Question 46

Which one of the following statements is true regarding autosomal recessive polycystic kidney disease?

A. Onset is typically in the third decade
B. Liver involvement is rare
C. Is due to a defect on chromosome 16
D. More common than autosomal dominant polycystic kidney disease
E. May be diagnosed on prenatal ultrasound

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ARPKD

Autosomal recessive polycystic kidney disease (ARPKD) is much less common than autosomal dominant disease (ADPKD). It is due to a defect in a gene located on chromosome 6

Diagnosis may be made on prenatal ultrasound or in early infancy with abdominal masses and renal failure. End-stage renal failure develops in childhood. Patients also typically have liver involvement, for example portal and interlobular fibrosis

Question 47

A 62-year-old man attends your clinic. He has a history of hypertension and atrial fibrillation for which he is anticoagulated with warfarin. A urine dipstick taken 8 weeks ago during a routine hypertension clinic appointment showed blood +. This has been repeated on two further occasions. What is the most appropriate action?

A. Take no further action
B. Send a 24-urine sample for protein estimation
C. Renal biopsy
D. Cystoscopy
E. Confirm with urine microscopy

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C. Renal biopsy
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E. Confirm with urine microscopy

The incidence of non-visible haematuria is similar in patients taking warfarin to the general population therefore these patients should be investigated as normal.

Haematuria

The management of patients with haematuria is often difficult due to the absence of widely followed guidelines. It is sometimes unclear whether patients are best managed in primary care, by urologists or by nephrologists.

The terminology surrounding haematuria is changing. Microscopic or dipstick positive haematuria is increasingly termed non-visible haematuria whilst macroscopic haematuria is termed visible haematuria.

Causes of transient or spurious non-visible haematuria
- urinary tract infection
- menstruation
- vigorous exercise
- sexual intercourse

Causes of persistent non-visible haematuria
- cancer (bladder, renal, prostate)
- stones
- benign prostatic hyperplasia
- prostatitis
- urethritis e.g. *Chlamydia*
- renal causes: IgA nephropathy, thin basement membrane disease

Management

Current evidence does not support screening for haematuria. The incidence of non-visible haematuria is similar in patients taking aspirin/warfarin to the general population hence these patients should also be investigated.

Testing
- urine dipstick is the test of choice for detecting haematuria
- urine microscopy may be used but time to analysis significantly affects the number of red blood cells detected

NICE urgent cancer referral guidelines
- of any age with painless macroscopic haematuria
- aged 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria
- aged 50 years and older who are found to have unexplained microscopic haematuria

Question 48

A 71-year-old man with chronic kidney disease stage 3 is reviewed in the cardiology clinic. He is known to have hypertension and ischaemic heart disease but a recent fasting glucose result confirmed he is not diabetic. A recent early morning urine result is reported as follows:
Albumin:creatinine ratio 5.2 mg/mmol

What is the most appropriate action?

A. Refer to a nephrologist
B. No action as not clinically significant
C. Obtain a 24-hour urine collection
D. Repeat using a late-evening sample
E. Arrange renovascular imaging

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C. Obtain a 24-hour urine collection
D. Repeat using a late-evening sample
E. Arrange renovascular imaging

As he is not diabetic this result is not clinically significant

Chronic kidney disease: proteinuria

Proteinuria is an important marker of chronic kidney disease, especially for diabetic nephropathy. NICE recommend using the albumin:creatinine ratio (ACR) in preference to the protein:creatinine ratio (PCR) when identifying patients with proteinuria as it has greater sensitivity. For quantification and monitoring of proteinuria, PCR can be used as an alternative, although ACR is recommended in diabetics. Urine reagent strips are not recommended unless they express the result as an ACR

Approximate equivalent values

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24 h)
30	50	0.5
70	100	1

Collecting an ACR sample

- by collecting a 'spot' sample it avoids the need to collect urine over a 24 hour period in order to detect or quantify proteinuria
- should be a first-pass morning urine specimen
- if the initial ACR is greater than 30 mg/mmol and less than 70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is greater than 70 mg/mmol a repeat sample need not be tested

Interpreting the ACR results

- in non-diabetics an ACR greater than 30 mg/mmol is considered clinically significant proteinuria
- in diabetics microalbuminuria (ACR greater than 2.5 mg/mmol in men and ACR greater than 3.5 mg/mmol in women) is considered clinically significant

Question 49

What is the most likely outcome following the diagnosis of minimal change nephropathy in a 15-year-old male?

A. Chronic kidney disease requiring renal replacement therapy within 30 years
B. Full recovery and no further episodes
C. Full recovery but with later relapses
D. Chronic kidney disease not requiring renal replacement therapy
E. Chronic kidney disease requiring renal replacement therapy within 10 years

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D. Chronic kidney disease not requiring renal replacement therapy
E. Chronic kidney disease requiring renal replacement therapy within 10 years

Whilst the prognosis in minimal change glomerulonephritis is good, relapses are common, with a third of patients having infrequent relapses and a further third having frequent relapses which usually stop before adulthood

Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:
- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

Features
- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria*
- renal biopsy: electron microscopy shows fusion of podocytes

Management
- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:
- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Question 50

A 12-year-old boy is investigated for a purpuric rash on the extensor surfaces of his lower legs. He also has a history of abdominal pain and an urticarial rash. The following results are obtained:

Urine dipstick: blood ++

What would be the likely finding on renal biopsy?

A. Linear IgG deposits
B. No change
C. Sclerosis within the glomerulus
D. Mesangial hypercellularity
E. Basement membrane thickening

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Features

- palpable purpuric rash (with localized oedema) over buttocks and extensor surfaces of arms and legs
- abdominal pain
- polyarthritis
- features of IgA nephropathy may occur e.g. haematuria, renal failure

Question 51

A 33-year-old man with a history of coeliac disease is admitted for investigation of recurrent macroscopic haematuria. His urine is typically brown and there is no history of passing clots. What is the most likely diagnosis?

A. Diffuse proliferative glomerulonephritis
B. IgA nephropathy
C. Membranous glomerulonephritis
D. Minimal change disease
E. Rapidly progressive glomerulonephritis

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B. IgA nephropathy
C. Membranous glomerulonephritis
D. Minimal change disease
E. Rapidly progressive glomerulonephritis

This man has IgA nephropathy which is associated with coeliac disease

IgA nephropathy

Basics
- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis
- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

Presentations
- young male, recurrent episodes of macroscopic haematuria
- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

Associated conditions
- alcoholic cirrhosis
- coeliac disease/dermatitis herpetiformis

Management
- steroids/immunosuppressants not be shown to be useful

Prognosis
- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD

Question 52

Each one of the following is a cause of sterile pyuria, except:

A. Renal stones
B. Membranous glomerulonephritis
C. Renal tuberculosis
D. *Chlamydia*
E. Appendicitis

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C. Renal tuberculosis
D. *Chlamydia*
E. Appendicitis

Tubulo-interstitial nephritis may cause sterile pyuria but it is not seen with acute glomerulonephritis

Sterile pyuria

Causes

- partially treated UTI
- urethritis e.g. *Chlamydia*
- renal tuberculosis
- renal stones
- appendicitis
- bladder/renal cell cancer
- adult polycystic kidney disease
- analgesic nephropathy

Question 53

Which one of the following is not a feature of HIV-associated nephropathy?

A. Small kidneys
B. Normotension
C. Elevated urea and creatinine
D. Proteinuria
E. Focal segmental glomerulosclerosis on renal biopsy

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C. Elevated urea and creatinine
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E. Focal segmental glomerulosclerosis on renal biopsy

HIV: renal involvement

Renal involvement in HIV patients may occur as a consequence of treatment or the virus itself. Protease inhibitors such as indinavir can precipitate intratubular crystal obstruction

HIV-associated nephropathy (HIVAN) accounts for up to 10% of end-stage renal failure cases in the United States. Antiretroviral therapy has been shown to alter the course of the disease. There are five key features of HIVAN:

- massive proteinuria
- normal or large kidneys
- focal segmental glomerulosclerosis with focal or global capillary collapse on renal biopsy
- elevated urea and creatinine
- normotension

Question 54

A 61-year-old man with a history of hypertension presents with central chest pain. Acute coronary syndrome is diagnosed and conventional management is given. A few days later a diagnostic coronary angiogram is performed. The following week a deteriorating of renal function is noted associated with a purpuric rash on his feet. What is the most likely diagnosis?

A. Aspirin-induced interstitial nephritis
B. Heparin-induced thrombocytopaenia
C. Renal artery stenosis
D. Cholesterol embolisation
E. Antiphospholipid syndrome

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B. Heparin-induced thrombocytopaenia
C. Renal artery stenosis
D. Cholesterol embolisation
E. Antiphospholipid syndrome

Cholesterol embolisation is a well-documented complication of coronary angiography

Cholesterol embolisation

Overview
- cholesterol emboli may break off causing renal disease
- seen more commonly in arteriopaths, abdominal aortic aneurysms

Features
- eosinophilia
- purpura
- renal failure
- livedo reticularis

Question 55

A 39-year-old woman with systemic lupus erythematosus presents for review in the rheumatology clinic. Dipstick urine on arrival at clinic shows protein ++. Further investigations reveal the following

Bicarbonate 22 mmol/l

Urea 7.1 mmol/l

Creatinine 134 µmol/l

24-hour urinary protein 2.6 g

What is the renal biopsy most likely to show?

A. Diffuse proliferative glomerulonephritis
B. Mesangiocapillary glomerulonephritis
C. Rapidly progressive glomerulonephritis
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Diffuse proliferative glomerulonephritis is the most common and severe form of renal disease in SLE patients

SLE: renal complications

WHO classification
- class I: normal kidney
- class II: mesangial glomerulonephritis
- class III: focal (and segmental) proliferative glomerulonephritis
- class IV: diffuse proliferative glomerulonephritis
- class V: diffuse membranous glomerulonephritis
- class VI: sclerosing glomerulonephritis

Class IV (diffuse proliferative glomerulonephritis) is the most common and severe form

Management
- treat hypertension
- corticosteroids if clinical evidence of disease
- immunosuppressants e.g. azathiopine/cyclophosphamide

Question 56

Which one of the following statements regarding minimal change glomerulonephritis is incorrect?

A. Has a good prognosis
B. The majority of cases are steroid responsive
C. Is a common cause of nephrotic syndrome
D. Hypertension is found in approximately 25% of patients
E. Haematuria is rare

Question 56

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B. The majority of cases are steroid responsive
C. Is a common cause of nephrotic syndrome
D. Hypertension is found in approximately 25% of patients
E. Haematuria is rare

Hypertension and haematuria are rare in minimal change glomerulonephritis

Minimal change glomerulonephritis

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The majority of cases are idiopathic, but in around 10-20% a cause is found:
- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

Features
- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria*
- renal biopsy: electron microscopy shows fusion of podocytes

Management
- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:
- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Question 57

A two-year old boy presents with an abdominal mass. Which of the following is associated with Wilm's tumour (nephroblastoma)?

A. Deletion on short arm of chromosome 12
B. Tuberose sclerosis
C. Beckwith-Wiedemann syndrome
D. Autosomal dominant polycystic kidney disease
E. Autosomal recessive polycystic kidney disease

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C. Beckwith-Wiedemann syndrome
D. Autosomal dominant polycystic kidney disease
E. Autosomal recessive polycystic kidney disease

Beckwith-Wiedemann syndrome is a inherited condition associated with organomegaly, macroglossia, abdominal wall defects, Wilm's tumour and neonatal hypoglycaemia.

Wilms tumour

Wilms nephroblastoma is one of the most common childhood malignancies. It typically presents in children under 5 years of age, with a median age of 3 years old.

Features
- abdominal mass (most common presenting feature)
- painless haematuria
- flank pain
- other features: anorexia, fever
- unilateral in 95% of cases
- metastases are found in 20% of patients (most commonly lung)

Associations
- Beckwith-Wiedemann syndrome
- as part of WAGR syndrome with Aniridia, Genitourinary malformations, mental Retardation
- hemihypertrophy
- around one-third of cases are associated with a mutation in the WT1 gene on chromosome 11

Management
- nephrectomy
- chemotherapy
- radiotherapy if advanced disease
- prognosis: good, 80% cure rate

Question 58

Which one of the following types of glomerulonephritis is most characteristically associated with Wegener's granulomatosis?

A. Mesangiocapillary glomerulonephritis
B. Membranous glomerulonephritis
C. Rapidly progressive glomerulonephritis
D. Focal segmental glomerulosclerosis
E. Diffuse proliferative glomerulonephritis

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B. Membranous glomerulonephritis
C. Rapidly progressive glomerulonephritis
D. Focal segmental glomerulosclerosis
E. Diffuse proliferative glomerulonephritis

Rapidly progressive glomerulonephritis, causes:
- Goodpasture's
- ANCA positive vasculitis

Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis
- presentation: proteinuria / nephrotic syndrome / CRF
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop CRF

IgA nephropathy - aka Berger's disease, mesangioproliferative GN
- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis
- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / ARF
- most common form of renal disease in SLE

Minimal change disease
- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

Focal segmental glomerulosclerosis
- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / CRF

Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis
- rapid onset, often presenting as ARF
- causes include Goodpasture's, ANCA positive vasculitis

Mesangiocapillary glomerulonephritis (membranoproliferative)
- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Question 59

Alport's syndrome is due to a defect in:

A. Fibrillin-2
B. Type II collagen
C. Fibrillin-1
D. Type IV collagen
E. Type V collagen

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Alport's syndrome is due to a defect in:

A. Fibrillin-2
B. Type II collagen
C. Fibrillin-1
D. Type IV collagen
E. Type V collagen

Alport's syndrome - type IV collagen defect

Alport's syndrome

Alport's syndrome is usually inherited in an X-linked dominant pattern*. It is due to a defect in the gene which codes for type IV collagen resulting in an abnormal glomerular-basement membrane (GBM). The disease is more severe in males with females rarely developing renal failure

A favourite question in the MRCP is an Alport's patient with a failing renal transplant. This may be caused by the presence of anti-GBM antibodies leading to a Goodpasture's syndrome like picture

Alport's syndrome usually presents in childhood. The following features may be seen:

- microscopic haematuria
- progressive renal failure
- bilateral sensorineural deafness
- lenticonus: protrusion of the lens surface into the anterior chamber
- retinitis pigmentosa

*in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing

Question 60

A 65-year-old man with a history of hypertension is reviewed. As part of routine blood tests to monitor his renal function whilst taking ramipril the following blood tests are received:

Na^+	140 mmol/l
K^+	4.8 mmol/l
Urea	6.2 mmol/l
Creatinine	102 µmol/l
eGFR	68 ml/min

A urine dipstick is subsequently performed which is normal and a renal ultrasound sound shows normal sized kidneys with no abnormality detected. What stage of chronic kidney disease does this patient have?

A. No chronic kidney disease
B. Chronic kidney disease stage 4
C. Chronic kidney disease stage 3
D. Chronic kidney disease stage 2
E. Chronic kidney disease stage 1

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B. Chronic kidney disease stage 4
C. Chronic kidney disease stage 3
D. Chronic kidney disease stage 2
E. Chronic kidney disease stage 1

CKD: only diagnose stages 1 & 2 if supporting evidence to accompany eGFR

Chronic kidney disease is only diagnosed in this situation if supporting tests such as urinalysis or renal ultrasound are abnormal

Chronic kidney disease: eGFR and classification

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were develop to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

CKD may be classified according to GFR:

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

*i.e. normal U&Es and no proteinuria

Question 61

A 45-year-old presents to the Emergency Department with chest pain. An ECG shows anterior ST elevation and he is thrombolysed with alteplase. His chest pain settles and he is started on aspirin, atorvastatin, bisoprolol and ramipril. Four days later his blood results are as follows:

Urea	22 mmol/l
Creatinine	277 µmol/l

What is the most likely cause for the deterioration in renal function?

A. Renal artery stenosis
B. NSAID related nephropathy
C. Statin nephropathy
D. Dressler's syndrome
E. Haemorrhage into renal cyst

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Flash pulmonary oedema, U&Es worse on ACE inhibitor, asymmetrical kidneys --> renal artery stenosis - do MR angiography

There is likely underlying renal artery stenosis revealed by the addition of an ACE inhibitor. Risk factors such as hypertension and hyperlipidaemia which have contributed to the development of his ischaemic heart disease also put him at risk of renal vascular disease

Renal vascular disease

Renal vascular disease is most commonly due to atherosclerosis (> 95% of patients). It is associated with risk factors such as smoking and hypertension that cause atheroma elsewhere in the body. It may present as hypertension, chronic renal failure or 'flash' pulmonary oedema. In younger patients however fibromuscular dysplasia (FMD) needs to be considered. FMD is more common in young women and characteristically has a 'string of beads' appearance on angiography. Patients respond well to balloon angioplasty

Investigation

- MR angiography is now the investigation of choice
- CT angiography
- conventional renal angiography is less commonly performed used nowadays, but may still have a role when planning surgery

Question 62

Which of the following types of renal stones are said to have a semi-opaque appearance on x-ray?

A. Calcium oxalate
B. Cystine stones
C. Urate stones
D. Xanthine stones
E. Triple phosphate stones

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D. Xanthine stones
E. Triple phosphate stones

Renal stones on x-ray
- cystine stones: semi-opaque
- urate + xanthine stones: radio-lucent

Renal stones: imaging

The table below summarises the appearance of different types of renal stone on x-ray

Type	Frequency	Radiograph appearance
Calcium oxalate	40%	Opaque
Mixed calcium oxalate/phosphate stones	25%	Opaque
Triple phosphate stones*	10%	Opaque
Calcium phosphate	10%	Opaque
Urate stones	5-10%	Radio-lucent
Cystine stones	1%	Semi-opaque, 'ground-glass' appearance
Xanthine stones	<1%	Radio-lucent

*stag-horn calculi involve the renal pelvis and extend into at least 2 calyces. They develop in alkaline urine and are composed of struvite (ammonium magnesium phosphate, triple phosphate). Ureaplasma urealyticum and Proteus infections predispose to their formation

Question 63

A 62-year-old man with a diabetic nephropathy and hypertension is reviewed. His current medication is insulin, bendroflumethiazide, ramipril and amlodipine. On examination blood pressure is 144/78 mmHg. Blood tests reveal the following:

Na^+	139 mmol/l
K^+	4.9 mmol/l
Urea	12.8 mmol/l
Creatinine	215 µmol/l
eGFR	29 ml/min

Renal function is similar to 3 months ago. What is the most appropriate action?

A. No change to his medication
B. Switch bendroflumethiazide for furosemide
C. Add a beta-blocker
D. Add spironolactone
E. Stop ramipril

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E. Stop ramipril

As the eGFR is 29 ml/min switching bendroflumethiazide for furosemide would be the next step in controlling his blood pressure. Please see the guidelines in the external links section

Chronic kidney disease: hypertension

The majority of patients with chronic kidney disease (CKD) will require more than two drugs to treat hypertension. ACE inhibitors are first line and are particularly helpful in proteinuric renal disease (e.g. diabetic nephropathy). As these drugs tend to reduce filtration pressure a small fall in glomerular filtration pressure (GFR) and rise in creatinine can be expected. Most nephrologists would accept a change of up to 15%. A rise greater than this may indicate underlying renovascular disease.

Furosemide is useful as a anti-hypertensive in patients with CKD, particularly when the GFR falls to below 45 ml/min*. It has the added benefit of lowering serum potassium. High doses are usually required. If the patient becomes at risk of dehydration (e.g. Gastroenteritis) then consideration should be given to temporarily stopping the drug

*the NKF K/DOQI guidelines suggest a lower cut-off of less than 30 ml/min

Question 64

A 24-year-old man who has a sister with adult polycystic kidney disease (ADPKD) asks if he could be screened for the disease. What is the most appropriate screening test?

A. PKD1 gene testing
B. CT abdomen
C. Urine microscopy
D. Ultrasound abdomen
E. Anti-polycystin 1 antibodies levels

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Ultrasound is the screening test for adult polycystic kidney disease

Genetic testing is still not routinely recommended for screening family members. Sensitivity for ADPKD1 is 99% for at-risk patients older than 20 years

ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	**ADPKD type 2**
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Question 65

A 67-year-old with chronic kidney disease stage 4 and metastatic prostate cancer presents as his pain is not controlled with co-codamol. Which one of the following opioids is it most appropriate to use given his impaired renal function?

A. Buprenorphine
B. Morphine
C. Hydromorphone
D. Diamorphine
E. Tramadol

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Alfentanil, buprenorphine and fentanyl are the preferred opioids in patients with chronic kidney disease.

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 66

A 45-year-old women with type 1 diabetes mellitus is reviewed in the diabetes clinic. Three months ago her blood tests were as followed:

K^+ 4.5 mmol/l

Creatinine 116 µmol/l

eGFR 47 ml/min

At the time she was started on lisinopril to treat both the hypertension and act as a renoprotective agent. Lisinopril had been titrated up to treatment dose. Her current bloods are as follows:

K^+ 4.9 mmol/l

Creatinine 123 µmol/l

eGFR 44 ml/min

Of the following options, what is the most appropriate course of action?

A. Stop lisinopril and arrange investigations to exclude renal artery stenosis
B. Switch to a angiotensin 2 receptor blocker
C. Switch to a different ACE inhibitor
D. No action
E. Reduce dose of lisinopril

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The small change in both the creatinine and eGFR are acceptable and below the threshold where ACE inhibitors should be stopped

Chronic kidney disease: hypertension

The majority of patients with chronic kidney disease (CKD) will require more than two drugs to treat hypertension. ACE inhibitors are first line and are particularly helpful in proteinuric renal disease (e.g. diabetic nephropathy). As these drugs tend to reduce filtration pressure a small fall in glomerular filtration pressure (GFR) and rise in creatinine can be expected. Most nephrologists would accept a change of up to 15%. A rise greater than this may indicate underlying renovascular disease.

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*the NKF K/DOQI guidelines suggest a lower cut-off of less than 30 ml/min

Question 67

A patient develops mesangiocapillary glomerulonephritis secondary to partial lipodystrophy. Which type of complement is likely to be low?

A. C3
B. C4
C. C2
D. C9
E. C6

Question 67

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A. C3
B. C4
C. C2
D. C9
E. C6

Mesangiocapillary glomerulonephritis (membranoproliferative) • type 1: cryoglobulinaemia, hepatitis C • type 2: partial lipodystrophy

Mesangiocapillary glomerulonephritis

Overview
- aka membranoproliferative glomerulonephritis
- may present as nephrotic syndrome, haematuria or proteinuria
- poor prognosis

Type 1
- subendothelial immune deposits
- cause: cryoglobulinaemia, hepatitis C

Type 2 - 'dense deposit disease'
- intramembranous deposits of electron dense material
- causes: partial lipodystrophy, factor H deficiency
- reduced serum complement
- C3b nephritic factor (an antibody against C3bBb) found in 70%

Type 3
- causes: hepatitis B and C

Management
- steroids may be effective

Question 68

Which one of the following is not a risk factor for the development of calcium oxalate and calcium phosphate renal stones?

A. Bendrofluazide
B. Aminophylline
C. Acetazolamide
D. Frusemide
E. Prednisolone

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B. Aminophylline
C. Acetazolamide
D. Frusemide
E. Prednisolone

Bendrofluazide may help prevent the formation of calcium based renal stones. It may however theoretically increase the risk of urate based stones

Renal stones: risk factors

Risk factors
- dehydration
- hypercalciuria, hyperparathyroidism, hypercalcaemia
- cystinuria
- high dietary oxalate
- renal tubular acidosis
- medullary sponge kidney, polycystic kidney disease
- beryllium or cadmium exposure

Risk factors for urate stones
- gout
- ileostomy: loss of bicarbonate and fluid results in acidic urine, causing the precipitation of uric acid

Drug causes
- drugs that promote calcium stones: loop diuretics, steroids, acetazolamide, theophylline
- thiazides can prevent calcium stones (increase distal tubular calcium resorption)

Question 69

A 54-year-old man is diagnosed as having gout. You are discussing ways to help prevent future attacks. Which one of the following is most likely to precipitate an attack of gout?

A. Chocolate
B. Brazil nuts
C. Eggs
D. Sardines
E. Smoking

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B. Brazil nuts
C. Eggs
D. Sardines
E. Smoking

Foods to avoid include those high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 70

Which one of the following may be useful in the prevention of oxalate renal stones?

A. Ferrous sulphate
B. Thiazide diuretics
C. Lithium
D. Pyridoxine
E. Allopurinol

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D. Pyridoxine
E. Allopurinol

Renal stones: management

Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic*. A second dose can be given after 30 minutes if necessary

Prevention of renal stones

Calcium stones

- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

Oxalate stones

- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

Uric acid stones

- allopurinol
- urinary alkalinization e.g. oral bicarbonate

*PR diclofenac is an alternative

Question 71

Which of the following factors would suggest that a patient has pre-renal uraemia rather than established acute tubular necrosis?

A. Urine sodium = 70 mmol/L
B. Fractional urea excretion = 20%
C. No response to fluid challenge
D. Urine:plasma urea ratio 5:1
E. Specific gravity = 1005

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E. Specific gravity = 1005

ATN or prerenal uraemia? In prerenal uraemia think of the kidneys holding on to sodium to preserve volume

ARF: ATN vs. prerenal uraemia

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	Pre-renal uraemia	**Acute tubular necrosis**
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	>35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

*fractional sodium excretion =
(urine sodium/plasma sodium) / (urine creatinine/plasma creatinine) x 100

**fractional urea excretion =
(urine urea /blood urea) / (urine creatinine/plasma creatinine) x 100

Question 72

Which one of the following is the most common type of SLE associated renal disease?

A. Class II: mesangial glomerulonephritis
B. Class III: focal (and segmental) proliferative glomerulonephritis
C. Class IV: diffuse proliferative glomerulonephritis
D. Class V: diffuse membranous glomerulonephritis
E. Class VI: sclerosing glomerulonephritis

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D. Class V: diffuse membranous glomerulonephritis
E. Class VI: sclerosing glomerulonephritis

Diffuse proliferative glomerulonephritis is the most common and severe form of renal disease in SLE patients

SLE: renal complications

WHO classification
- class I: normal kidney
- class II: mesangial glomerulonephritis
- class III: focal (and segmental) proliferative glomerulonephritis
- class IV: diffuse proliferative glomerulonephritis
- class V: diffuse membranous glomerulonephritis
- class VI: sclerosing glomerulonephritis

Class IV (diffuse proliferative glomerulonephritis) is the most common and severe form

Management
- treat hypertension
- corticosteroids if clinical evidence of disease
- immunosuppressants e.g. azathiopine/cyclophosphamide

Question 73

Autosomal dominant polycystic kidney disease type 2 is associated with a gene defect in:

A. Chromosome 4
B. Chromosome 8
C. Chromosome 12
D. Chromosome 16
E. Chromosome 20

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ADPKD type 2 = chromosome 4 = 15% of cases

ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	**ADPKD type 2**
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Question 1 of 164

A 76-year-old man is admitted with a right hemiparesis. CT scan shows an ischaemic stroke and aspirin 300mg is commenced. In terms of further management in the acute phase, which one of the following values should not be corrected?

- A. BP 210/110
- B. Blood glucose 11.2 mmol/l
- C. Oxygen saturation 94%
- D. Temp 38.3ºC
- E. Blood glucose 3.5 mmol/l

Question 1 of 164

A 76-year-old man is admitted with a right hemiparesis. CT scan shows an ischaemic stroke and aspirin 300mg is commenced. In terms of further management in the acute phase, which one of the following values should not be corrected?

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- B. Blood glucose 11.2 mmol/l
- C. Oxygen saturation 94%
- D. Temp 38.3ºC
- E. Blood glucose 3.5 mmol/l

Hypertension should not be treated in the initial period following a stroke

Elevated blood pressure should not be treated in the acute phase following a stroke unless complications develop. Other physiological parameters should be kept within normal limits - an aggressive approach with respect to this has been shown to improve outcome

Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued guidelines in 2008.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commence on a statin

Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

*SIGN recommend a window of 4.5 hours

Question 2 of 164

A 27-year-old man presents to the Emergency Department with 2 day history of severe headache and pyrexia (38.2ºC). A CT scan is reported as follows:

CT: Brain

Petechial haemorrhages in the temporal and inferior frontal lobes. No mass effect. Brain parenchyma otherwise normal

What is the most likely diagnosis?

- A. Brain abscess
- B. Meningococcal meningitis
- C. Cerebral malaria
- D. Herpes simplex encephalitis
- E. New variant CJD

Question 2 of 164

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CT head showing temporal lobe changes - think herpes simplex encephalitis

Herpes simplex encephalitis

Herpes simplex (HSV) encephalitis is a common topic in the MRCP. The virus characteristically affects the temporal lobes - questions may give the result of imaging or describe temporal lobe signs e.g. aphasia

Features
- fever, headache, psychiatric symptoms, seizures, vomiting
- focal features e.g. aphasia
- peripheral lesions (e.g. cold sores) have no relation to presence of HSV encephalitis

Pathophysiology
- HSV-1 responsible for 95% of cases in adults
- typically affects temporal and inferior frontal lobes

Investigation
- CSF: lymphocytosis, elevated protein
- PCR for HSV
- CT: medial temporal and inferior frontal changes (e.g. petechial haemorrhages) - normal in one-third of patients
- MRI is better
- EEG pattern: lateralised periodic discharges at 2 Hz

Treatment
- intravenous aciclovir

The prognosis is dependent on whether aciclovir is commenced early. If treatment is started promptly the mortality is 10-20%. Left untreated the mortality approaches 80%

Question 3 of 164

A 64-year-old man with a history of Parkinson's disease is reviewed in clinic and a decision has been made to start him on cabergoline. Which one of the following adverse effects is most strongly associated with this drug?

- A. Optic neuritis
- B. Transient rise in liver function tests
- C. Pulmonary fibrosis
- D. Renal failure
- E. Thrombocytopenia

Question 3 of 164

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- D. Renal failure
- E. Thrombocytopenia

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 4 of 164

A 29-year-old man presents complaining of visual disturbance. Examination reveals a right superior homonymous quadrantanopia. Where is the lesion most likely to be?

- A. Optic chiasm
- B. Left temporal lobe
- C. Right temporal lobe
- D. Left optic nerve
- E. Left parietal lobe

Question 4 of 164

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- C. Right temporal lobe
- D. Left optic nerve
- E. Left parietal lobe

Visual field defects:
- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects= optic radiation lesion or occipital cortex

Visual field defects

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Homonymous hemianopia
- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias
- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Question 5 of 164

A 34-year-old female presents with vomiting preceded by an occipital headache of acute onset. On examination she was conscious and alert with photophobia but no neck stiffness. CT brain is reported as normal. What is the most appropriate further management?

- A. CT brain with contrast
- B. Repeat CT brain in 24h
- C. CSF examination
- D. Cerebral angiography
- E. MRI brain

Question 5 of 164

A 34-year-old female presents with vomiting preceded by an occipital headache of acute onset. On examination she was conscious and alert with photophobia but no neck stiffness. CT brain is reported as normal. What is the most appropriate further management?

- A. CT brain with contrast
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- C. CSF examination
- D. Cerebral angiography
- E. MRI brain

If the CSF examination revealed xanthochromia, or there was still a high level of clinical suspicion, then cerebral angiography would be the next step

Subarachnoid haemorrhage

Causes
- 85% are due to rupture of berry aneurysms (conditions associated with berry aneurysms include adult polycystic kidney disease, Ehlers-Danlos syndrome and coarctation of the aorta)
- AV malformations
- trauma
- tumours

Investigations
- CT: negative in 5%
- LP: done after 12 hrs (allowing time for xanthochromia to develop)

Complications
- rebleeding (in 30%)
- obstructive hydrocephalus (due to blood in ventricles)
- vasospasm leading to cerebral ischaemia

Management
- neurosurgical opinion: no clear evidence over early surgical intervention against delayed intervention
- nimodipine (e.g. 60mg / 4 hrly, if BP allows) has been shown to reduce the severity of neurological deficits but doesn't reduce rebleeding*

*the way nimodipine works in subarachnoid haemorrhage is not fully understood. It has been previously postulated that it reduces cerebral vasospasm (hence maintaining cerebral perfusion) but this has not been demonstrated in studies

Question 6 of 164

A 73-year-old female with a history of recurrent falls at home and alcohol excess is brought to the Emergency Department due to episodes of confusion over the past 5 days. Between these episodes she is apparently her normal self. On examination her GCS is 14/15 and she has nystagmus on left lateral gaze. What is the most likely diagnosis?

- A. Subdural haemorrhage
- B. Subarachnoid haemorrhage
- C. Meningitis
- D. Herpes simplex encephalitis
- E. Alzheimer's disease

Question 6 of 164

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- A. Subdural haemorrhage
- B. Subarachnoid haemorrhage
- C. Meningitis
- D. Herpes simplex encephalitis
- E. Alzheimer's disease

Fluctuating consciousness = subdural haemorrhage

The combination of falls, alcohol excess, fluctuating episodes of confusion and focal neurology points towards a diagnosis of subdural haemorrhage. The phrase 'fluctuating conscious level' is common in questions and should always bring to mind subdural haemorrhage

Subdural haemorrhage

Basics
- most commonly secondary to trauma e.g. old person/alcohol falling over
- initial injury may be minor and is often forgotten
- caused by bleeding from damaged bridging veins between cortex and venous sinuses

Features
- headache
- classically fluctuating conscious level
- raised ICP

Treatment
- needs neurosurgical review ? burr hole

Question 7 of 164

A 24-year-old female presents with a headache. She has a past history of epilepsy and is known to suffer from migraines, but has previously managed attacks with a combination of paracetamol and metoclopramide. This combination is however not working for the current episode.

What second line medication is it most appropriate to use?

- A. Codeine
- B. Pizotifen
- C. Zolmitriptan
- D. Methysergide
- E. Ergotamine

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Epilepsy is not a contraindication to the use of triptans. Opioids are not recommended in the management of migraine

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment

Standard analgesia

- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans

- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine

- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis

Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line

- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines

- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists

- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 8 of 164

Which of the following features is least likely to be found in a patient with tuberose sclerosis?

- A. Adenoma sebaceum
- B. Café-au-lait spots
- C. Retinal hamartomas
- D. 'Ash-leaf' spots
- E. Lisch nodules

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- D. 'Ash-leaf' spots
- E. Lisch nodules

Lisch nodules are seen in neurofibromatosis

Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

Cutaneous features
- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots* may be seen

Neurological features
- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

Also
- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Question 9 of 164

A 27-year-old man presents with a history of fits consistent with tonic-clonic seizures. What is the most suitable first-line treatment?

- A. Gabapentin
- B. Lamotrigine
- C. Sodium valproate
- D. Carbamazepine
- E. Phenytoin

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Epilepsy medication: first-line
- generalised seizure: sodium valproate
- partial seizure: carbamazepine

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:
- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures
- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)
- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures
- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures
- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 10 of 164

A 33-year-old man presents complaining of visual disturbance. Examination reveals a bitemporal hemianopia with predominately the upper quadrants being affected. What is the most likely lesion?

- A. Craniopharyngioma
- B. Brainstem lesion
- C. Pituitary macroadenoma
- D. Frontal lobe lesion
- E. Right occipital lesion

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Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

An upper quadrant defect implies inferior chiasmal compression making a pituitary macroadenoma the most likely diagnosis

Visual field defects

The main points for the exam are:
- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
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Question 11 of 164

A 29-year-old man with a history of schizophrenia is taken to the local Emergency Department as he is generally unwell. He is currently taking olanzapine and citalopram. On examination he is noted to have a temperature of 37.0ºC and his blood pressure is 170/100 mmHg. Which other examination finding would best support a diagnosis of neuroleptic malignant syndrome?

- A. Ataxia
- B. Hyperreflexia
- C. Muscle rigidity
- D. Tremor
- E. Papilloedema

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- E. Papilloedema

Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics

Features

- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

Management

- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene may be useful in selected cases
- bromocriptine, dopamine agonist, may also be used

Question 12 of 164

A 75-year-old female presents with weakness of her left hand. On examination wasting of the hypothenar eminence is seen and there is weakness of finger abduction. Thumb adduction is also weak. Where is the lesion most likely to be?

- A. C7
- B. Median nerve
- C. Radial nerve
- D. Anterior interosseous nerve
- E. Ulnar nerve

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- C. Radial nerve
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- E. Ulnar nerve

Ulnar nerve

Overview
- arises from medial cord of brachial plexus (C8, T1)

Motor to
- medial two lumbricals
- aDductor pollicis
- interossei
- hypothenar muscles: abductor digiti minimi, flexor digiti minimi
- flexor carpi ulnaris

Sensory to
- medial 1 1/2 fingers (palmar and dorsal aspects)

Patterns of damage

Damage at wrist
- 'claw hand'
- wasting and paralysis of intrinsic hand muscles (except lateral two lumbricals)
- wasting and paralysis of hypothenar muscles
- sensory loss to the medial 1 1/2 fingers (palmar and dorsal aspects)

Damage at elbow
- as above
- radial deviation of wrist

Question 13 of 164

Which one of the following is least associated with normal pressure hydrocephalus?

- A. Papilloedema
- B. Dementia
- C. Urinary incontinence
- D. Gait abnormality
- E. Enlarged fourth ventricle

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- A. Papilloedema
- B. Dementia
- C. Urinary incontinence
- D. Gait abnormality
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Urinary incontinence + gait abnormality + dementia = normal pressure hydrocephalus

Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis

A classical triad of features is seen
- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson's disease)

Imaging
- hydrocephalus with an enlarged fourth ventricle

Management
- ventriculoperitoneal shunting

Question 14 of 164

In patients with Guillain-Barre syndrome, respiratory function should be monitored with:

- A. Oxygen saturations
- B. PEFR
- C. Flow volume loop
- D. Arterial blood gases
- E. FVC

Question 14 of 164

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- C. Flow volume loop
- D. Arterial blood gases
- E. FVC

FVC is used to monitor respiratory function in Guillain-Barre syndrome

Guillain-Barre syndrome: management

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

Management
- plasma exchange
- IV immunoglobulins
- steroids and immunosuppressants have not been shown to be beneficial
- FVC regularly to monitor respiratory function

Prognosis
20% suffer permanent disability, 5% die

Question 15 of 164

A 56-year-old woman presents with facial asymmetry. Whilst brushing her teeth this morning she noted that the right hand corner of her mouth was drooping. She is generally well but noted some pain behind her right ear yesterday and says her right eye is becoming dry. On examination she has a complete paralysis of the facial nerve on the right side, extending from the forehead to the mouth. Ear, nose and throat examination is normal. Clinical examination of the peripheral nervous system is normal. What is the most likely diagnosis?

- A. Ramsey-Hunt syndrome
- B. Bell's palsy
- C. Stroke
- D. Multiple sclerosis
- E. Parotid tumour

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- B. Bell's palsy
- C. Stroke
- D. Multiple sclerosis
- E. Parotid tumour

The pain around the ear raises the possibility of Ramsey-Hunt syndrome but this is actually quite common in Bell's palsy - some studies suggest it is seen in 50% of patients. The normal ear exam also goes against this diagnosis.

Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously.

Features

- lower motor neuron facial nerve palsy - forehead affected*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes

Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 25mg bd for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

*upper motor neuron lesion 'spares' upper face

Question 16 of 164

Which one of the following statements regarding the development of a headache following lumbar puncture is incorrect?

- A. Occurs in one-third of patients
- B. May last several days
- C. More common in females
- D. Usually develops within the first 24 hours
- E. Worsens with upright position

Question 16 of 164

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Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline

Question 17 of 164

Which type of motor neuron disease carries the worst prognosis?

- A. Relapsing-remitting
- B. Bulbar palsy
- C. Progressive muscular atrophy
- D. Spinocerebellar ataxia
- E. Amyotrophic lateral sclerosis

Question 17 of 164

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Motor neuron disease: types

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, primary lateral sclerosis, progressive muscular atrophy and bulbar palsy. In some patients however, there is a combination of clinical patterns

Amyotrophic lateral sclerosis (50% of patients)
- typically LMN signs in arms and UMN signs in legs
- in familial cases the gene responsible lies on chromosome 21 and codes for superoxide dismutase

Primary lateral sclerosis
- UMN signs only

Progressive muscular atrophy
- LMN signs only
- affects distal muscles before proximal
- carries best prognosis

Bulbar palsy
- palsy of the tongue, muscles of chewing/swallowing and facial muscles due to loss of function of brainstem motor nuclei
- carries worst prognosis

Question 18 of 164

You are called to the obstetric ward to see a women who is fitting. She is 34-weeks pregnant and currently an inpatient for the treatment of severe pre-eclampsia. The anaesthetist has secured the airway and is giving 100% oxygen. What is the most appropriate next step?

- A. IV calcium gluconate
- B. IV labetalol
- C. IV methyldopa
- D. IV lorazepam
- E. IV magnesium sulphate

Question 18 of 164

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- D. IV lorazepam
- E. IV magnesium sulphate

Eclampsia - give magnesium sulphate first-line

Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

Question 19 of 164

An obese 24-year-old female presents with headaches and blurred vision. Examination reveals bilateral blurring of the optic discs but is otherwise unremarkable with no other neurological signs. Blood pressure is 130/74 and she is apyrexial. What is the most likely underlying diagnosis?

- A. Multiple sclerosis
- B. Meningococcal meningitis
- C. Brain abscess
- D. Normal pressure hydrocephalus
- E. Idiopathic intracranial hypertension

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Obese, young female with headaches / blurred vision think idiopathic intracranial hypertension

The combination of a young, obese female with papilloedema but otherwise normal neurology makes idiopathic intracranial hypertension the most likely diagnosis

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

Features
- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

Risk factors
- obesity
- female sex
- pregnancy
- drugs: oral contraceptive pill, steroids, tetracycline, vitamin A

Management
- weight loss
- diuretics e.g. acetazolamide
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

Question 20 of 164

Which of the following visual field changes would be most consistent with a left parietal lobe lesion?

- A. Right homonymous hemianopia
- B. Left inferior homonymous quadrantanopia
- C. Left superior homonymous quadrantanopia
- D. Right superior homonymous quadrantanopia
- E. Right inferior homonymous quadrantanopia

Question 20 of 164

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Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Question 21 of 164

A patient is referred due to the development of a third nerve palsy associated with a headache. On examination meningism is present. Which one of the following diagnoses needs to be urgently excluded?

- A. Weber's syndrome
- B. Internal carotid artery aneurysm
- C. Multiple sclerosis
- D. Posterior communicating artery aneurysm
- E. Anterior communicating artery aneurysm

Question 21 of 164

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- A. Weber's syndrome
- B. Internal carotid artery aneurysm
- C. Multiple sclerosis
- D. Posterior communicating artery aneurysm
- E. Anterior communicating artery aneurysm

Painful third nerve palsy = posterior communicating artery aneurysm

Given the combination of a headache and third nerve palsy it is important to exclude a posterior communicating artery aneurysm

Third nerve palsy

Features
- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

Causes
- diabetes mellitus
- vasculitis e.g. temporal arteritis, SLE
- false localizing sign* due to uncal herniation through tentorium if raised ICP
- posterior communicating artery aneurysm (pupil dilated)
- cavernous sinus thrombosis
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia -caused by midbrain strokes
- other possible causes: amyloid, multiple sclerosis

*this term is usually associated with sixth nerve palsies but it may be used for a variety of neurological presentations

Question 22 of 164

A 52-year-old man is prescribed apomorphine. What type of receptors does apomorphine act on?

- A. Opioid receptors
- B. GABA receptors
- C. Cholinergic receptors
- D. Dopamine receptors
- E. Muscarinic receptors

Question 22 of 164

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Apomorphine is one of the older dopamine receptor agonists. Newer agents such as ropinirole and cabergoline have since been developed

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 23 of 164

A 29-year-old woman with a past history of hypothyroidism presents to the surgery complaining of weakness, particularly of her arms, for the past four months. She has also developed double vision towards the end of the day, despite having a recent normal examination at the opticians. What is the most likely diagnosis?

- A. Chronic fatigue syndrome
- B. Polymyositis
- C. Polymyalgia rheumatica
- D. Multiple sclerosis
- E. Myasthenia gravis

Question 23 of 164

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- E. Myasthenia gravis

Myasthenia gravis

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 90% of cases*. Myasthenia is more common in women (2:1)

Features
- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

Associations
- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmine thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

Investigations
- Tensilon test: IV edrophonium reduces muscle weakness temporarily
- CT thorax to exclude thymoma
- CK normal

Management
- long-acting anticholinesterase e.g. Pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

Management of myasthenic crisis
- plasmapheresis
- intravenous immunoglobulins

*antibodies are less commonly seen in disease limited to the ocular muscles

Question 24 of 164

Which one of the following features is most associated with frontal lobe lesions?

- A. Wernicke's aphasia
- B. Gerstmann's syndrome
- C. Perseveration
- D. Cortical blindness
- E. Superior homonymous quadrantanopia

Question 24 of 164

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- C. Perseveration
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Brain anatomy

The following neurological disorders/features may allow localisation of a brain lesion:

Parietal lobe lesions
- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

Occipital lobe lesions
- homonymous hemianopia
- cortical blindness
- visual agnosia

Temporal lobe lesion
- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia

Frontal lobes lesions
- expressive (Broca's) aphasia: located
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Question 25 of 164

A 21-year-old female is seen in the first seizure clinic in the outpatient department. A decision is made not to start her on anti-epileptic medication. What restrictions on driving should she be informed about?

- A. No restrictions but inform DVLA
- B. No restrictions, no need to inform DVLA if not on medication
- C. Cannot drive for 1 month from date of seizure
- D. Cannot drive for 6 months from date of seizure
- E. Cannot drive for 1 year from date of seizure

Question 25 of 164

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- E. Cannot drive for 1 year from date of seizure

Patients cannot drive for 6 months following a seizure

DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- first seizure: 6 months off driving*. For patients with established epilepsy they must be fit free for 12 months before being able to drive
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving**
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

*previously rule was 12 months. It is now 6 months off driving if the licence holder has undergone assessment by an appropriate specialist and no relevant abnormality has been identified on investigation, for example EEG and brain scan where indicated

**if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

Question 26 of 164

A 23-year-old man is referred to neurology clinic. He describes episodes of leg weakness following bouts of laughing whilst out with friends. The following weekend his friends described a brief collapse following a similar episode. What is the most likely diagnosis?

- A. Stokes-Adams attack
- B. Cataplexy
- C. Hypokalaemic periodic paralysis
- D. Absence seizure
- E. Myasthenia gravis

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- C. Hypokalaemic periodic paralysis
- D. Absence seizure
- E. Myasthenia gravis

Cataplexy

Cataplexy describes the loss of muscular tone caused by strong emotion (e.g. laughter, being frightened). Around two-thirds of patients with narcolepsy have cataplexy

Features range from buckling knees to collapse

Question 27 of 164

A 45-year-old man presents with dizziness and right-sided hearing loss. Which one of the following tests would most likely indicate an acoustic neuroma?

- A. Jerky nystagmus
- B. Left homonymous hemianopia
- C. Tongue deviated to the left
- D. Fasciculation of the tongue
- E. Absent corneal reflex

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- D. Fasciculation of the tongue
- E. Absent corneal reflex

Loss of corneal reflex - think acoustic neuroma

Acoustic neuroma

Acoustic neuromas account for approximately five percent of intracranial tumours and 90 percent of cerebellopontine angle

Features can be predicted by the affected cranial nerves
- cranial nerve VIII: hearing loss, vertigo, tinnitus
- cranial nerve V: absent corneal reflex
- cranial nerve VII: facial palsy

Bilateral acoustic neuromas are seen in neurofibromatosis type 2

MRI of the cerebellopontine angle is the investigation of choice

Question 28 of 164

A 55-year-old man is diagnosed with amyotrophic lateral sclerosis. Which one of the following drugs has been shown to confer a survival benefit?

- A. Rituximab
- B. Riluzole
- C. Interferon-beta
- D. Cyclophosphamide
- E. Interferon-alpha

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- D. Cyclophosphamide
- E. Interferon-alpha

Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

Riluzole
- anti-glutamate drug
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months
- expensive

Respiratory care
- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

Prognosis
- poor: 50% of patients die within 3 years

Question 29 of 164

A 41-year-old man presents with a two week history of headaches around the left side of his face associated with watery eyes. He describes having about two episodes a day each lasting around 30 minutes. On examination he has a red left eye and a partial left ptosis. There is no past medical history of note other than migraines as a child. What is the likely diagnosis?

- A. Atypical migraine
- B. Cluster headache
- C. Trigeminal neuralgia
- D. Acute angle closure glaucoma
- E. Cavernous sinus thrombosis

Question 29 of 164

A 41-year-old man presents with a two week history of headaches around the left side of his face associated with watery eyes. He describes having about two episodes a day each lasting around 30 minutes. On examination he has a red left eye and a partial left ptosis. There is no past medical history of note other than migraines as a child. What is the likely diagnosis?

- A. Atypical migraine
- B. Cluster headache
- C. Trigeminal neuralgia
- D. Acute angle closure glaucoma
- E. Cavernous sinus thrombosis

Episodic eye pain, lacrimation, nasal stuffiness occurring daily - cluster headache

Cluster headache

Cluster headaches* are more common in men (5:1) and smokers

Features

- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

Management

- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

Question 30 of 164

Which one of the following is least characteristic of Wernicke's encephalopathy?

- A. Ataxia
- B. Confusion
- C. Ophthalmoplegia
- D. Confabulation
- E. Nystagmus

Question 30 of 164

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- D. Confabulation
- E. Nystagmus

An inability to acquire new memories and confabulation suggests the development of Korsakoff's syndrome

Wernicke's encephalopathy

Wernicke's encephalopathy is a neuropsychiatric disorder caused by thiamine deficiency which is most commonly seen in alcoholics. Rarer causes include: persistent vomiting, stomach cancer, dietary deficiency. A classic triad of nystagmus, ophthalmoplegia and ataxia may occur. In Wernicke's encephalopathy petechial haemorrhages occur in a variety of structures in the brain including the mamillary bodies and ventricle walls

Features
- nystagmus
- ophthalmoplegia
- ataxia
- confusion, altered GCS
- peripheral sensory neuropathy

Investigations
- decreased red cell transketolase
- MRI

Treatment is with urgent replacement of thiamine

Question 31 of 164

A 55-year-old man presents due to an uncontrollable urge to move his legs during the night-time. He has also experience the sensation of spiders crawling over his legs. Simple measures such as walking and massaging the affected limb have not alleviated the problem. What is the most appropriate medical therapy?

- A. Selective serotonin reuptake inhibitor
- B. Low-dose tricyclic antidepressant
- C. Dopamine agonist
- D. 5-HT3 antagonist
- E. Dopamine antagonist

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Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

Question 32 of 164

A 25-year-old female with a history of bilateral vitreous haemorrhage is referred due to progressive ataxia. What is the likely diagnosis?

- A. Neurofibromatosis type I
- B. Neurofibromatosis type II
- C. Tuberose sclerosis
- D. Von Hippel-Lindau syndrome
- E. Sarcoidosis

Question 32 of 164

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- B. Neurofibromatosis type II
- C. Tuberose sclerosis
- D. Von Hippel-Lindau syndrome
- E. Sarcoidosis

Retinal and cerebellar haemangiomas are key features of Von Hippel-Lindau syndrome. Retinal haemangiomas are bilateral in 25% of patients and may lead to vitreous haemorrhage

Von Hippel-Lindau syndrome

Von Hippel-Lindau (VHL) syndrome is an autosomal dominant condition predisposing to neoplasia. It is due to an abnormality in the VHL gene located on short arm of chromosome 3

Features

- cerebellar haemangiomas:
- retinal haemangiomas: vitreous haemorrhage
- renal cysts (premalignant)
- phaeochromocytoma
- extra-renal cysts: epididymal, pancreatic, hepatic
- endolymphatic sac tumours

Question 33 of 164

A 45-year-old man presents to the Emergency Department following the sudden onset of pain in the right side of his face whilst hammering a nail into the wall. The pain is described as severe with occasional exacerbations. On examination he has a mild right ptosis and small right pupil. What is the most likely diagnosis?

- A. Trigeminal neuralgia
- B. Glaucoma
- C. Carotid artery dissection
- D. Syringomyelia
- E. Migraine

Question 33 of 164

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- E. Migraine

This patient has Horner's syndrome caused by a carotid artery dissection. This may be caused by relatively benign trauma to the neck such as hyperextension whilst doing DIY. Cluster headache would be a differential diagnosis

Horner's syndrome

Features
- miosis (small pupil)
- ptosis
- enophthalmos* (sunken eye)
- anhydrosis (loss of sweating one side)

Distinguishing between causes
- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	**Pre-ganglionic lesions**	**Post-ganglionic lesions**
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke **S**yringomyelia Multiple **s**clerosis Tumour Encephalitis	Pancoast's **t**umour **T**hyroidectomy **T**rauma Cervical rib	**C**arotid artery dissection **C**arotid aneurysm **C**avernous sinus thrombosis **C**luster headache

*in reality the appearance is due to a narrow palpebral aperture rather than true enophthalmos

Question 34 of 164

A 54-year-old man presents with a persistent tremor. On examination there is 6-8 Hz tremor of the arms which is worse when his arms are outstretched. His father suffered from a similar complaint. What is the most suitable first-line treatment?

- A. Amitriptyline
- B. Propranolol
- C. D-penicillamine
- D. Levodopa
- E. Diazepam

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Essential tremor is an AD condition that is made worse when arms are outstretched, made better by alcohol and propranolol

This patient has a typical history of essential tremor. Propranolol is generally considered the first-line treatment

Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

Features
- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

Management
- propranolol is first-line
- primidone is sometimes used

Question 35 of 164

A 65-year-old man is referred to the neurology outpatient clinic due to a resting tremor of his right hand. A diagnosis of Parkinson's disease is made. He is otherwise well and is not currently disabled by his symptoms. What is the most appropriate treatment?

- A. Selegiline
- B. No treatment
- C. New generation dopamine receptor agonist e.g. ropinirole
- D. Conventional dopamine receptor agonist e.g. bromocriptine
- E. Antimuscarinics

Question 35 of 164

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Dopamine receptor agonists
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- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
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- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 36 of 164

A 54-year-old man is admitted to the Emergency Department with a left hemiplegia. His symptoms started around 4 hours ago and he has had no headache, visual disturbance or loss of consciousness. On examination a dense left hemiplegia is noted. Blood pressure is 120/78 mmHg, GCS is 15/15 and pupils are equal and reactive to light. An urgent CT scan is performed shortly after his arrival. This demonstrates no abnormality. What is the most appropriate initial management?

- A. Enoxaparin
- B. Alteplase
- C. Dexamethasone
- D. Warfarin
- E. Aspirin

Question 36 of 164

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- C. Dexamethasone
- D. Warfarin
- E. Aspirin

Stroke thrombolysis - only consider if less than 3 hours and haemorrhage excluded

This patient has had an ischaemic stroke. He is however outside the thrombolytic window and should therefore be treated with aspirin

Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued guidelines in 2008.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commence on a statin

Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

*SIGN recommend a window of 4.5 hours

Question 37 of 164

A 63-year-old female is reviewed in the rapid access transient ischaemic attack clinic. For the past three weeks she has been having episode of transient loss of vision in the right eye. Carotid ultrasound reveals a 48% stenosis of her right carotid artery and an ECG shows sinus rhythm. What is the most appropriate management of this patient?

- A. Warfarin
- B. Aspirin and clopidogrel
- C. Carotid endarterectomy
- D. Aspirin
- E. Aspirin and dipyridamole

Question 37 of 164

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- A. Warfarin
- B. Aspirin and clopidogrel
- C. Carotid endarterectomy
- D. Aspirin
- E. Aspirin and dipyridamole

Carotid artery endarterectomy is recommend if the patient has suffered a stroke or TIA in the carotid territory and is not severely disabled. It should only be considered if the carotid stenosis is greater than 70% or 50%, depending on the reporting criteria used - please see below.

Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who've had a suspected TIA:

	Criteria	Points
A	**A**ge = 60 years	1
B	**B**lood pressure = 140/90 mmHg	1
C	**C**linical features - Unilateral weakness - Speech disturbance, no weakness	 2 1
D	**D**uration of symptoms - > 60 minutes - 10-59 minutes	 2 1
	Patient has diabetes	1

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision on brain imaging
- if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2005 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- low-dose aspirin combined with modified-release dipyridamole is recommended as first-line treatment. After 2 years treatment should revert to low-dose aspirin alone
- if aspirin cannot be taken, clopidogrel alone

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST* criteria or > 50% according to NASCET** criteria

*European Carotid Surgery Trialists' Collaborative Group
**North American Symptomatic Carotid Endarterectomy Trial

Question 38 of 164

Neurofibromatosis type 1 is associated with a gene defect on which chromosome?

- A. Chromosome 4
- B. Chromosome 11
- C. Chromosome 16
- D. Chromosome 17
- E. Chromosome 22

Question 38 of 164

Neurofibromatosis type 1 is associated with a gene defect on which chromosome?

- A. Chromosome 4
- B. Chromosome 11
- C. Chromosome 16
- D. Chromosome 17
- E. Chromosome 22

One of our registered users sent the following mnemonic to us:

- NF1: chromosome 17 - as neurofibromatosis has 17 characters
- NF2: chromosome 22 - all the 2's

Neurofibromatosis

There are two types of neurofibromatosis, NF1 and NF2. Both are inherited in an autosomal dominant fashion

NF1 is also known as von Recklinghausen's syndrome. It is caused by a gene mutation on chromosome 17 which encodes neurofibromin and affects around 1 in 4,000

NF2 is caused by gene mutation on chromosome 22 and affects around 1 in 100,000

Features

NF1	NF2
Café-au-lait spots (= 6, 15 mm in diameter) Axillary/groin freckles Peripheral neurofibromas Iris: Lisch nodules in > 90% Scoliosis	Bilateral acoustic neuromas

Question 39 of 164

Which one of the following is least associated with the development of chorea?

- A. Haemochromatosis
- B. Ataxic telangiectasia
- C. Carbon monoxide poisoning
- D. SLE
- E. Huntington's disease

Question 39 of 164

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Chorea

Chorea describes rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus

Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

Question 40 of 164

A 19-year-old female presents complaining of visual disturbance. Examination reveals a bitemporal hemianopia with predominately the lower quadrants being affected. What is the most likely lesion?

- A. Brainstem lesion
- B. Craniopharyngioma
- C. Frontal lobe lesion
- D. Pituitary macroadenoma
- E. Right occipital lesion

Question 40 of 164

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Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Visual field defects

The main points for the exam are:
- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

Homonymous hemianopia
- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias*
- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details: http://www.ncbi.nlm.nih.gov/pubmed/9109741

Question 41 of 164

A 78-year-old man is seen in the Memory clinic. His daughter reports that for the past 12 months he has become increasingly forgetful and has now started to wonder around at night. A mini-mental test is performed and he scores 18 out of 30. Neurological examination is unremarkable. A full blood screen is also requested, all of which comes back as normal. What is the most appropriate next step?

- A. Arrange a MRI head
- B. Perform carotid Dopplers
- C. Give practical advice + advise family to contact Alzheimer's Society
- D. Prescribe aspirin + simvastatin
- E. Prescribe donepezil

Question 41 of 164

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Neuroimaging is required to diagnose dementia

Dementia

Dementia is though to affect over 700,000 people in the UK and accounts for a large amount of health and social care spending. The most common cause of dementia in the UK is Alzheimer's disease followed by vascular and Lewy body dementia. These conditions may coexist.

Features

- diagnosis can be difficult and is often delayed
- the mini-mental state examination is widely used. A score of less than 24 out of 30 suggests dementia

Management

- in primary care a blood screen is usually sent to exclude reversible causes (e.g. Hypothyroidism). NICE recommend the following tests: FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. Patients are now commonly referred on to old-age psychiatrists (sometimes working in 'memory clinics').
- in secondary care neuroimaging is performed* to exclude other reversible conditions (e.g. Subdural haematoma, normal pressure hydrocephalus) and help provide information on aetiology to guide prognosis and management

*in the 2006 NICE guidelines structural imaging was said to be essential for diagnosis

Question 42 of 164

A 34-year-old man is reviewed in the neurology clinic. He has been established on sodium valproate for primary generalised epilepsy. Despite now taking a therapeutic dose he continues to have seizures and is troubled by weight gain since starting sodium valproate. He asks to stop the his current medication and try a different drug. Which one of the following drugs would be the most appropriate second-line treatment?

- A. Lamotrigine
- B. Ethosuximide
- C. Pregabalin
- D. Gabapentin
- E. Tiagabine

Question 42 of 164

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- D. Gabapentin
- E. Tiagabine

Monotherapy with another drug should be attempted before combination therapy is started. Caution should be exercised when combining sodium valproate and lamotrigine as serious skin rashes such as Steven-Johnson's syndrome may be provoked

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures

- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 43 of 164

Which one of the following features is most suggestive of Lewy body dementia

- A. Disinhibition
- B. Emotional lability
- C. Symptoms worsen with neuroleptics
- D. Urinary incontinence
- E. Paucity of extrapyramidal signs

Question 43 of 164

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Lewy body dementia

Lewy body dementia is an increasingly recognised cause of dementia, accounting for up to 20% of cases. The characteristic pathological feature is cytoplasmic neuronal inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas

The relationship between Parkinson's disease and Lewy body dementia is complicated, particularly as dementia is often seen in Parkinson's disease. Also, up to 40% of patients with Alzheimer's have Lewy bodies

Neuroleptics should be avoided in Lewy body dementia as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent

Features

- progressive cognitive impairment
- parkinsonism
- visual hallucinations (other features such as delusions and non-visual hallucinations may also be seen)

Question 44 of 164

Which one of the following features is not associated with an oculomotor nerve palsy?

- A. Miosis
- B. Ptosis
- C. Eye is deviated 'down and out'
- D. Pain if due to a posterior communicating artery aneurysm
- E. Diplopia

Question 44 of 164

Which one of the following features is not associated with an oculomotor nerve palsy?

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- B. Ptosis
- C. Eye is deviated 'down and out'
- D. Pain if due to a posterior communicating artery aneurysm
- E. Diplopia

Ptosis + dilated pupil = third nerve palsy; ptosis + constricted pupil = Horner's

Oculomotor nerve palsy is typically associated with a dilated pupil

Third nerve palsy

Features
- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

Causes
- diabetes mellitus
- vasculitis e.g. temporal arteritis, SLE
- false localizing sign* due to uncal herniation through tentorium if raised ICP
- posterior communicating artery aneurysm (pupil dilated)
- cavernous sinus thrombosis
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia -caused by midbrain strokes
- other possible causes: amyloid, multiple sclerosis

*this term is usually associated with sixth nerve palsies but it may be used for a variety of neurological presentations

Question 45 of 164

A 40-year-old woman presents with recurrent episode of vertigo associated with a feeling or 'fullness' and 'pressure' in her ears. She thinks his hearing is worse during the attacks. Clinical examination is unremarkable. What is the most likely diagnosis?

- A. Meniere's disease
- B. Benign paroxysmal positional vertigo
- C. Acoustic neuroma
- D. Multiple sclerosis
- E. Somatisation

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- B. Benign paroxysmal positional vertigo
- C. Acoustic neuroma
- D. Multiple sclerosis
- E. Somatisation

Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours

Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit

Question 46 of 164

A 55-year-old man is referred to the neurology clinic due to a resting tremor and an abnormal gait characterised by short, shuffling steps. Which one of the following features would point towards a diagnosis of Parkinson's disease rather than parkinsonism of another cause?

- A. Asymmetrical tremor
- B. Bradykinesia
- C. Impairment of vertical gaze
- D. Confusion
- E. Poor response to levodopa therapy

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- C. Impairment of vertical gaze
- D. Confusion
- E. Poor response to levodopa therapy

Asymmetrical symptoms suggests idiopathic Parkinson's

Parkinson's disease: features

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

Bradykinesia
- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

Tremor
- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

Rigidity
- lead pipe
- cogwheel: due to superimposed tremor

Other characteristic features
- flexed posture
- short, shuffling steps
- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur

Question 47 of 164

A 76-year-old man is reviewed in the Elderly Medicine clinic. He is concerned about his increasing forgetfulness over the past six months. His daughter notes he has generally 'slowed down' and struggles to follow conversations. Over the past month he has noted increasingly frequent episodes of urinary incontinence. He has also had one episode of faecal incontinence in the past week. On examination he is noted to have brisk reflexes and a short, shuffling gait. No cerebellar signs are noted. What is the most likely diagnosis?

- A. Multiple system atrophy
- B. Parkinson's disease
- C. Normal pressure hydrocephalus
- D. Urinary tract infection
- E. Pick's disease

Question 47 of 164

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- B. Parkinson's disease
- C. Normal pressure hydrocephalus
- D. Urinary tract infection
- E. Pick's disease

Urinary incontinence + gait abnormality + dementia = normal pressure hydrocephalus

The presence of dementia and absence of cerebellar signs point away from a diagnosis of multiple system atrophy

Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis

A classical triad of features is seen
- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson's disease)

Imaging
- hydrocephalus with an enlarged fourth ventricle

Management
- ventriculoperitoneal shunting

Question 48 of 164

During a routine cranial nerve examination the following findings are observed:
Rinne's test: Air conduction > bone conduction in both ears
Weber's test: Localises to the right side

What do these tests imply?

- A. Left conductive deafness
- B. Normal hearing
- C. Right conductive deafness
- D. Right sensorineural deafness
- E. Left sensorineural deafness

Question 48 of 164

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- D. Right sensorineural deafness
- E. Left sensorineural deafness

In Weber's test if there is a sensorineural problem the sound is localised to the unaffected side (right) indicating a problem on the left side

Rinne's and Weber's test

Performing both Rinne's and Weber's test allows differentiation of conductive and sensorineural deafness

Rinne's test

- tuning fork is placed over mastoid process, followed by repositioning just over external acoustic meatus
- air conduction (AC) is normally better than bone conduction (BC)
- if BC > AC then conductive deafness

Weber's test

- tuning fork is placed over middle of forehead, patient is asked which side is loudest
- in unilateral sensorineural deafness, sound is localised to the 'good' side
- in unilateral conductive deafness, sound is localised to the 'bad' side

Question 499 of 164

A 54-year-old man with small cell lung cancer complains of muscle weakness. Each one of the following are features of Lambert-Eaton syndrome, except:

- A. Proximal muscles more commonly affected
- B. Hyporeflexia
- C. Dry mouth
- D. Repeated muscle contractions lead to decreased muscle strength
- E. Impotence

Question 499 of 164

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- B. Hyporeflexia
- C. Dry mouth
- D. Repeated muscle contractions lead to decreased muscle strength
- E. Impotence

In myasthenia gravis repeated muscle contractions lead to reduced muscle strength. The opposite is however classically seen in the related disorder Lambert-Eaton syndrome

Lambert-Eaton syndrome

Lambert-Eaton myasthenic syndrome is seen in association with small cell lung cancer, and to a lesser extent breast and ovarian cancer. It may also occur independently as an autoimmune disorder. Lambert-Eaton myasthenic syndrome is caused by an antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system

Features
- repeated muscle contractions lead to increased muscle strength* (in contrast to myasthenia gravis)
- limb girdle weakness (affects lower limbs first)
- hyporeflexia
- autonomic symptoms: dry mouth, impotence, difficultly micturating
- ophthalmoplegia and ptosis not commonly a feature (unlike in myasthenia gravis)

EMG
- incremental response to repetitive electrical stimulation

Management
- treatment of underlying cancer
- immunosuppression, for example with prednisolone and/or azathioprine
- 3,4-diaminopyridine is currently being trialled**
- intravenous immunoglobulin therapy and plasma exchange may be beneficial

*in reality this is seen in only 50% of patients and following prolonged muscle use muscle strength will eventually decrease

**works by blocking potassium channel efflux in the nerve terminal so that the action potential duration is increased. Calcium channels can then be open for a longer time and allow greater acetylcholine release to the stimulate muscle at the end plate

Question 50 of 164

A 69-year-old man who is known to have Alzheimer's disease is reviewed in clinic. His latest Mini Mental State Examination (MMSE) score is 18 out of 30. What is the most appropriate management?

A. Supportive care + memantine

B. Supportive care + trial of citalopram

C. Supportive care

D. Supportive care + donepezil + low-dose aspirin

E. Supportive care + donepezil

Question 50 of 164

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- C. Supportive care
- D. Supportive care + donepezil + low-dose aspirin
- E. Supportive care + donepezil

Alzheimer's disease

Alzheimer's disease is a progressive degenerative disease of the brain accounting for the majority of dementia seen in the UK

Genetics

- most cases are sporadic
- 5% are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form
- apoprotein E allele E4 - encodes a cholesterol transport protein

Pathological changes

- macroscopic = widespread cerebral atrophy, particularly involving the cortex and hippocampus
- microscopic = intraneuronal neurofibrillary tangles, neuronal plaques, deficiency of neurons
- biochemical = deposition of type A-Beta-amyloid protein in cortex, deficit of Ach from damage to an ascending forebrain projection

Neurofibrillary tangles

- paired helical filaments are partly made from a protein called tau
- in AD are tau proteins are excessively phosphorylated

Management

- cholinesterase inhibitor (e.g. donepezil) - currently licensed for patients with Alzheimer's disease of moderate severity only*, classified as a Mini-Mental State Examination (MMSE) score of 10-20 out of 30

*draft guidance from NICE in 2010 suggests that donepezil may soon be recommended for patients with disease of mild severity as well

Question 51 of 164

Each of the following features are seen in myotonic dystrophy, except:

- A. Mild mental impairment
- B. Round face
- C. Frontal balding
- D. Myotonia
- E. Cataracts

Question 51 of 164

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Dystrophia myotonica - **D**M1
- **d**istal weakness initially
- autosomal **d**ominant
- **d**iabetes
- **d**ysarthria

Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics
- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	**DM2**
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features
- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features
- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Question 52 of 164

A 34-year-old man from West Africa is admitted due to confusion associated with left-sided weakness and ataxia. He is known to be HIV positive but is not on anti-retroviral treatment. The following results are obtained:

CD4 43 u/l

CT head Low attenuation diffusely.
No mass effect or enhancement

What is the most likely diagnosis?

- A. Toxoplasmosis
- B. Tuberculosis
- C. Progressive multifocal leukoencephalopathy
- D. *Cryptococcus*
- E. Cerebral lymphoma

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HIV: neurocomplications

Generalised neurological disease

Encephalitis
- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

Cryptococcus
- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

Progressive multifocal leukoencephalopathy (PML)
- widespread demyelination
- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment
- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

AIDS dementia complex
- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy

Focal neurological lesions

Toxoplasmosis
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

Tuberculosis
- single enhancing lesion

Question 53 of 164

Which one of the following features is most associated with temporal lobe lesions?

- A. Astereognosis
- B. Auditory agnosia
- C. Visual agnosia
- D. Disinhibition
- E. Expressive (Broca's) aphasia

Question 53 of 164

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- E. Expressive (Broca's) aphasia

Brain anatomy

The following neurological disorders/features may allow localisation of a brain lesion:

Parietal lobe lesions
- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

Occipital lobe lesions
- homonymous hemianopia
- cortical blindness
- visual agnosia

Temporal lobe lesion
- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia

Frontal lobes lesions
- expressive (Broca's) aphasia: located
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Question 54 of 164

A 33-year-old female with multiple sclerosis complains that her vision becomes blurred during a hot bath. What is this an example of?

- A. Uhthoff's phenomenon
- B. Oppenheim's sign
- C. Werdnig-Hoffman's sign
- D. Lambert's sign
- E. Lhermitte's sign

Question 54 of 164

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- B. Oppenheim's sign
- C. Werdnig-Hoffman's sign
- D. Lambert's sign
- E. Lhermitte's sign

This is Uhthoff's phenomenon. Lhermitte's sign describes paraesthesiae in the limbs on neck flexion

Oppenheim's sign is seen when scratching of the inner side of leg leads to extension of the toes. It is a sign of cerebral irritation and is not related to multiple sclerosis

Werdnig-Hoffman's disease is also known as spinal muscular atrophy

Multiple sclerosis: features

Visual
- optic neuritis: common presenting feature
- optic atrophy
- Uhthoff's phenomenon: worsening of vision following rise in body temperature
- internuclear ophthalmoplegia

Sensory
- pins/needles
- numbness
- trigeminal neuralgia
- Lhermitte's syndrome: paraesthesiae in limbs on neck flexion

Motor
- spastic weakness

Cerebellar
- ataxia
- tremor

Others
- urinary incontinence
- sexual dysfunction
- intellectual deterioration

Question 55 of 164

Which of the following factors indicate a poor prognosis in multiple sclerosis?

- A. Relapsing-remitting disease
- B. Presence of sensory symptoms
- C. Young age of onset
- D. Male sex
- E. Long interval between first two relapses

Question 55 of 164

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Multiple sclerosis: prognostic features

Good prognosis features
- female sex
- young age of onset
- relapsing-remitting disease
- sensory symptoms
- long interval between first two relapses

Ways of remembering prognostic features
- the typical patient carries a better prognosis than an atypical presentation

Question 56 of 164

A 25-year-old female is found to have a left hemiparesis following a deep vein thrombosis. An ECG shows RBBB with right axis deviation. What is the most likely underlying diagnosis?

- A. Ventricular septal defect
- B. Patent ductus arteriosus
- C. Ostium primum atrial septal defect
- D. Ostium secundum atrial septal defect
- E. Tetralogy of Fallot

Question 56 of 164

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- C. Ostium primum atrial septal defect
- D. Ostium secundum atrial septal defect
- E. Tetralogy of Fallot

The ostium secundum in this patient has allowed passage of an embolus from the right-sided circulation to the left causing a stroke

Atrial septal defects

Atrial septal defects (ASDs) are the most likely congenital heart defect to be found in adulthood. They carry a significant mortality, with 50% of patients being dead at 50 years. Two types of ASDs are recognised, ostium secundum and ostium primum. Ostium secundum are the most common

Features
- ejection systolic murmur, fixed splitting of S2
- embolism may pass from venous system to left side of heart causing a stroke

Ostium secundum (70% of ASDs)
- associated with Holt-Oram syndrome (tri-phalangeal thumbs)
- ECG: RBBB with RAD

Ostium primum
- present earlier than ostium secundum defects
- associated with abnormal AV valves
- ECG: RBBB with LAD, prolonged PR interval

Question 57 of 164

Which one of the following drugs is used in the management of multiple sclerosis?

- A. Beta-interferon
- B. Gamma-interferon
- C. Infliximab
- D. Rituximab
- E. Alpha-interferon

Question 57 of 164

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- D. Rituximab
- E. Alpha-interferon

Multiple sclerosis: management

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure. High dose steroids (e.g. IV methylprednisolone) may be given for 3-5 days to shorten the length of an acute relapse. Baclofen is helpful in controlling spasticity. Hallucinations are occasionally seen on the withdrawal of baclofen

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:

- relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
- secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
- reduces number of relapses and MRI changes, however doesn't reduce overall disability

Other drugs used in the management of multiple sclerosis include:

- glatiramer acetate: immunomodulating drug
- natalizumab: a recombinant monoclonal antibody that antagonises Alpha4Beta1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium into parenchymal tissue

Symptom control

- spasticity: baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine

Question 58 of 164

A 45-year-old woman presents complaining of visual disturbance. Examination reveals a left congruous homonymous hemianopia. Where is the lesion most likely to be?

- A. Optic chiasm
- B. Left occipital cortex
- C. Right optic tract
- D. Right occipital cortex
- E. Left optic tract

Question 58 of 164

A 45-year-old woman presents complaining of visual disturbance. Examination reveals a left congruous homonymous hemianopia. Where is the lesion most likely to be?

- A. Optic chiasm
- B. Left occipital cortex
- C. Right optic tract
- D. Right occipital cortex
- E. Left optic tract

Visual field defects:
- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects= optic radiation lesion or occipital cortex

Visual field defects

The main points for the exam are:
- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

Homonymous hemianopia
- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias
- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Question 59 of 164

Which one of the following features is most associated with parietal lobe lesions?

- A. Gerstmann's syndrome
- B. Perseveration
- C. Cortical blindness
- D. Superior homonymous quadrantanopia
- E. Wernicke's aphasia

Question 59 of 164

Which one of the following features is most associated with parietal lobe lesions?

- A. Gerstmann's syndrome
- B. Perseveration
- C. Cortical blindness
- D. Superior homonymous quadrantanopia
- E. Wernicke's aphasia

Brain anatomy

The following neurological disorders/features may allow localisation of a brain lesion:

Parietal lobe lesions
- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

Occipital lobe lesions
- homonymous hemianopia
- cortical blindness
- visual agnosia

Temporal lobe lesion
- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia

Frontal lobes lesions
- expressive (Broca's) aphasia: located
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Question 60 of 164

A 34-year-old is reviewed following an episode of 'collapse' whilst at church. She describes feeling hot and nauseous after standing up to sing a hymn. A few moments later she could 'feel herself going' and proceeded to fall to the ground. Her husband describes how her arms twitched at one point, but there was no tongue biting or urinary incontinence. She made a quick recovery and continued to finish the church service. Neurological examination today is unremarkable. What is the most appropriate advice regarding driving?

- A. Cannot drive for 6 months
- B. Cannot drive until investigations including ECG and neuroimaging have been performed
- C. No need to inform DVLA
- D. Cannot drive for 4 weeks
- E. Inform DVLA but can continue to drive

Question 60 of 164

A 34-year-old is reviewed following an episode of 'collapse' whilst at church. She describes feeling hot and nauseous after standing up to sing a hymn. A few moments later she could 'feel herself going' and proceeded to fall to the ground. Her husband describes how her arms twitched at one point, but there was no tongue biting or urinary incontinence. She made a quick recovery and continued to finish the church service. Neurological examination today is unremarkable. What is the most appropriate advice regarding driving?

- A. Cannot drive for 6 months
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- C. No need to inform DVLA
- D. Cannot drive for 4 weeks
- E. Inform DVLA but can continue to drive

DVLA - simple faint - no need to inform DVLA

This is a typical history of a simple faint - there are no features to suggest epilepsy or another organic cause

DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- first seizure: 1 year off driving
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

Question 61 of 164

A 24-year-old woman who is 14 weeks pregnant presents with a severe migraine. She has a long history of migraine and stopped propranolol prophylaxis when she found out she was pregnant. Unfortunately the headache has not responded to paracetamol 1g. What is the most appropriate next step?

- A. Ergotamine
- B. Nasal zolmitriptan
- C. Ibuprofen 400mg
- D. Almotriptan 12.5mg
- E. Codeine 30mg

Question 61 of 164

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- D. Almotriptan 12.5mg
- E. Codeine 30mg

Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

Migraine during pregnancy

- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

Migraine and the combined oral contraceptive (COC) pill

- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

Migraine and menstruation

- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefanamic acid or a combination of aspirin, parcetamol and caffeine. Triptans are also recommended in the acute situation

Migraine and hormone replacement therapy (HRT)

- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

Question 62 of 164

A 66-year-old woman is investigated for ascites and found to have ovarian cancer. She presents due to 'unsteadiness'. On examination there is evidence of nystagmus and past-pointing. Which one of the following antibodies is most likely to be present?

- A. Anti-Hu
- B. Anti-Yo
- C. Anti-Ri
- D. Anti-Ro
- E. Anti-La

Question 62 of 164

A 66-year-old woman is investigated for ascites and found to have ovarian cancer. She presents due to 'unsteadiness'. On examination there is evidence of nystagmus and past-pointing. Which one of the following antibodies is most likely to be present?

- A. Anti-Hu
- B. Anti-Yo
- C. Anti-Ri
- D. Anti-Ro
- E. Anti-La

This lady has developed cerebellar syndrome secondary to anti-Yo antibodies.

Paraneoplastic syndromes affecting nervous system

Lambert-Eaton myasthenic syndrome
- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

Anti-Hu
- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

Anti-Yo
- associated with ovarian and breast cancer
- cerebellar syndrome

Anti-GAD antibody
- associated with breast, colorectal and small cell lung carcinoma
- stiff person’s syndrome or diffuse hypertonia

Anti-Ri
- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

Question 63 of 164

A 24-year-old man is seen in the 'First Seizure' clinic. He has been referred by the local the Emergency Department following a single episode of a witnessed seizure. Which one of the following factors would be least relevant when deciding whether to start anti-epileptic drugs after a single seizure?

- A. Brain imaging shows a structural abnormality
- B. The patient has a neurological deficit
- C. The EEG shows unequivocal epileptic activity
- D. The patient is less than 45 years old
- E. The patient considers the risk of having a further seizure unacceptable

Question 63 of 164

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- B. The patient has a neurological deficit
- C. The EEG shows unequivocal epileptic activity
- D. The patient is less than 45 years old
- E. The patient considers the risk of having a further seizure unacceptable

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures

- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 64 of 164

You are asked to perform a neurological exam of the lower limbs on a patient with multiple sclerosis. Which one of the following findings is least typical?

- A. Decreased tone
- B. Patellar clonus
- C. Upgoing plantars
- D. Weakness
- E. Brisk reflexes

Question 64 of 164

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- B. Patellar clonus
- C. Upgoing plantars
- D. Weakness
- E. Brisk reflexes

In multiple sclerosis there is demyelination of the central nervous system and hence upper motor neuron signs are seen

Multiple sclerosis: features

Visual
- optic neuritis: common presenting feature
- optic atrophy
- Uhthoff's phenomenon: worsening of vision following rise in body temperature
- internuclear ophthalmoplegia

Sensory
- pins/needles
- numbness
- trigeminal neuralgia
- Lhermitte's syndrome: paraesthesiae in limbs on neck flexion

Motor
- spastic weakness

Cerebellar
- ataxia
- tremor

Others
- urinary incontinence
- sexual dysfunction
- intellectual deterioration

Question 65 of 164

A 23-year-old man is admitted following the sudden onset of an occipital headache. On examination GCS is 15/15, neurological examination is unremarkable but neck stiffness is noted. A subarachnoid haemorrhage is suspected but the CT scan is normal. At what time should a lumbar puncture be done to exclude the diagnosis?

- A. Immediately
- B. 2 hours post-headache
- C. 4 hours post-headache
- D. 12 hours post-headache
- E. 24 hours post-headache

Question 65 of 164

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- A. Immediately
- B. 2 hours post-headache
- C. 4 hours post-headache
- D. 12 hours post-headache
- E. 24 hours post-headache

If the patient was acutely unwell or had an altered GCS then discussion with neurosurgery may be appropriate rather than waiting 12 hours

Subarachnoid haemorrhage

Causes
- 85% are due to rupture of berry aneurysms (conditions associated with berry aneurysms include adult polycystic kidney disease, Ehlers-Danlos syndrome and coarctation of the aorta)
- AV malformations
- trauma
- tumours

Investigations
- CT: negative in 5%
- LP: done after 12 hrs (allowing time for xanthochromia to develop)

Complications
- rebleeding (in 30%)
- obstructive hydrocephalus (due to blood in ventricles)
- vasospasm leading to cerebral ischaemia

Management
- neurosurgical opinion: no clear evidence over early surgical intervention against delayed intervention
- nimodipine (e.g. 60mg / 4 hrly, if BP allows) has been shown to reduce the severity of neurological deficits but doesn't reduce rebleeding*

*the way nimodipine works in subarachnoid haemorrhage is not fully understood. It has been previously postulated that it reduces cerebral vasospasm (hence maintaining cerebral perfusion) but this has not been demonstrated in studies

Question 66 of 164

Which one of the following is least associated with the development of chorea?

- A. Ataxic telangiectasia
- B. SLE
- C. Wilson's disease
- D. Oral contraceptive pill
- E. Infective endocarditis

Question 66 of 164

Which one of the following is least associated with the development of chorea?

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- B. SLE
- C. Wilson's disease
- D. Oral contraceptive pill
- E. Infective endocarditis

Chorea can be a very rare manifestation of infective endocarditis, following embolisation to the basal ganglia. It is however the least likely of the above five options

Chorea

Chorea describes rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus

Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

Question 67 of 164

A 67-year-old man is reviewed in the neurology clinic due to concerns about increasing clumsiness. Examination reveals an ataxic gait and increased upper limb tone with cog-wheel rigidity. Blood pressure is 135/80 lying and 95/70 standing. What is the most likely diagnosis?

- A. Motor neuron disease
- B. Progressive supranuclear palsy
- C. Parkinson's disease
- D. Multiple sclerosis
- E. Multiple system atrophy

Question 67 of 164

A 67-year-old man is reviewed in the neurology clinic due to concerns about increasing clumsiness. Examination reveals an ataxic gait and increased upper limb tone with cog-wheel rigidity. Blood pressure is 135/80 lying and 95/70 standing. What is the most likely diagnosis?

- A. Motor neuron disease
- B. Progressive supranuclear palsy
- C. Parkinson's disease
- D. Multiple sclerosis
- E. Multiple system atrophy

Whilst postural hypotension may be seen in Parkinson's disease the cerebellar signs point towards a diagnosis of multiple system atrophy

Multiple system atrophy

Shy-Drager syndrome is a type of multiple system atrophy

Features
- Parkinsonism
- autonomic disturbance (atonic bladder, postural hypotension)
- cerebellar signs

Question 68 of 164

Which of the following drugs is least likely to cause peripheral neuropathy?

- A. Amiodarone
- B. Vincristine
- C. Trimethoprim
- D. Isoniazid
- E. Nitrofurantoin

Question 68 of 164

Which of the following drugs is least likely to cause peripheral neuropathy?

- A. Amiodarone
- B. Vincristine
- C. Trimethoprim
- D. Isoniazid
- E. Nitrofurantoin

Trimethoprim is not listed in the BNF as causing peripheral neuropathy

Drugs causing peripheral neuropathy

Drugs causing a peripheral neuropathy
- antibiotics: nitrofurantoin, metronidazole
- amiodarone
- isoniazid
- vincristine
- tricyclic antidepressants

Question 69 of 164

A 14-year-old male is noted to have optic atrophy on fundoscopy. Neurological exam reveals dysarthric speech and nystagmus. Knee and ankle jerks are absent but there is an extensor plantar response. What is the likely diagnosis?

- A. Leber's optic atrophy
- B. Ataxic telangiectasia
- C. Friedreich's ataxia
- D. Subacute combined degeneration of the cord
- E. Multiple sclerosis

Question 69 of 164

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- B. Ataxic telangiectasia
- C. Friedreich's ataxia
- D. Subacute combined degeneration of the cord
- E. Multiple sclerosis

Multiple sclerosis would be unlikely at this age

Friedreich's ataxia

Friedreich's ataxia is the most common of the early-onset hereditary ataxias. It is an autosomal recessive, trinucleotide repeat disorder characterised by a GAA repeat in the X25 gene on chromosome 9 (frataxin). Friedreich's ataxia is unusual amongst trinucleotide repeat disorders in not demonstrating the phenomenon of anticipation

The typical age of onset is 10-15 years old

Neurological features
- absent ankle jerks/extensor plantars
- cerebellar ataxia
- optic atrophy
- spinocerebellar tract degeneration

Other features
- hypertrophic obstructive cardiomyopathy (90%, most common cause of death)
- diabetes mellitus (10-20%)
- high-arched palate

Question 70 of 164

A 29-year-old female presents complaining of weakness in her arms, leading to increasing difficulties at work. On examination she has a bilateral ptosis and loss of the red-reflex in both eyes. Urine testing also reveals glycosuria. What is the most likely diagnosis?

- A. Myotonic dystrophy
- B. Homocystinuria
- C. Multiple sclerosis
- D. Myasthenia gravis
- E. HIV

Question 70 of 164

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- A. Myotonic dystrophy
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- C. Multiple sclerosis
- D. Myasthenia gravis
- E. HIV

Dystrophia myotonica - **D**M1

- **d**istal weakness initially
- autosomal **d**ominant
- **d**iabetes
- **d**ysarthria

These features are typical of myotonic dystrophy. The red-reflex is lost due to bilateral cataracts

Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	**DM2**
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Question 71 of 164

Which of the following is least associated with Parkinsonism?

- A. Chlorpromazine
- B. Progressive supranuclear palsy
- C. Dementia pugilistica
- D. Lead poisoning
- E. Wilson's disease

Question 71 of 164

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Parkinsonism

Causes of Parkinsonism
- Parkinson's disease
- drug-induced e.g. antipsychotics, metoclopramide - see below
- progressive supranuclear palsy
- multiple system atrophy
- Wilson's disease
- post-encephalitis
- dementia pugilistica (secondary to chronic head trauma e.g. boxing)
- toxins: carbon monoxide, MPTP

Drugs causing Parkinsonism
- phenothiazines: e.g. chlorpromazine
- butyrophenones: haloperidol, droperidol
- metoclopramide

Domperidone does not cross the blood-brain barrier and therefore does not cause extra-pyramidal side-effects

Question 72 of 164

Which one of the following is most likely to cause a bilateral facial nerve palsy?

- A. Acoustic neuroma
- B. Cholesteatoma
- C. Bell's palsy
- D. Sarcoidosis
- E. Amyloidosis

Question 72 of 164

Which one of the following is most likely to cause a bilateral facial nerve palsy?

- A. Acoustic neuroma
- B. Cholesteatoma
- C. Bell's palsy
- D. Sarcoidosis
- E. Amyloidosis

Facial nerve

Supply - 'face, ear, taste, tear'
- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy
- sarcoidosis
- Guillain-Barre syndrome
- polio, Lyme disease

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron	Upper motor neuron
• Bell's palsy • Ramsay-Hunt syndrome (due to herpes zoster) • acoustic neuroma • parotid tumours • HIV • multiple sclerosis* • diabetes mellitus	• stroke

LMN vs. UMN
- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

*may also cause an UMN palsy

Question 73 of 164

A 47-year-old man presents to the Emergency Department with a three day history of severe headache associated with vomiting. There is no past medical history of note. On examination blood pressure is 98/62 mmHg, pulse is 108 bpm and temperature is 37.0ºC. There is mild neck stiffness and a partial third nerve palsy of the left eye. Blood rests reveal:

Hb	14.8 g/dl
Plt	373 * 10^9/l
WBC	15.6 * 10^9/l
Na^+	133 mmol/l
K^+	5.1 mmol/l
Urea	4.2 mmol/l
Creatinine	99 µmol/l
Free T4	9 pmol/l (range 10-22)

What is the most likely diagnosis?

- A. Subarachnoid haemorrhage
- B. Cavernous sinus thrombosis
- C. Meningitis
- D. Pituitary apoplexy
- E. Lateral sinus thrombosis

Question 73 of 164

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Na^+	133 mmol/l
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Urea	4.2 mmol/l
Creatinine	99 µmol/l
Free T4	9 pmol/l (range 10-22)

What is the most likely diagnosis?

- A. Subarachnoid haemorrhage
- B. Cavernous sinus thrombosis
- C. Meningitis
- D. Pituitary apoplexy
- E. Lateral sinus thrombosis

The hypotension, electrolytes and low free T4 point towards hypopituitarism. Clinically, pituitary apoplexy can mimic a subarachnoid haemorrhage

Pituitary apoplexy

Sudden enlargement of pituitary tumour secondary to haemorrhage or infarction

Features

- sudden onset headache similar to that seen in subarachnoid haemorrhage
- vomiting
- neck stiffness
- visual field defects: classically bitemporal superior quadrantic defect
- extraocular nerve palsies
- features of pituitary insufficiency e.g. Hypotension secondary to hypoadrenalism

Question 74 of 164

Which one of the following is least recognised as a cause of autonomic neuropathy

- A. Guillain-Barre syndrome
- B. New variant CJD
- C. Diabetes
- D. Parkinson's
- E. HIV

Question 74 of 164

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- A. Guillain-Barre syndrome
- B. New variant CJD
- C. Diabetes
- D. Parkinson's
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Autonomic neuropathy

Features
- impotence, inability to sweat, postural hypotension
- postural hypotension e.g. drop of 30/15 mmHg
- loss of decrease in heart rate following deep breathing
- pupils: dilates following adrenaline instillation

Causes
- diabetes
- Guillain-Barre syndrome
- multisystem atrophy (MSA), Shy-Drager syndrome
- Parkinson's
- infections: HIV, Chagas' disease, neurosyphilis
- drugs: antihypertensives, tricyclics
- craniopharyngioma

Question 75 of 164

Which one of the following causes of peripheral neuropathy is most associated with demyelination?

- A. Vasculitis
- B. Alcohol
- C. Hereditary sensorimotor neuropathies (HSMN) type I
- D. Vitamin B12 deficiency
- E. Diabetes mellitus

Question 75 of 164

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- B. Alcohol
- C. Hereditary sensorimotor neuropathies (HSMN) type I
- D. Vitamin B12 deficiency
- E. Diabetes mellitus

Peripheral neuropathy: demyelinating vs. axonal

Demyelinating pathology
- Guillain-Barre syndrome
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- amiodarone
- hereditary sensorimotor neuropathies (HSMN) type I
- paraprotein neuropathy

Axonal pathology
- alcohol
- diabetes mellitus*
- vasculitis
- vitamin B12 deficiency*
- hereditary sensorimotor neuropathies (HSMN) type II

* may also cause a demyelinating picture

Question 76 of 164

A patient is noted to have absent ankle jerks combined with extensor plantars on examination. Which one of the following is least likely?

- A. Multiple sclerosis
- B. Subacute combined degeneration of the cord
- C. Syringomyelia
- D. Syphilis
- E. Motor neuron disease

Question 76 of 164

A patient is noted to have absent ankle jerks combined with extensor plantars on examination. Which one of the following is least likely?

- A. Multiple sclerosis
- B. Subacute combined degeneration of the cord
- C. Syringomyelia
- D. Syphilis
- E. Motor neuron disease

Multiple sclerosis would not give this combination of physical signs

Absent ankle jerks, extensor plantars

Typically caused by lesion producing both upper motor neuron (extensor plantars) and lower motor neuron (absent ankle jerk) signs

Causes

- subacute combined degeneration of the cord
- motor neuron disease
- Friedreich's ataxia
- syringomyelia
- taboparesis (syphilis)
- conus medullaris lesion

Question 77 of 164

A 25-year-old female presents 5 days after discharge from hospital following an admission for suspected meningitis. A lumbar puncture was performed which showed no evidence of infection. Unfortunately she developed a headache 48 hours after discharge. This has now lasted 3 days and has failed to settle with analgesia. Which one of the following treatment options should be considered?

- A. Intrathecal steroids
- B. Repeat lumbar puncture
- C. Course of oral prednisolone
- D. Blood patch
- E. Intravenous fluids on top of oral fluid intake

Question 77 of 164

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Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline

Question 78 of 164

A 34-year-old female is reviewed in the neurology clinic due to a number of 'funny-dos'. She describes a sensation that her surroundings are unreal, 'like a dream'. Following this she has been told that she starts to smack her lips, although she has no recollection of doing this. What is the most likely diagnosis?

- A. Myoclonic seizure
- B. Simple partial seizure
- C. Complex partial seizure
- D. Partial seizure progressing to generalised seizure
- E. Absence seizure

Question 78 of 164

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- C. Complex partial seizure
- D. Partial seizure progressing to generalised seizure
- E. Absence seizure

With simple partial seizures there is no disturbance of consciousness or awareness. Lip smacking is an example of an automatism - an automatic, repetitive act

Epilepsy: classification

Basics
- two main categories are generalised and partial seizures
- partial seizures may progress to general seizures
- other types: myoclonic, atypical absence, atonic and tonic seizures are usually seen in childhood

Generalised - no focal features, consciousness lost immediately
- grand mal (tonic-clonic)
- petit mal (absence seizures)
- partial seizures progressing to generalised seizures

Partial - focal features depending on location
- simple (no disturbance of consciousness or awareness)
- complex (consciousness is disturbed)
- temporal lobe --> aura, déjà vu, jamais vu; motor --> Jacksonian

Myoclonus
- occur in a variety of conditions

Question 79 of 164

A 52-year-old women presents with a two week history of dizziness when she rolls over in bed. She says it feels like the room is spinning around her. Examination of her ears and cranial nerves is unremarkable. Given the likely diagnosis of benign paroxysmal positional vertigo what is the most appropriate management?

- A. Trial of prochlorperazine
- B. Request MRI brain
- C. Advise review by an optician
- D. Perform Epley manoeuvre
- E. Trial of cinnarizine

Question 79 of 164

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- E. Trial of cinnarizine

Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo encountered. It is characterised by the sudden onset of dizziness and vertigo triggered by changes in head position

Features

- vertigo triggered by change in head position (e.g. rolling over in bed or gazing upwards)
- may be associated with nausea
- each episode typically lasts 10-20 seconds
- positive Halpike manoeuvre

BPPV has a good prognosis and usually resolves spontaneously after a few weeks to months. Symptomatic relief may be gained by:

- Epley manoeuvre (successful in around 80% of cases)

Medication is often prescribed (e.g. betahistine) but it tends to be of limited value

Question 80 of 164

A 46-year-old female presents with a burning sensation over the antero-lateral aspect of her right thigh. A diagnosis of meralgia paraesthetica is suspected. Which nerve is most likely to be affected?

- A. Common peroneal nerve
- B. Anterior cutaneous nerve of thigh
- C. Posterior cutaneous nerve of thigh
- D. Lateral cutaneous nerve of thigh
- E. Sciatic nerve

Question 80 of 164

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- D. Lateral cutaneous nerve of thigh
- E. Sciatic nerve

Burning thigh pain - ? meralgia paraesthetica - lateral cutaneous nerve of thigh compression

Meralgia paraesthetica

Basics

- caused by compression of lateral cutaneous nerve of thigh
- typically burning sensation over antero-lateral aspect of thigh

Question 81 of 164

A 19-year-old man is admitted following a generalised seizure. No past history is available as the man is currently in a postictal state. On examination it is noted that he has three patches of hypopigmented skin and fibromata under two of his finger nails. What is the most likely diagnosis?

- A. Neurofibromatosis
- B. Systemic lupus erythematous
- C. Vitiligo
- D. Solvent abuse
- E. Tuberous sclerosis

Question 81 of 164

A 19-year-old man is admitted following a generalised seizure. No past history is available as the man is currently in a postictal state. On examination it is noted that he has three patches of hypopigmented skin and fibromata under two of his finger nails. What is the most likely diagnosis?

- A. Neurofibromatosis
- B. Systemic lupus erythematous
- C. Vitiligo
- D. Solvent abuse
- E. Tuberous sclerosis

This man has a neurocutaneous syndrome which raises the possibility of neurofibromatosis or tuberous sclerosis. Given the areas of hypopigmentation and subungual fibromas the most likely diagnosis is tuberous sclerosis

Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

Cutaneous features
- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots* may be seen

Neurological features
- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

Also
- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Question 82 of 164

A 5-year-old boy is diagnosed as having absence seizures. What is the chance he will be seizure free by the age of 16-years-old?

- A. 5-10%
- B. 20-25%
- C. 40-45%
- D. 65-70%
- E. 90-95%

Question 82 of 164

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- C. 40-45%
- D. 65-70%
- E. 90-95%

Absence seizures - good prognosis: 90-95% become seizure free in adolescence

Absence seizures

Absence seizures (petit mal) are a form of generalised epilepsy that is mostly seen in children. The typical age of onset of 3-10 years old and girls are affected twice as commonly as boys

Features

- absences last a few seconds and are associated with a quick recovery
- seizures may be provoked by hyperventilation or stress
- the child is usually unaware of the seizure
- they may occur many times a day
- EEG: bilateral, symmetrical 3Hz spike and wave pattern

Management

- sodium valproate and ethosuximide are first-line treatment
- good prognosis - 90-95% become seizure free in adolescence

Question 83 of 164

Which one of the following is least likely to cause a raised protein level in the cerebrospinal fluid?

- A. Tuberculous meningitis
- B. Guillain-Barre syndrome
- C. Fungal meningitis
- D. Spinal block
- E. Systemic lupus erythematous

Question 83 of 164

Which one of the following is least likely to cause a raised protein level in the cerebrospinal fluid?

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- B. Guillain-Barre syndrome
- C. Fungal meningitis
- D. Spinal block
- E. Systemic lupus erythematous

Cerebrospinal fluid: raised protein

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose = > 2/3 blood glucose
- cells: red cells = 0, white cells < 5/mm^3

The following conditions are associated with raised protein levels

- Guillain-Barre syndrome
- tuberculous, fungal and bacterial meningitis
- spinal block (Froin's syndrome*)
- viral encephalitis

*describes an increase in CSF protein below a spinal canal blockage (e.g. tumour, disc, infection)

Question 84 of 164

A 34-year-old female with a history of primary generalised epilepsy asks for advice in the neurology clinic as she plans to start a family. She currently takes sodium valproate as monotherapy. What advice should be given regarding the prevention of neural tube defects?

- A. Folic acid 400 mcg per day once pregnancy has been confirmed
- B. Folic acid 1 mg per day once pregnancy has been confirmed
- C. Folic acid 5 mg per day starting nowi
- D. Folic acid 10 mg per day starting now
- E. Folic acid 400 mcg per day starting now

Question 84 of 164

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- B. Folic acid 1 mg per day once pregnancy has been confirmed
- C. Folic acid 5 mg per day starting now
- D. Folic acid 10 mg per day starting now
- E. Folic acid 400 mcg per day starting now

Epilepsy + pregnancy = 5mg folic acid

Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects

Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- phenytoin: associated with cleft palate

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

Question 85 of 164

Which one of the following is not a recognised causes of miosis?

- A. Old age
- B. Pontine haemorrhage
- C. Holmes-Adie pupil
- D. Argyll-Robertson pupil
- E. Horner's syndrome

Question 85 of 164

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- D. Argyll-Robertson pupil
- E. Horner's syndrome

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil

Miosis

Causes of miosis (small pupil)
- Horner's syndrome
- Argyll-Robertson pupil
- senile miosis
- pontine haemorrhage
- congenital

Drugs causes
- opiates
- parasympathomimetics: pilocarpine
- organophosphate toxicity

Question 86 of 164

A 62-year-old man is referred to the neurology clinic with worsening symptoms over the past few months. The neurologist suspects the patient has progressive supranuclear palsy. Which one of the following features is least likely to be seen in this patient?

- A. Poor response to L-dopa
- B. Impairment of horizontal gaze
- C. Falls
- D. Cognitive impairment
- E. Slurring of speech

Question 86 of 164

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- B. Impairment of horizontal gaze
- C. Falls
- D. Cognitive impairment
- E. Slurring of speech

Progressive supranuclear palsy: parkinsonism, impairment of vertical gaze

Impairment of vertical gaze is seen in progressive supranuclear palsy. Horizontal gaze impairment is sometimes seen later as the disease progresses, but would be atypical in a newly diagnosed patient.

Progressive supranuclear palsy

Overview
- aka Steele-Richardson-Olszewski syndrome
- a 'Parkinson Plus' syndrome

Features
- impairment of vertical gaze (down gaze worse than up gaze - patients may complain of difficultly reading or descending stairs)
- parkinsonism
- falls
- slurring of speech
- cognitive impairment

Management
- poor response to L-dopa

Question 87 of 164

A 15-year-old boy is reviewed. He has been referred by his GP with ptosis, diplopia and night blindness. On examination he is noted to have a degree of ophthalmoplegia, bilateral partial ptosis and evidence of retinitis pigmentosa during fundoscopy. His mother developed a similar problem when she was 18-years-old. What is the most likely diagnosis?

- A. Kearns-Sayre syndrome
- B. Alport's syndrome
- C. Usher syndrome
- D. Refsum disease
- E. Lawrence-Moon-Biedl syndrome

Question 87 of 164

A 15-year-old boy is reviewed. He has been referred by his GP with ptosis, diplopia and night blindness. On examination he is noted to have a degree of ophthalmoplegia, bilateral partial ptosis and evidence of retinitis pigmentosa during fundoscopy. His mother developed a similar problem when she was 18-years-old. What is the most likely diagnosis?

- A. Kearns-Sayre syndrome
- B. Alport's syndrome
- C. Usher syndrome
- D. Refsum disease
- E. Lawrence-Moon-Biedl syndrome

Kearns-Sayre syndrome
- mitochondrial inheritance
- onset < 20-years-old
- external ophthalmoplegia
- retinitis pigmentosa

Mitochondrial diseases

Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria. It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:
- inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote
- all children of affected males will not inherit the disease
- all children of affected females will inherit it
- generally encode rare neurological diseases
- poor genotype:phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

Histology
- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:
- Leber's optic atrophy
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

Question 88 of 164

A 29-year-old female presents complaining of double vision and unsteadiness. She has no past medical history of note. On examination she has limited movement of her eyes in all directions. Pupils are 3 mm, equal and reactive to light. Examination of the peripheral nervous system is normal other than reduced reflexes and the plantars are down going. Some past-pointing is also noted. What is the most likely diagnosis?

- A. Multiple sclerosis
- B. Conversion disorder
- C. Miller-Fisher syndrome
- D. Ataxic telangiectasia
- E. Friedreich's ataxia

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- B. Conversion disorder
- C. Miller-Fisher syndrome
- D. Ataxic telangiectasia
- E. Friedreich's ataxia

Miller-Fisher syndrome - areflexia, ataxia, ophthalmoplegia

This patient has Miller-Fisher syndrome, a variant of Guillain-Barre syndrome

Guillain-Barre syndrome

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

Pathogenesis
- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

Miller-Fisher syndrome
- variant of Guillain-Barre syndrome
- associated with areflexia, ataxia, ophthalmoplegia
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barre syndrome
- anti-GQ1b antibodies are present in 90% of cases

Question 89 of 164

In the treatment of migraine, sumatriptan is an example of a:

- A. Beta-blocker
- B. Alpha-blocker and a partial 5-HT2 agonist
- C. Specific 5-HT1 agonist
- D. 5-HT2 antagonist
- E. Tricyclic antidepressant

Question 89 of 164

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- D. 5-HT2 antagonist
- E. Tricyclic antidepressant

Migraine
- acute: 5-HT1 agonist
- prophylaxis: beta-blocker, 5-HT2 antagonist

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment
Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis
Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 90 of 164

A 54-year-old man presents concerned about leg weakness. On examination he is noted to have increased tone in both legs, brisk reflexes and weakness in both lower limbs. Examination of his upper limbs is normal. Which one of the following is least likely to produce these symptoms?

- A. HIV
- B. Amyloidosis
- C. Hereditary spastic paraplegia
- D. Multiple sclerosis
- E. Parasagittal meningioma

Question 90 of 164

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- C. Hereditary spastic paraplegia
- D. Multiple sclerosis
- E. Parasagittal meningioma

Amyloidosis is the least likely of the above options to result in a spastic paraparesis

Spastic paraparesis

Spastic paraparesis describes a upper motor neuron pattern of weakness in the lower limbs

Causes

- demyelination e.g. multiple sclerosis
- cord compression: trauma, tumour
- parasagittal meningioma
- tropical spastic paraparesis
- transverse myelitis e.g. HIV
- syringomyelia
- hereditary spastic paraplegia
- osteoarthritis of the cervical spine

Question 91 of 164

Which one of the following side-effects is least associated with the use of levodopa?

- A. Psychosis
- B. 'On-off' effect
- C. Postural hypotension
- D. Cardiac arrhythmias
- E. Galactorrhoea

Question 91 of 164

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- B. 'On-off' effect
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- D. Cardiac arrhythmias
- E. Galactorrhoea

Levodopa

Overview
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of L-dopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- no use in neuroleptic induced parkinsonism

Adverse effects
- dyskinesia
- 'on-off' effect
- postural hypotension
- cardiac arrhythmias
- nausea & vomiting
- psychosis
- reddish discolouration of urine upon standing

Question 92 of 164

Which one of the following antibodies are associated with painful sensory neuropathy in patients with small cell lung cancer?

- A. Anti-Ri
- B. Anti-GAD
- C. Anti-Ro
- D. Anti-Hu
- E. Anti-Yo

Question 92 of 164

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- B. Anti-GAD
- C. Anti-Ro
- D. Anti-Hu
- E. Anti-Yo

Paraneoplastic syndromes affecting nervous system

Lambert-Eaton myasthenic syndrome
- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

Anti-Hu
- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

Anti-Yo
- associated with ovarian and breast cancer
- cerebellar syndrome

Anti-GAD antibody
- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

Anti-Ri
- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

Question 93 of 164

A 62-year-old man presents with left-sided eye pain and diplopia for the past 2 days. Examination of his eyes shows his pupils equal and reactive to light with no proptosis. There is however an apparent palsy of the 6th cranial nerve associated with a partial 3rd nerve palsy on the left side. Examining the remaining cranial demonstrates hyperaesthesia of the upper face on the left side. Where is the likely lesion?

- A. Cavernous sinus
- B. Orbital apex
- C. Pons
- D. Cerebropontine angle
- E. Medulla

Question 93 of 164

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- B. Orbital apex
- C. Pons
- D. Cerebropontine angle
- E. Medulla

Intracranial venous thrombosis

Overview
- can cause cerebral infarction, much lesson common than arterial causes
- 50% of patients have isolated sagittal sinus thromboses - the remainder have coexistent lateral sinus thromboses and cavernous sinus thromboses

Features
- headache (may be sudden onset)
- nausea & vomiting
- papilloedema

Sagittal sinus thrombosis
- may present with seizures and hemiplegia
- parasagittal biparietal or bifrontal haemorrhagic infarctions are sometimes seen

Cavernous sinus thrombosis
- other causes of cavernous sinus syndrome: local infection (e.g. sinusitis), neoplasia, trauma
- ophthalmoplegia due to IIIrd, IVth and VIth nerve damage
- trigeminal nerve involvement may lead to hyperaesthesia of upper face and eye pain
- central retinal vein thrombosis
- swollen eyelids

Lateral sinus thrombosis
- VIth and VIIth cranial nerve palsies

Question 94 of 164

Lateral medullary syndrome is caused by occlusion of which one of the following blood vessels?

- A. Anterior inferior cerebellar artery
- B. Posterior cerebral artery
- C. Lateral sinus thrombosis
- D. Middle cerebral artery
- E. Posterior inferior cerebellar artery

Question 94 of 164

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Lateral medullary syndrome - PICA lesion - cerebellar signs, contralateral sensory loss & ipsilateral Horner's

Lateral medullary syndrome

Lateral medullary syndrome, also known as Wallenberg's syndrome, occurs following occlusion of the posterior inferior cerebellar artery

Cerebellar features
- ataxia
- nystagmus

Brainstem features
- ipsilateral: dysphagia, facial numbness, cranial nerve palsy e.g. Horner's
- contralateral: limb sensory loss

Question 95 of 164

A 63-year-old man is prescribed ropinirole for Parkinson's disease. What is the mechanism of action?

- A. MAO-B inhibitor
- B. Antimuscarinic
- C. Dopamine receptor agonist
- D. Dopamine receptor antagonist
- E. Decarboxylase inhibitor

Question 95 of 164

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- D. Dopamine receptor antagonist
- E. Decarboxylase inhibitor

Ropinirole - dopamine receptor agonist

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 96 of 164

How long should a patient stop driving for following a stroke?

- A. No restriction unless physical/visual impairment
- B. 1 month
- C. 3 month
- D. 6 months
- E. 12 months

Question 96 of 164

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- D. 6 months
- E. 12 months

DVLA advice post CVA: cannot drive for 1 month

DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- first seizure: 6 months off driving
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

Question 97 of 164

A 63-year-old man is prescribed selegiline for Parkinson's disease. What is the mechanism of action?

- A. Dopamine receptor antagonist
- B. Dopamine receptor agonist
- C. Monoamine Oxidase-B inhibitor
- D. Antimuscarinic
- E. Catechol-O-Methyl Transferase inhibitor

Question 97 of 164

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Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 98 of 164

A 63-year-old man is diagnosed as having restless legs syndrome. What is the most relevant blood test to perform?

- A. ESR
- B. Ferritin
- C. Blood glucose
- D. Urea and electrolytes
- E. Liver function tests

Question 98 of 164

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- B. Ferritin
- C. Blood glucose
- D. Urea and electrolytes
- E. Liver function tests

A case could be made for all the above tests but a low serum ferritin is most likely to be a cause of secondary restless legs syndrome

Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

Question 99 of 164

Which one of the following medications is most useful for helping to prevent attacks of Meniere's disease?

- A. Promethazine
- B. Prochlorperazine
- C. Betahistine
- D. Chlorphenamine
- E. Cinnarizine

Question 99 of 164

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- E. Cinnarizine

Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours

Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit

Question 100 of 164

Each one of the following is associated with ataxic telangiectasia, except:

- A. Telangiectasia
- B. Cerebellar ataxia
- C. Autosomal dominant inheritance
- D. Recurrent chest infections
- E. Increased risk of malignancy

Question 100 of 164

Each one of the following is associated with ataxic telangiectasia, except:

- A. Telangiectasia
- B. Cerebellar ataxia
- C. Autosomal dominant inheritance
- D. Recurrent chest infections
- E. Increased risk of malignancy

Ataxic telangiectasia

Basics
- autosomal recessive disorder
- combined immunodeficiency disorder

Features
- cerebellar ataxia
- telangiectasia
- recurrent chest infections
- 10% risk of developing malignancy, lymphoma or leukaemia, but also non-lymphoid tumours

Question 101 of 164

A 43-year-old woman with multiple sclerosis presents for review. She is having increasing problems with painful involuntary contractions of the leg muscles. What is the most appropriate first-line therapy?

- A. Referral for relaxation therapy
- B. Baclofen
- C. Diazepam
- D. Dantrolene
- E. Natalizumab

Question 101 of 164

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- E. Natalizumab

Multiple sclerosis: management

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure. High dose steroids (e.g. IV methylprednisolone) may be given for 3-5 days to shorten the length of an acute relapse. Baclofen is helpful in controlling spasticity. Hallucinations are occasionally seen on the withdrawal of baclofen

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:

- relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
- secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
- reduces number of relapses and MRI changes, however doesn't reduce overall disability

Other drugs used in the management of multiple sclerosis include:

- glatiramer acetate: immunomodulating drug
- natalizumab: a recombinant monoclonal antibody that antagonises Alpha4Beta1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium into parenchymal tissue

Symptom control

- spasticity: baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine

Question 102 of 164

A 75-year-old man is seen with his family who are concerned about his memory and behaviour over the past six months. A cognitive assessment is performed which seems to confirm the families concerns. A series of blood tests are performed to exclude reversible causes. A full blood count, urea and electrolytes, liver function tests and bone profile are requested. Which other blood tests is it most appropriate to request?

- A. Thyroid function tests, vitamin B12, glucose, syphilis, HIV
- B. Thyroid function tests, vitamin B12, folate, glucose
- C. Thyroid function tests, vitamin B12, folate, glucose, syphilis
- D. Thyroid function tests, vitamin B12
- E. Thyroid function tests, vitamin B12, syphilis, HIV

Question 102 of 164

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- B. Thyroid function tests, vitamin B12, folate, glucose
- C. Thyroid function tests, vitamin B12, folate, glucose, syphilis
- D. Thyroid function tests, vitamin B12
- E. Thyroid function tests, vitamin B12, syphilis, HIV

NICE do not recommend routine testing for syphilis and HIV.

Dementia

Dementia is though to affect over 700,000 people in the UK and accounts for a large amount of health and social care spending. The most common cause of dementia in the UK is Alzheimer's disease followed by vascular and Lewy body dementia. These conditions may coexist.

Features
- diagnosis can be difficult and is often delayed
- the mini-mental state examination is widely used. A score of less than 24 out of 30 suggests dementia

Management
- in primary care a blood screen is usually sent to exclude reversible causes (e.g. Hypothyroidism). NICE recommend the following tests: FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. Patients are now commonly referred on to old-age psychiatrists (sometimes working in 'memory clinics').
- in secondary care neuroimaging is performed* to exclude other reversible conditions (e.g. Subdural haematoma, normal pressure hydrocephalus) and help provide information on aetiology to guide prognosis and management

*in the 2006 NICE guidelines structural imaging was said to be essential for diagnosis

Question 103 of 164

The following drugs commonly exacerbate myasthenia gravis, except:

- A. Methotrexatei
- B. Gentamicin
- C. Beta-blockers
- D. Quinidine
- E. Penicillamine

Question 103 of 164

The following drugs commonly exacerbate myasthenia gravis, except:

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- B. Gentamicin
- C. Beta-blockers
- D. Quinidine
- E. Penicillamine

Myasthenia gravis: exacerbating factors

The most common exacerbating factor is exertion resulting in fatigability, which is the hallmark feature of myasthenia gravis . Symptoms become more marked during the day

The following drugs may exacerbate myasthenia:

- penicillamine
- quinidine, procainamide
- beta-blockers
- lithium
- phenytoin
- gentamicin

Question 104 of 164

Each one of the following is associated with Friedreich's ataxia, except:

- A. Increased risk of deep vein thrombosis
- B. Optic atrophy
- C. Cardiomyopathy
- D. Nystagmus
- E. High-arched palate

Question 104 of 164

Each one of the following is associated with Friedreich's ataxia, except:

- A. Increased risk of deep vein thrombosis
- B. Optic atrophy
- C. Cardiomyopathy
- D. Nystagmus
- E. High-arched palate

Friedreich's ataxia

Friedreich's ataxia is the most common of the early-onset hereditary ataxias. It is an autosomal recessive, trinucleotide repeat disorder characterised by a GAA repeat in the X25 gene on chromosome 9 (frataxin). Friedreich's ataxia is unusual amongst trinucleotide repeat disorders in not demonstrating the phenomenon of anticipation

The typical age of onset is 10-15 years old

Neurological features
- absent ankle jerks/extensor plantars
- cerebellar ataxia
- optic atrophy
- spinocerebellar tract degeneration

Other features
- hypertrophic obstructive cardiomyopathy (90%, most common cause of death)
- diabetes mellitus (10-20%)
- high-arched palate

Question 105 of 164

A 60-year-old man is diagnosed with Bell's palsy. What is the current evidenced base approach to the management of this condition?

- A. Refer for urgent surgical decompression
- B. Aciclovir
- C. No treatment
- D. Aciclovir + prednisolone
- E. Prednisolone

Question 105 of 164

A 60-year-old man is diagnosed with Bell's palsy. What is the current evidenced base approach to the management of this condition?

- A. Refer for urgent surgical decompression
- B. Aciclovir
- C. No treatment
- D. Aciclovir + prednisolone
- E. Prednisolone

Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously.

Features

- lower motor neuron facial nerve palsy - forehead affected*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes

Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 25mg bd for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

*upper motor neuron lesion 'spares' upper face

Question 106 of 164

A 70-year-old man is investiged for involuntary, jerking movements of his arms. His symptoms seem to resolve when he is asleep. Damage to which one of the following structures may lead to hemiballism?

- A. Substantia nigra
- B. Red nucleus
- C. Subthalamic nucleus
- D. Globus pallidus
- E. Frontal lobe

Question 106 of 164

A 70-year-old man is investiged for involuntary, jerking movements of his arms. His symptoms seem to resolve when he is asleep. Damage to which one of the following structures may lead to hemiballism?

- A. Substantia nigra
- B. Red nucleus
- C. Subthalamic nucleus
- D. Globus pallidus
- E. Frontal lobe

Hemiballism is caused by damage to the subthalamic nucleus

Hemiballism

Hemiballism occurs following damage to the subthalamic nucleus. Ballisic movements are involuntary, sudden, jerking movements which occur contralateral to the side of the lesion. The ballisic movements primarily affect the proximal limb musculature whilst the distal muscles may display more choreiform-like movements

Symptoms may decrease whilst the patient is asleep.

Antidopaminergic agents (e.g. Haloperidol) are the mainstay of treatment

Question 107 of 164

Which one of the following causes of Horner's syndrome is due to a lesion in the post-ganglionic part of the nerve supply?

- A. Internal carotid aneurysm
- B. Stroke
- C. Syringomyelia
- D. Pancoast's tumour
- E. Thyroidectomy

Question 107 of 164

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- B. Stroke
- C. Syringomyelia
- D. Pancoast's tumour
- E. Thyroidectomy

Horner's syndrome - anhydrosis determines site of lesion:
- head, arm, trunk = central lesion: stroke, syringomyelia
- just face = pre-ganglionic lesion: Pancoast's, cervical rib
- absent = post-ganglionic lesion: carotid artery

Horner's syndrome

Features
- miosis (small pupil)
- ptosis
- enophthalmos (sunken eye)
- anhydrosis (loss of sweating one side)

Distinguishing between causes
- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	**Pre-ganglionic lesions**	**Post-ganglionic lesions**
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke **S**yringomyelia Multiple **s**clerosis Tumour Encephalitis	Pancoast's **t**umour **T**hyroidectomy **T**rauma Cervical rib	**C**arotid artery dissection **C**arotid aneurysm **C**avernous sinus thrombosis **C**luster headache

Question 108 of 164

Which one of the following is most associated with downbeat nystagmus?

- A. Arnold-Chiari malformation
- B. Pseudobulbar palsy
- C. Jugular foramen syndrome
- D. Acoustic neuroma
- E. Cerebellar vermis lesions

Question 108 of 164

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- A. Arnold-Chiari malformation
- B. Pseudobulbar palsy
- C. Jugular foramen syndrome
- D. Acoustic neuroma
- E. Cerebellar vermis lesions

Nystagmus

Upbeat nystagmus
- cerebellar vermis lesions

Downbeat nystagmus - foramen magnum lesions
- Arnold-Chiari malformation

Question 109 of 164

A 27-year-old female presents complaining of generalised weakness. Examination of her face reveals bilateral ptosis, dysarthric speech and a slow-relaxing grip. What is the most likely diagnosis?

- A. Myotonic dystrophy
- B. Myasthenia gravis
- C. Multiple sclerosis
- D. Ataxic telangiectasia
- E. Friedreich's ataxia

Question 109 of 164

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- E. Friedreich's ataxia

Dystrophia myotonica - **D**M1

- **d**istal weakness initially
- autosomal **d**ominant
- **d**iabetes
- **d**ysarthria

The slow-relaxing grip may be noticed on initial hand-shake with the patient and is typical of myotonic dystrophy. Dysarthric speech is secondary to myotonia of the tongue and pharynx

Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Question 110 of 164

A 19-year-old man presents with a two-day history of a diffuse headache and sore throat. He is pyrexial at 37.8ºC and is reluctant to have a fundoscopy due to photophobia. A lumbar puncture is performed:

Serum glucose 5.9 mmol/l

Lumbar puncture reveals:

Appearance	Clear
Glucose	4.1 mmol/l
Protein	0.3 g/l
White cells	lymphocytes 2 /mm³ polymorphs 0 /mm³

What is the most likely diagnosis?

- A. Guillain-Barre syndrome
- B. Viral meningitis
- C. Bacterial meningitis
- D. Cerebral malaria
- E. Normal CSF result

Question 110 of 164

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What is the most likely diagnosis?

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- B. Viral meningitis
- C. Bacterial meningitis
- D. Cerebral malaria
- E. Normal CSF result

There results are consistent with normal CSF - an alternative diagnosis should be considered

Meningitis: CSF analysis

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	Bacterial	**Viral**	**Tuberculous**
Appearance	Cloudy	Clear/cloudy	Fibrin web
Glucose	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
Protein	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
White cells	10 - 5,000 polymorphs/mm³	15 - 1,000 lymphocytes/mm³	10 - 1,000 lymphocytes/mm³

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Question 111 of 164

A 19-year-old man is diagnosed as having myoclonic seizures. What is the most appropriate first line antiepileptic?

- A. Sodium valproate
- B. Carbamazepine
- C. Topiramate
- D. Phenytoin
- E. Ethosuximide

Question 111 of 164

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- B. Carbamazepine
- C. Topiramate
- D. Phenytoin
- E. Ethosuximide

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures

- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 112 of 164

A 63-year-old woman with motor neuron disease is reviewed in clinic. Which one of the following interventions will have the greatest effect on survival?

- A. Regular chest physiotherapy
- B. Total parental nutrition
- C. Riluzole
- D. Antioxidant supplementation
- E. Non-invasive ventilation

Question 112 of 164

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- B. Total parental nutrition
- C. Riluzole
- D. Antioxidant supplementation
- E. Non-invasive ventilation

Motor neuron disease - treatment: NIV is better than riluzole

Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

Riluzole
- anti-glutamate drug
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months
- expensive

Respiratory care
- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

Prognosis
- poor: 50% of patients die within 3 years

Question 113 of 164

Which one of the following is least associated with ptosis?

- A. Horner's syndrome
- B. Myotonic dystrophy
- C. Lambert-Eaton syndrome
- D. Third nerve palsy
- E. Motor neuron disease

Question 113 of 164

Which one of the following is least associated with ptosis?

- A. Horner's syndrome
- B. Myotonic dystrophy
- C. Lambert-Eaton syndrome
- D. Third nerve palsy
- E. Motor neuron disease

Ptosis

Ptosis may be unilateral or bilateral

Causes of bilateral ptosis:
- myotonic dystrophy
- myasthenia gravis*
- syphilis
- congenital

Causes of unilateral ptosis, as above plus:
- third nerve palsy
- Horner's

*ptosis is much less common in Lambert-Eaton syndrome than myasthenia gravis

Question 114 of 164

A 68-year-old woman presents with a two month history of electric shock like pains on the right side of her face. She describes having around 10-20 episodes a day which, each lasting for around 30-60 seconds. A recent dental check was normal. Neurological examination is unremarkable. What is the most suitable first-line management?

- A. Amitriptyline
- B. Sodium valproate
- C. Carbamazepine
- D. Atenolol
- E. Zolmitriptan

Question 114 of 164

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- E. Zolmitriptan

Trigeminal neuralgia - carbamazepine is first-line

Trigeminal neuralgia

Trigeminal neuralgia is a pain syndrome characterised by severe unilateral pain. The vast majority of cases are idiopathic but compression of the trigeminal roots by tumours or vascular problems may occur

The International Headache Society defines trigeminal neuralgia as:

- a unilateral disorder characterised by brief electric shock-like pains, abrupt in onset and termination, limited to one or more divisions of the trigeminal nerve
- the pain is commonly evoked by light touch, including washing, shaving, smoking, talking, and brushing the teeth (trigger factors), and frequently occurs spontaneously
- small areas in the nasolabial fold or chin may be particularly susceptible to the precipitation of pain (trigger areas)
- the pains usually remit for variable periods

Management

- carbamazepine is first-line
- failure to respond to treatment or atypical features (e.g. < 50 years old) should prompt referral to neurology

Question 115 of 164

A 49-year-old man presents to the Emergency Department complaining of visual disturbance. Examination reveals a right incongruous homonymous hemianopia. Where is the lesion most likely to be?

- A. Left optic tract
- B. Left optic radiation
- C. Right optic tract
- D. Right optic radiation
- E. Optic chiasm

Question 115 of 164

A 49-year-old man presents to the Emergency Department complaining of visual disturbance. Examination reveals a right incongruous homonymous hemianopia. Where is the lesion most likely to be?

- A. Left optic tract
- B. Left optic radiation
- C. Right optic tract
- D. Right optic radiation
- E. Optic chiasm

Visual field defects:
- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects= optic radiation lesion or occipital cortex

Visual field defects

The main points for the exam are:
- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

Homonymous hemianopia
- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias
- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Question 116 of 164

A 31-year-old female with progressive leg weakness has nerve conduction studies for suspected Guillain-Barre syndrome. Which one of the following findings would be most consistent with this diagnosis?

- A. Reduced conduction velocity
- B. Extended series of repetitive discharges lasting up to 30 seconds
- C. Increased conduction velocity
- D. Diminished response to repetitive stimulation
- E. Reduced wave amplitude

Question 116 of 164

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- E. Reduced wave amplitude

Slowing of the nerve conduction velocity usually indicates there is damage to the myelin sheath, as in Guillain-Barre syndrome

Nerve conduction studies

Nerve conduction studies (NCS) are useful in determining between axonal and demyelinating pathology

Axonal
- normal conduction velocity
- reduced amplitude

Demyelinating
- reduced conduction velocity
- normal amplitude

Question 117 of 164

An 84-year-old female is admitted for a urinary tract infection. On the second night of admission she is found wandering outside the ward in an agitated state. Despite appropriate antibiotic therapy, nursing care and modification of her environment she remains agitated and aggressive and it is judged a potential danger to herself. What is the most appropriate management?

- A. Haloperidol 5 mg orally
- B. Lorazepam 2 mg intramuscularly
- C. Haloperidol 0.5 mg orally
- D. Lorazepam 0.5 mg orally
- E. Ask for on-call psychiatric opinion for consideration of section under the Mental Health Act

Question 117 of 164

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D. Lorazepam 0.5 mg orally

E. Ask for on-call psychiatric opinion for consideration of section under the Mental Health Act

Whilst many doctors may use oral lorazepam in this situation the Royal College of Physicians recommend haloperidol as the first-line sedative

Acute confusional state

Acute confusional state is also known as delirium or acute organic brain syndrome. It affects up to 30% of elderly patients admitted to hospital

Features - wide variety of presentations
- memory disturbances (loss of short term > long term)
- may be very agitated or withdrawn
- disorientation
- mood change
- visual hallucinations
- disturbed sleep cycle
- poor attention

Management
- treatment of underlying cause
- modification of environment
- the 2006 Royal College of Physicians publication 'The prevention, diagnosis and management of delirium in older people: concise guidelines' recommended haloperidol 0.5 mg as the first-line sedative

Question 118 of 164

A 62-year-old man is admitted to the Emergency Deparment with a left hemiplegia. His symptoms started around 5 hours but he initially thought he had slept in an awkward position. He has no past medical history of note but on examination is found to have and irregular pulse of 150 / min. The ECG confirms atrial fibrillation. A CT head is immediately arranged and reported as normal. What is the most appropriate initial management?

- A. Aspirin
- B. Aspirin + dipyridamole
- C. Alteplase
- D. Warfarin
- E. Aspirin + warfarin

Question 118 of 164

A 62-year-old man is admitted to the Emergency Deparment with a left hemiplegia. His symptoms started around 5 hours but he initially thought he had slept in an awkward position. He has no past medical history of note but on examination is found to have and irregular pulse of 150 / min. The ECG confirms atrial fibrillation. A CT head is immediately arranged and reported as normal. What is the most appropriate initial management?

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- C. Alteplase
- D. Warfarin
- E. Aspirin + warfarin

Rate control should also be initiated. He is outside the thombolysis window so alteplase is not an option. The 2004 RCP guidelines recommend that anticoagulation should be commenced 14 days after an ischaemic stroke. Earlier anticoagulation may exacerbate any secondary haemorrhage.

Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued guidelines in 2008.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commence on a statin

Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

*SIGN recommend a window of 4.5 hours

Question 119 of 164

A 23-year-old female with a history of migraine presents for review. Her headaches are now occurring about once a week. She describes unilateral, throbbing headaches that may last over 24 hours. Neurological examination is unremarkable. Other than a history of asthma she is fit and well. What is the most suitable therapy to reduce the frequency of migraine attacks?

- A. Propranolol
- B. Zolmitriptan
- C. Sodium valproate
- D. Carbamazepine
- E. Pizotifen

Question 119 of 164

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- B. Zolmitriptan
- C. Sodium valproate
- D. Carbamazepine
- E. Pizotifen

Pizotifen is used less commonly nowadays due to side-effects such as weight gain. Propranolol should be avoided in asthmatics.

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment

Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis

Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 120 of 164

Which one of the following statements regarding the stopping of anti-epileptic drugs (AED) is most correct?

- A. Can be considered if seizure free for > 5 years, with AEDs being stopped over 2-3 months
- B. Can be considered if seizure free for > 2 years, with AEDs being stopped over 2-3 months
- C. Can be considered if seizure free for > 1 year, with AEDs being stopped over 2-3 months
- D. Can be considered if seizure free for > 5 years, with AEDs being stopped over 8-12 months
- E. Can be considered if seizure free for > 1 year, with AEDs being stopped over 8-12 months

Question 120 of 164

Which one of the following statements regarding the stopping of anti-epileptic drugs (AED) is most correct?

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C. Can be considered if seizure free for > 1 year, with AEDs being stopped over 2-3 months
D. Can be considered if seizure free for > 5 years, with AEDs being stopped over 8-12 months
E. Can be considered if seizure free for > 1 year, with AEDs being stopped over 8-12 months

The above reflects 2004 NICE guidelines and should be done under the guidance of a specialist. Benzodiazepines should be withdrawn over a longer period.

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures

- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 121 of 164

What is the most common clinical pattern seen in motor neuron disease?

- A. Progressive muscular atrophy
- B. Bulbar palsy
- C. Spinocerebellar ataxia
- D. Relapsing-remitting
- E. Amyotrophic lateral sclerosis

Question 121 of 164

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- C. Spinocerebellar ataxia
- D. Relapsing-remitting
- E. Amyotrophic lateral sclerosis

Motor neuron disease: types

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, primary lateral sclerosis, progressive muscular atrophy and bulbar palsy. In some patients however, there is a combination of clinical patterns

Amyotrophic lateral sclerosis (50% of patients)
- typically LMN signs in arms and UMN signs in legs
- in familial cases the gene responsible lies on chromosome 21 and codes for superoxide dismutase

Primary lateral sclerosis
- UMN signs only

Progressive muscular atrophy
- LMN signs only
- affects distal muscles before proximal
- carries best prognosis

Bulbar palsy
- palsy of the tongue, muscles of chewing/swallowing and facial muscles due to loss of function of brainstem motor nuclei
- carries worst prognosis

Question 122 of 164

A 72-year-old woman with a past history of treated hypertension presents to the Emergency Department. Yesterday she had a 2 hour episode where she couldn't find the right word when speaking. This has never happened before and there were no associated features. Neurological examination is unremarkable and blood pressure was 150/100 mmHg. Her only current medication is amlodipine. What is the most appropriate management?

- A. Aspirin 300mg immediately + specialist review within 2 weeks
- B. Specialist review within 2 weeks
- C. Aspirin 300mg immediately + specialist review within 24 hours
- D. Aspirin 75mg + outpatient CT brain
- E. Specialist review within 24 hours

Question 122 of 164

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- B. Specialist review within 2 weeks
- C. Aspirin 300mg immediately + specialist review within 24 hours
- D. Aspirin 75mg + outpatient CT brain
- E. Specialist review within 24 hours

This patients age, blood pressure and duration of symptoms would put her in a higher risk category. Current guidelines advocate specialist review within 24 hours

Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who've had a suspected TIA:

	Criteria	Points
A	**A**ge = 60 years	1
B	**B**lood pressure = 140/90 mmHg	1
C	**C**linical features - Unilateral weakness - Speech disturbance, no weakness	 2 1
D	**D**uration of symptoms - > 60 minutes - 10-59 minutes	 2 1
	Patient has diabetes	1

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision on brain imaging
- if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2005 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- low-dose aspirin combined with modified-release dipyridamole is recommended as first-line treatment. After 2 years treatment should revert to low-dose aspirin alone
- if aspirin cannot be taken, clopidogrel alone

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST* criteria or > 50% according to NASCET** criteria

*European Carotid Surgery Trialists' Collaborative Group

**North American Symptomatic Carotid Endarterectomy Trial

Question 123 of 164

A 27-year-old woman is reviewed due to sudden loss of vision in her left eye. She has is known to have severe rheumatoid arthritis and is treated currently with methotrexate, infliximab and prednisolone. She has in the past also used sulfasalazine and hydroxychloroquine. For the past 6 weeks she has developed troublesome headaches. Examination demonstrates bilateral papilloedema. Which one of the following is most likely to be responsible for this presentation?

- A. Chloroquine retinopathy
- B. Prednisolone
- C. Infliximab
- D. Methotrexate
- E. Keratoconjunctivitis sicca

Question 123 of 164

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- B. Prednisolone
- C. Infliximab
- D. Methotrexate
- E. Keratoconjunctivitis sicca

This patient has developed intracranial hypertension probably secondary to prednisolone. Patients may lose sight suddenly if the optic nerve becomes compressed

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

Features
- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

Risk factors
- obesity
- female sex
- pregnancy
- drugs: oral contraceptive pill, steroids, tetracycline, vitamin A

Management
- weight loss
- diuretics e.g. acetazolamide
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

Question 124 of 164

A 52-year-old man is reviewed in the neurology clinic. He has been referred due to the development of difficultly in finding the right words whilst speaking. His comprehension of normal conversation has however remained normal. Where is the likely lesion?

- A. Anterior temporal lobe
- B. Posterior temporal lobe
- C. Parietal lobe
- D. Posterior frontal lobe
- E. Anterior frontal lobe

Question 124 of 164

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- A. Anterior temporal lobe
- B. Posterior temporal lobe
- C. Parietal lobe
- D. Posterior frontal lobe
- E. Anterior frontal lobe

This man has expressive aphasia due to a lesion in Broca's area, located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus

Brain anatomy

The following neurological disorders/features may allow localisation of a brain lesion:

Parietal lobe lesions
- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

Occipital lobe lesions
- homonymous hemianopia
- cortical blindness
- visual agnosia

Temporal lobe lesion
- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia

Frontal lobes lesions
- expressive (Broca's) aphasia: located
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Question 125 of 164

A 34-year-old accountant presents with a one week history of pain around his right eye occurring once or twice a day. They are described as being very severe and lasting between 10-30 minutes each. He also describes a feeling of a blocked nose. What is the treatment of choice to treat this current episode?

- A. Ibuprofen
- B. Acetazolamide + topical pilocarpine
- C. Prednisolone
- D. Subcutaneous sumatriptan
- E. Ergotamine

Question 125 of 164

A 34-year-old accountant presents with a one week history of pain around his right eye occurring once or twice a day. They are described as being very severe and lasting between 10-30 minutes each. He also describes a feeling of a blocked nose. What is the treatment of choice to treat this current episode?

- A. Ibuprofen
- B. Acetazolamide + topical pilocarpine
- C. Prednisolone
- D. Subcutaneous sumatriptan
- E. Ergotamine

Cluster headache - acute treatment: subcutaneous sumatriptan + 100% O2

Standard analgesia is rarely effective in cluster headaches. 100% oxygen may also be used

Cluster headache

Cluster headaches* are more common in men (5:1) and smokers

Features
- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

Management
- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

Question 126 of 164

Which one of the following is most associated with a good prognosis in Guillain-Barre syndrome?

- A. Age > 40 years
- B. Female sex
- C. No history of a diarrhoeal illness
- D. High anti-GM1 antibody titre
- E. Low peak expiratory flow rate

Question 126 of 164

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Preceding gastrointestinal infections are associated with a poor prognosis in Guillain-Barre syndrome. The sex of the patient has not been shown to correlate with outcome

Guillain-Barre syndrome: prognosis

Guillain-Barre syndrome (GBS) describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

Poor prognostic features

- age > 40 years
- poor upper extremity muscle strength
- previous history of a diarrhoeal illness (specifically *Campylobacter jejuni*)
- high anti-GM1 antibody titre
- need for ventilatory support

There is currently contradictory evidence as to whether a gradual or rapid onset of GBS is associated with a poor outcome

Question 127 of 164

A 61-year-old woman presents with bilateral tinnitus. She reports no change in her hearing or other ear-related symptoms. Ear and cranial nerve examination is unremarkable. Which medication is she most likely to have recently started?

- A. Ciprofloxacin
- B. Nifedipine
- C. Repaglinide
- D. Quinine
- E. Bendroflumethiazide

Question 127 of 164

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Tinnitus

Causes of tinnitus include:

Meniere's disease	Associated with hearing loss, tinnitus and sensation of fullness or pressure in one or both ears
Otosclerosis	Onset is usually at 20-40 years Conductive deafness Tinnitus Normal tympanic membrane* Positive family history
Acoustic neuroma	Hearing loss, vertigo, tinnitus Absent corneal reflex is important sign Associated with neurofibromatosis type 2
Hearing loss	Causes include excessive loud noise and presbycusis
Drugs	Aspirin Aminoglycosides Loop diuretics Quinine

Other causes include

- impacted ear wax
- chronic suppurative otitis media

*10% of patients may have a 'flamingo tinge', caused by hyperaemia

Question 128 of 164

Which one of the following anti-epileptic drugs is most likely to cause visual field defects?

- A. Lamotrigine
- B. Phenytoin
- C. Ethosuximide
- D. Vigabatrin
- E. Pregabalin

Question 128 of 164

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V for Vigabatrin - V for Visual field defects

Vigabatrin

Key points

- 40% of patients develop visual field defects, which may be irreversible
- visual fields should be checked every 6 months

Question 129 of 164

A 45-year-old female is diagnosed with a glioma in the parietal lobe after being investigated for new onset seizures. Which one of the following features is she most likely to develop?

- A. Visual agnosia
- B. Auditory agnosia
- C. Acalculia
- D. Inability to generate a list
- E. Expressive (Broca's) aphasia

Question 129 of 164

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Frontal lobes lesions
- expressive (Broca's) aphasia: located
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Question 130 of 164

A 62-year-old man is seen in the rapid access transient ischaemic attack clinic following three episodes over the past two weeks of transient left sided weakness. What is the most appropriate advice to give with regards to driving?

- A. Cannot drive for 12 months
- B. Cannot drive until investigations complete
- C. Inform DVLA but can continue driving
- D. Cannot drive for 3 months
- E. Cannot drive for 1 month

Question 130 of 164

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- C. Inform DVLA but can continue driving
- D. Cannot drive for 3 months
- E. Cannot drive for 1 month

DVLA advice post multipler TIAs: cannot drive for 3 months

DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

Specific rules

- first seizure: 6 months off driving
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

Question 131 of 164

A 19-year-old presents as she would like to start a combined oral contraceptive pill. During the history she states that in the past she has had migraine with aura in the past. She asks why the combined oral contraceptive pill is contraindicated. What is the most appropriate response?

- A. Theoretical risk of ischaemic stroke
- B. Significantly increased risk of ischaemic stroke
- C. Increased frequency of migraines
- D. Migraine is an independent risk factor for venous thromboembolism
- E. Increased severity of migraines

Question 131 of 164

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Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

Migraine during pregnancy
- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

Migraine and the combined oral contraceptive (COC) pill
- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

Migraine and menstruation
- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefanamic acid or a combination of aspirin, parcetamol and caffeine. Triptans are also recommended in the acute situation

Migraine and hormone replacement therapy (HRT)
- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

Question 132 of 164

A 31-year-old woman presents with a 4 month history of headache. She has brought a headache diary which demonstrates that her symptoms are present on around 20-25 days of each month. The headache is typically unilateral and she is currently taking paracetamol 1g qds and ibuprofen 400mg tds everyday to try and relieve her symptoms. A diagnosis of medication overuse headache is suspected. What is the most appropriate management?

- A. Add metoclopramide + start propranolol
- B. Gradually withdraw analgesics + start propranolol
- C. Abruptly stop analgesics
- D. Gradually withdraw analgesics
- E. Continue analgesics + start propranolol

Question 132 of 164

A 31-year-old woman presents with a 4 month history of headache. She has brought a headache diary which demonstrates that her symptoms are present on around 20-25 days of each month. The headache is typically unilateral and she is currently taking paracetamol 1g qds and ibuprofen 400mg tds everyday to try and relieve her symptoms. A diagnosis of medication overuse headache is suspected. What is the most appropriate management?

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- D. Gradually withdraw analgesics
- E. Continue analgesics + start propranolol

Medication overuse headache • simple analgesia + triptans: stop abruptly • opioid analgesia: withdraw gradually

This answer may seem counterintuitive but it is line with recent guidelines from SIGN, please see the link provided.

Medication overuse headache

Medication overuse headache is one of the most common causes of chronic daily headache. It may affect up to 1 in 50 people

Features
- present for 15 days or more per month
- developed or worsened whilst taking regular symptomatic medication
- patients using opioids and triptans are at most risk
- may be psychiatric co-morbidity

Management (from 2008 SIGN guidelines)
- simple analgesics and triptans should be withdrawn abruptly (may initially worsen headaches)
- opioid analgesics should be gradually withdrawn

Question 133 of 164

Which one of the following is least recognised as causing idiopathic intracranial hypertension?

- A. Oral contraceptive pill
- B. Tetracycline
- C. Ciclosporin
- D. Prednisolone
- E. Vitamin A

Question 133 of 164

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Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

Features
- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

Risk factors
- obesity
- female sex
- pregnancy
- drugs: oral contraceptive pill, steroids, tetracycline, vitamin A

Management
- weight loss
- diuretics e.g. acetazolamide
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

Question 134 of 164

A 42-year-old woman with a history of myasthenia gravis is admitted to the Emergency Department. She is currently taking pyridostigmine but there has been a significant worsening of her symptoms following antibiotic treatment for a chest infection. On examination she is dyspnoeic and cyanotic with quiet breath sounds in both lungs. Other than respiratory support, what are the two treatments of choice?

- A. IV methylprednisolone or plasmapheresis
- B. IV methylprednisolone or intravenous immunoglobulins
- C. Plasmapheresis or atropine
- D. IV methylprednisolone or atropine
- E. Plasmapheresis or intravenous immunoglobulins

Question 134 of 164

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This patient is having a myasthenic crisis. Opinions vary as to whether plasmapheresis or intravenous immunoglobulins should be given first-line. Plasmapheresis usually works quicker but involves more expensive equipment

Myasthenia gravis

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 90% of cases*. Myasthenia is more common in women (2:1)

Features
- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

Associations
- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmine thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

Investigations
- Tensilon test: IV edrophonium reduces muscle weakness temporarily
- CT thorax to exclude thymoma
- CK normal

Management
- long-acting anticholinesterase e.g. Pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

Management of myasthenic crisis
- plasmapheresis
- intravenous immunoglobulins

*antibodies are less commonly seen in disease limited to the ocular muscles

Question 135 of 164

Which one of the following is least associated with Miller-Fisher syndrome?

- A. Anti-GQ1b antibodies
- B. Areflexia
- C. Ataxia
- D. Postural hypotension
- E. Ophthalmoplegia

Question 135 of 164

Which one of the following is least associated with Miller-Fisher syndrome?

- A. Anti-GQ1b antibodies
- B. Areflexia
- C. Ataxia
- D. Postural hypotension
- E. Ophthalmoplegia

Postural hypotension due to autonomic involvement is not a feature of Miller-Fisher syndrome, but may be seen in Guillain-Barre syndrome

Guillain-Barre syndrome

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

Pathogenesis

- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

Miller-Fisher syndrome

- variant of Guillain-Barre syndrome
- associated with areflexia, ataxia, ophthalmoplegia
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barre syndrome
- anti-GQ1b antibodies are present in 90% of cases

Question 136 of 164

Which one of the following statements regarding the use of 5-HT1 agonists in the treatment of migraine is incorrect?

- A. May be given subcutaneously
- B. Are second line therapy in the management of acute migraine
- C. Should be taken as soon as possible after the onset of an aura
- D. Should be avoided in patients with ischaemic heart disease
- E. Adverse effects include tingling and chest tightness

Question 136 of 164

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- D. Should be avoided in patients with ischaemic heart disease
- E. Adverse effects include tingling and chest tightness

Triptans should be taken when the headache starts, rather than the aura

Triptans

Triptans are specific 5-HT1 agonists used in the acute treatment of migraine. They are generally used second line when standard analgesics such as paracetamol and ibuprofen are ineffective

Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease

Question 137 of 164

A 64-year-old man who is under investigation for parkinsonian symptoms is brought to the GP by his wife. She is concerned he husband is becoming increasingly agitated. The GP prescribes haloperidol. One week later the GP is called out to see the patient as his parkinsonian symptoms have deteriorated markedly. What is the most likely underlying diagnosis?

- A. Lewy body dementia
- B. Normal pressure hydrocephalus
- C. Progressive supranuclear palsy
- D. Multiple system atrophy
- E. Dementia pugilistica

Question 137 of 164

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- D. Multiple system atrophy
- E. Dementia pugilistica

Patients with Lewy body dementia are extremely sensitive to neuroleptic agents

Lewy body dementia

Lewy body dementia is an increasingly recognised cause of dementia, accounting for up to 20% of cases. The characteristic pathological feature is cytoplasmic neuronal inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas

The relationship between Parkinson's disease and Lewy body dementia is complicated, particularly as dementia is often seen in Parkinson's disease. Also, up to 40% of patients with Alzheimer's have Lewy bodies

Neuroleptics should be avoided in Lewy body dementia as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent

Features

- progressive cognitive impairment
- parkinsonism
- visual hallucinations (other features such as delusions and non-visual hallucinations may also be seen)

Question 138 of 164

A 23-year-old female has a lumbar puncture to exclude subarachnoid haemorrhage following a negative CT scan. Which one of the following factors would be most likely to influence the incidence of post-lumbar puncture headache?

- A. Position of the patient
- B. Increased fluid intake post procedure
- C. Opening pressure of CSF
- D. Bed rest following the procedure
- E. Replacing the stylet

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Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline

Question 139 of 164

A 49-year-old man is prescribed procyclidine for Parkinson's disease. What is the mechanism of action?

- A. Antimuscarinic
- B. Dopamine receptor agonist
- C. Decarboxylase inhibitor
- D. Dopamine receptor antagonist
- E. Monoamine Oxidase-B inhibitor

Question 139 of 164

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Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 140 of 164

A 24-year-old woman with Charcot-Marie-Tooth disease asks how likely it is that any future children will have the disease. What is the most accurate answer?

- A. Three times as likely as background population
- B. 25%
- C. Between 5 - 10%
- D. Same as background population
- E. 50%

Question 140 of 164

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- B. 25%
- C. Between 5 - 10%
- D. Same as background population
- E. 50%

Charcot-Marie-Tooth disease (hereditary sensorimotor neuropathy type I) is an autosomal dominant condition and therefore 50% of children will be affected

HSMN

Hereditary sensorimotor neuropathy (HSMN) is a relatively new term which encompasses Charcot-Marie-Tooth disease (also known as peroneal muscular atrophy). Over 7 types have been characterised - however only 2 are common to clinical practice

- HSMN type I: primarily due to demyelinating pathology
- HSMN type II: primarily due to axonal pathology

HSMN type I

- autosomal dominant
- due to defect in PMP-22 gene (which codes for myelin)
- features often start at puberty
- motor symptoms predominate
- distal muscle wasting, pes cavus, clawed toes
- foot drop, leg weakness often first features

Question 141 of 164

A 65-year-old female is admitted with a right hemiparesis. Examination reveals she is in atrial fibrillation. CT confirms an ischaemic stroke and aspirin 300mg is commenced. If the patient is well and develops no new problems at what point should warfarin be started?

- A. After 14 days
- B. Immediately
- C. After 7 days
- D. Following a repeat CT at 28 days to exclude secondary haemorrhage
- E. Following a repeat CT at 14 days to exclude secondary haemorrhage

Question 141 of 164

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- B. Immediately
- C. After 7 days
- D. Following a repeat CT at 28 days to exclude secondary haemorrhage
- E. Following a repeat CT at 14 days to exclude secondary haemorrhage

The 2004 RCP guidelines recommend that anticoagulation should be commenced 14 days after an ischaemic stroke. Earlier anticoagulation may exacerbate any secondary haemorrhage

Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued guidelines in 2008.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commence on a statin

Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

*SIGN recommend a window of 4.5 hours

Question 142 of 164

A 34-year-old man presents with headache and blurred vision for a few weeks. Investigations reveal:

Prolactin 21,500 mu/l

CT brain Large pituitary mass encroaching on the optic chiasm with evidence of midline shift

What is the most appropriate treatment?

- A. Dopamine agonist
- B. Trans-cranial hypophysectomy
- C. Trans-sphenoidal hypophysectomy
- D. Pituitary irradiation
- E. Somatostatin

Question 142 of 164

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- D. Pituitary irradiation
- E. Somatostatin

Prolactinoma management - medical therapy is almost always first-line

Prolactinomas are unusual as medical therapy is first line, even if visual field defects are present. The main indications for surgery are tumours resistant to dopamine agonists

Pituitary tumours

Hormones secreted

- PRL - 35%
- no obvious hormone, 'non-functioning', 'chromophobe' - 30%
- GH - 20%
- PRL and GH - 7%
- ACTH - 7%
- others: TSH, LH, FSH - 1%

Question 143 of 164

A 55-year-old man presents complaining of visual disturbance. Examination reveals a right congruous homonymous hemianopia with macula sparing. Where is the lesion most likely to be?

- A. Right optic nerve
- B. Left optic radiation
- C. Left optic tract
- D. Left occipital cortex
- E. Optic chiasm

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- C. Left optic tract
- D. Left occipital cortex
- E. Optic chiasm

Visual field defects:
- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects= optic radiation lesion or occipital cortex

Visual field defects

The main points for the exam are:
- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

Homonymous hemianopia
- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias
- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia
- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

Question 144 of 164

A 76-year-old man is admitted with a right hemiparesis. On examination his blood pressure is 120/78 mmHg, pulse 84 bpm and oxygen saturations 96% on room air. A CT scan excludes intracerebral haemorrhage and he is given aspirin 300mg. What is the most appropriate management with regards to oxygen therapy in the first 12 hours following admission?

- A. 35% via Venturi mask
- B. 24% via Venturi mask
- C. No oxygen therapy
- D. 28% via Venturi mask
- E. 2 litres/minute via nasal cannulae

Question 144 of 164

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- A. 35% via Venturi mask
- B. 24% via Venturi mask
- C. No oxygen therapy
- D. 28% via Venturi mask
- E. 2 litres/minute via nasal cannulae

Both the NICE stroke guidelines and British Thoracic Society oxygen guidelines do not support giving oxygen in this scenario.

Oxygen therapy

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

Oxygen saturation targets

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

Management of COPD patients

- prior to the availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO2 is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

Question 145 of 164

A 34-ear-old man who is known to suffer from complex partial seizures is reviewed in the neurology clinic. He has not been able to tolerate either carbamazepine or sodium valproate. What is the most appropriate next line drug?

- A. Phenytoin
- B. Lamotrigine
- C. Ethosuximide
- D. Topiramate
- E. Clonazepam

Question 145 of 164

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- D. Topiramate
- E. Clonazepam

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Partial seizures

- carbamazepine
- second line: lamotrigine**, sodium valproate

*carbamazepine may actually exacerbate absence seizure

**the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Question 146 of 164

Which one of the following statements regarding restless legs syndrome is incorrect?

- A. Movements may be seen during sleep
- B. May be secondary to uraemia
- C. Affects approximately 5% of the general population
- D. Family history is found in up to 50% of patients
- E. It is three times as common in females

Question 146 of 164

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- D. Family history is found in up to 50% of patients
- E. It is three times as common in females

Males and females are thought to be equally affected, with only one study showing a slightly increased incidence in females

Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

Question 147 of 164

Which one of the following conditions is least recognised as a cause of a seventh nerve palsy?

- A. Acoustic neuroma
- B. Herpes zoster
- C. HIV
- D. Systemic lupus erythematous
- E. Diabetes mellitus

Question 147 of 164

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Facial nerve

Supply - 'face, ear, taste, tear'
- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy
- sarcoidosis
- Guillain-Barre syndrome
- polio, Lyme disease

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron	Upper motor neuron
• Bell's palsy • Ramsay-Hunt syndrome (due to herpes zoster) • acoustic neuroma • parotid tumours • HIV • multiple sclerosis* • diabetes mellitus	• stroke

LMN vs. UMN
- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

*may also cause an UMN palsy

Question 148 of 164

Each one of the following is associated with the development of chorea, except:

- A. Sarcoidosis
- B. Wilson's disease
- C. Anti-phospholipid syndrome
- D. Pregnancy
- E. Rheumatic fever

Question 148 of 164

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Chorea

Chorea describes rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus

Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

Question 149 of 164

A 22-year-old female presents with a history of fits, describing focal seizures associated with impairment of consciousness. What is the most suitable first-line treatment?

- A. Phenytoin
- B. Sodium valproate
- C. Gabapentin
- D. Levetiracetam
- E. Carbamazepine

Question 149 of 164

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Epilepsy medication: first-line
- generalised seizure: sodium valproate
- partial seizure: carbamazepine

The 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:
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Question 150 of 164

Which one of the following is least likely to produce a lymphocytosis in the cerebrospinal fluid?

- A. Systemic lupus erythematous
- B. Guillain-Barre syndrome
- C. Viral encephalitis
- D. Partially treated bacterial meningitis
- E. Behcet's syndrome

Question 150 of 164

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- E. Behcet's syndrome

Cerebrospinal fluid: raised lymphocytes

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose = > 2/3 blood glucose
- cells: red cells = 0, white cells < 5/mm^3

The following conditions are associated with raised lymphocytes

- viral meningitis/encephalitis
- TB meningitis
- partially treated bacterial meningitis
- Lyme disease
- Behcet's, SLE
- lymphoma, leukaemia

Question 151 of 164

Which one of the following statements regarding absence seizures is incorrect?

- A. Typical age of onset of 3-10 years old
- B. Sodium valproate and ethosuximide are first-line treatments
- C. Seizures may be provoked by a child holding their breath
- D. There is a good prognosis
- E. Characteristic EEG changes are seen

Question 151 of 164

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- B. Sodium valproate and ethosuximide are first-line treatments
- C. Seizures may be provoked by a child holding their breath
- D. There is a good prognosis
- E. Characteristic EEG changes are seen

Seizures are characteristically provoked by hyperventilation

Absence seizures

Absence seizures (petit mal) are a form of generalised epilepsy that is mostly seen in children. The typical age of onset of 3-10 years old and girls are affected twice as commonly as boys

Features

- absences last a few seconds and are associated with a quick recovery
- seizures may be provoked by hyperventilation or stress
- the child is usually unaware of the seizure
- they may occur many times a day
- EEG: bilateral, symmetrical 3Hz spike and wave pattern

Management

- sodium valproate and ethosuximide are first-line treatment
- good prognosis - 90-95% become seizure free in adolescence

Question 152 of 164

A 24-year-old female presents to her GP due to increased frequency of migraine attacks. She is now having around four migraines per month. Which type of medication would it be most appropriate to prescribe to reduce the frequency of migraine attacks?

- A. Specific 5-HT2 agonist
- B. 5-HT1 antagonist
- C. Tricyclic antidepressant
- D. Beta-blocker
- E. Specific 5-HT1 agonist

Question 152 of 164

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- A. Specific 5-HT2 agonist
- B. 5-HT1 antagonist
- C. Tricyclic antidepressant
- D. Beta-blocker
- E. Specific 5-HT1 agonist

Migraine
- acute: 5-HT1 agonist
- prophylaxis: beta-blocker, 5-HT2 antagonist

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment

Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis

Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 153 of 164

Which of the following features is least likely to be found in a patient with tuberose sclerosis?

- A. Shagreen patches
- B. Café-au-lait spots
- C. Retinal hamartomas
- D. Axillary freckling
- E. Renal angiomyolipomata

Question 153 of 164

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- B. Café-au-lait spots
- C. Retinal hamartomas
- D. Axillary freckling
- E. Renal angiomyolipomata

Axillary freckling is seen in neurofibromatosis

Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

Cutaneous features
- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots* may be seen

Neurological features
- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

Also
- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Question 154 of 164

A 65-year-old man who is known to have metastatic colorectal cancer presents for review. Since last been seen he reports being generally stiff and on examination is noted to have diffuse hypertonia. Which antibodies are most likely to be responsible for this presentation?

- A. Anti-GAD
- B. Anti-Ri
- C. Anti-Hu
- D. Anti-La
- E. Anti-Yo

Question 154 of 164

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- C. Anti-Hu
- D. Anti-La
- E. Anti-Yo

This patient has developed stiff person's syndrome.

Paraneoplastic syndromes affecting nervous system

Lambert-Eaton myasthenic syndrome
- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

Anti-Hu
- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

Anti-Yo
- associated with ovarian and breast cancer
- cerebellar syndrome

Anti-GAD antibody
- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

Anti-Ri
- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

Question 155 of 164

Which one of the following features is least typically of motor neuron disease?

- A. Fasciculation
- B. Dysarthria
- C. Increased muscle tone
- D. Ataxia
- E. Absent reflexes

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Cerebellar signs are not seen in motor neuron disease

Motor neuron disease: features

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

There are a number of clues which point towards a diagnosis of motor neuron disease:

- fasciculation
- absence of sensory signs/symptoms*
- lower motor neuron signs in arms and upper motor neuron signs in legs
- wasting of the small hand muscles/tibialis anterior is common

Other features

- doesn't affect external ocular muscles
- no cerebellar signs
- abdominal reflexes are usually preserved and sphincter dysfunction if present is a late feature

The diagnosis of motor neuron disease is clinical, but nerve conduction studies will show normal motor conduction and can help exclude a neuropathy. Electromyography shows a reduced number of action potentials with an increased amplitude. MRI is usually performed to exclude the differential diagnosis of cervical cord compression and myelopathy

*vague sensory symptoms may occur early in the disease (e.g. limb pain) but 'never' sensory signs

Question 156 of 164

A 45-year-old female with a past medical history of asthma is diagnosed as having essential tremor. What is the most suitable management?

- A. Amitriptyline
- B. Propranolol
- C. Sodium valproate
- D. Carbamazepine
- E. Primidone

Question 156 of 164

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- A. Amitriptyline
- B. Propranolol
- C. Sodium valproate
- D. Carbamazepine
- E. Primidone

Essential tremor is an AD condition that is made worse when arms are outstretched, made better by alcohol and propranolol

Propranolol is generally considered first-line in essential but given the history of asthma primidone should be used

Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

Features
- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

Management
- propranolol is first-line
- primidone is sometimes used

Question 157 of 164

Which one of the following statements regarding Meniere's disease is correct?

- A. More common in patients from the Indian Subcontinent
- B. Symptoms resolve in the majority of patients after 6-12 months
- C. It is very rare that patients develop permanent hearing loss
- D. More common in children
- E. Approximately equal incidence in males and females

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Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours

Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit

Question 158 of 164

A 51-year-old man with a history of schizophrenia is reviewed. He has developed parkinsonism secondary to his antipsychotic medication. Which one of the following drugs is most useful in the management of tremor?

- A. Apomorphine
- B. Cabergoline
- C. Selegiline
- D. Amantadine
- E. Benzhexol

Question 158 of 164

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- C. Selegiline
- D. Amantadine
- E. Benzhexol

Benzhexol is now more commonly referred to as trihexyphenidyl. It is now mainly used for drug-induced parkinsonism rather than idiopathic Parkinson's disease

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 159 of 164

Each of the following are causes of peripheral neuropathy. Which one is associated with predominately sensory loss?

- A. Diphtheria
- B. Hereditary sensorimotor neuropathies
- C. Porphyria
- D. Lead poisoning
- E. Uraemia

Question 159 of 164

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Peripheral neuropathy

Peripheral neuropathy may be divided into conditions which predominately cause a motor or sensory loss

Predominately motor loss
- Guillain-Barre syndrome
- porphyria
- lead poisoning
- hereditary sensorimotor neuropathies (HSMN) - Charcot-Marie-Tooth
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- diphtheria

Predominately sensory loss
- diabetes
- uraemia
- leprosy
- alcoholism
- vitamin B12 deficiency
- amyloidosis

Alcoholic neuropathy
- secondary to both direct toxic effects and reduced absorption of B vitamins
- sensory symptoms typically present prior to motor symptoms

Vitamin B12 deficiency
- subacute combined degeneration of spinal cord
- dorsal column usually affected first (joint position, vibration) prior to distal paraesthesia

Question 160 of 164

A 39-year-old man is diagnosed as having cluster headaches. He has received subcutaneous sumatriptan on two occasions but would like to start medication to help prevent further attacks. Of the following options, which one is the most suitable treatment?

- A. Atenolol
- B. Amitriptyline
- C. Sodium valproate
- D. Verapamil
- E. Gabapentin

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Cluster headache

Cluster headaches* are more common in men (5:1) and smokers

Features
- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

Management
- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

Question 161 of 164

Which one of the following causes of peripheral neuropathy is most associated with an axonal, rather than demyelinating, pathology?

- A. Paraprotein neuropathy
- B. Guillain-Barre syndrome
- C. Hereditary sensorimotor neuropathies (HSMN) type I
- D. Amiodarone
- E. Vasculitis

Question 161 of 164

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- D. Amiodarone
- E. Vasculitis

The other causes are associated with a demyelinating pathology

Peripheral neuropathy: demyelinating vs. axonal

Demyelinating pathology
- Guillain-Barre syndrome
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- amiodarone
- hereditary sensorimotor neuropathies (HSMN) type I
- paraprotein neuropathy

Axonal pathology
- alcohol
- diabetes mellitus*
- vasculitis
- vitamin B12 deficiency*
- hereditary sensorimotor neuropathies (HSMN) type II

* may also cause a demyelinating picture

Question 162 of 164

Which one of the following antibiotics is most likely to exacerbate myasthenia gravis?

- A. Metronidazole
- B. Ceftriaxone
- C. Trimethoprim
- D. Doxycycline
- E. Gentamicin

Question 162 of 164

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Myasthenia gravis: exacerbating factors

The most common exacerbating factor is exertion resulting in fatigability, which is the hallmark feature of myasthenia gravis . Symptoms become more marked during the day

The following drugs may exacerbate myasthenia:

- penicillamine
- quinidine, procainamide
- beta-blockers
- lithium
- phenytoin
- gentamicin

Question 163 of 164

Each one of the following drugs may be used to prevent migraine attacks, except:

- A. Pizotifen
- B. Amitriptyline
- C. Propranolol
- D. Methysergide
- E. Sumatriptan

Question 163 of 164

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- C. Propranolol
- D. Methysergide
- E. Sumatriptan

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment
Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis
Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 164 of 164

Which one of the following is least associated with myotonic dystrophy?

- A. Dysphagia
- B. Aortic regurgitation
- C. Diabetes mellitus
- D. Testicular atrophy
- E. Learning difficulties

Question 164 of 164

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- A. Dysphagia
- B. Aortic regurgitation
- C. Diabetes mellitus
- D. Testicular atrophy
- E. Learning difficulties

Dystrophia myotonica - **D**M1
- **d**istal weakness initially
- autosomal **d**ominant
- **d**iabetes
- **d**ysarthria

Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics
- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features
- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features
- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Question 1 of 143

A 34-year-old man with a past history of HIV infection presents to the Emergency Department with watery diarrhoea. Cryptosporidium infection is confirmed on ZN staining. What is the most suitable management?

- A. Metronidazole
- B. Sulfadiazine + pyrimethamine
- C. Supportive therapy
- D. Rifampicin + ethambutol + clarithromycin
- E. Co-trimoxazole

Question 1 of 143

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- E. Co-trimoxazole

Supportive therapy is the mainstay of treatment in Cryptosporidium diarrhoea

HIV: diarrhoea

Diarrhoea is common in patients with HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes

- Cryptosporidium + other protozoa (most common)
- Cytomegalovirus
- *Mycobacterium avium intracellulare*
- Giardia

Cryptosporidium is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of Cryptosporidium. Treatment is difficult, with the mainstay of management being supportive therapy*

Mycobacterium avium intracellulare is an atypical mycobacteria seen with the CD4 count is below 50. Typical features include fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with rifabutin, ethambutol and clarithromycin

*nitazozanide is licensed in the US for immunocompetent patients

Question 2 of 143

A 39-year-old man is admitted to hospital with decompensated liver disease of unknown aetiology. As part of a liver screen the following results are obtained:

Anti-HBs	Positive
Anti-HBc	Negative
HBs antigen	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen

What is this man's hepatitis B status?

- A. Chronic hepatitis B - highly infectious
- B. Previous immunisation to hepatitis B
- C. Probable hepatitis D infection
- D. Acute hepatitis B infection
- E. Chronic hepatitis B - not infectious

Question 2 of 143

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- B. Previous immunisation to hepatitis B
- C. Probable hepatitis D infection
- D. Acute hepatitis B infection
- E. Chronic hepatitis B - not infectious

Question 3 of 143

A 34-year-old man from Zimbabwe is admitted with abdominal pain to the Emergency Department. An abdominal x-ray reveals urinary bladder calcification. What is the most likely cause?

- A. Schistosoma mansoni
- B. Sarcoidosis
- C. Leishmaniasis
- D. Tuberculosis
- E. Schistosoma haematobium

Question 3 of 143

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- B. Sarcoidosis
- C. Leishmaniasis
- D. Tuberculosis
- E. Schistosoma haematobium

Schistosoma **haem**atobium causes **haem**aturia

Schistosomiasis is the most common cause of bladder calcification worldwide

Schistosomiasis

Schistosomiasis, or bilharzia, is a parasitic flatworm infection. The following types of schistosomiasis are recognised:

- Schistosoma mansoni and Schistosoma intercalatum: intestinal schistosomiasis
- Schistosoma haematobium: urinary schistosomiasis

Schistosoma **haematobium**

This typically presents as a 'swimmer's itch' in patients who have recently returned from Africa. Schistosoma haematobium is a risk factor for squamous cell bladder cancer

Features

- frequency
- haematuria
- bladder calcification

Management

- single oral dose of praziquantel

Question 4 of 143

A 34-year-old postman attends the Emergency Department following a dog bite to his right hand. What is the most appropriate antibiotic therapy?

- A. Metronidazole + amoxicillin
- B. Erythromycin
- C. Co-amoxiclav
- D. Metronidazole
- E. Flucloxacillin + penicillin

Question 4 of 143

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- A. Metronidazole + amoxicillin
- B. Erythromycin
- C. Co-amoxiclav
- D. Metronidazole
- E. Flucloxacillin + penicillin

A combination of doxycycline and metronidazole is recommended in the BNF if the patient is penicillin allergic

Animal bites

Management

- cleanse wound
- current BNF recommendation is co-amoxiclav
- if penicillin-allergic then doxycycline + metronidazole is recommended

Question 5 of 143

A 35-year-old homosexual man is referred to the local genitourinary clinic following the development of a solitary painless penile ulcer associated with painful inguinal lymphadenopathy. He has recently developed rectal pain and tenesmus. What is the most likely diagnosis?

- A. Herpes simplex infection
- B. Syphilis
- C. Granuloma inguinale
- D. Chancroid
- E. Lymphogranuloma venereum

Question 5 of 143

A 35-year-old homosexual man is referred to the local genitourinary clinic following the development of a solitary painless penile ulcer associated with painful inguinal lymphadenopathy. He has recently developed rectal pain and tenesmus. What is the most likely diagnosis?

- A. Herpes simplex infection
- B. Syphilis
- C. Granuloma inguinale
- D. Chancroid
- E. Lymphogranuloma venereum

Genital ulcers • painful: herpes >> chancroid • painless: syphilis > lymphogranuloma venereum + granuloma inguinale

Lymphogranuloma venereum usually involves three stages:
- 1 - small painless pustule which later forms an ulcer
- 2 - painful inguinal lymphadenopathy
- 3 - proctocolitis

STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages
- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

Other causes of genital ulcers
- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis**

*previously called *Calymmatobacterium granulomatis*

Question 6 of 143

A 30-year-old man is diagnosed as having malaria following a recent trip to Zimbabwe. Which one of the following is most likely to indicate severe malaria?

- A. Parasitaemia 1%
- B. Heart rate 102 per minute
- C. White blood cells 18.2 * 10^9/l
- D. Platelets 105 * 10^9/l
- E. Respiratory rate 30 per minute

Question 6 of 143

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- E. Respiratory rate 30 per minute

A respiratory rate of 30 per minute may indicate acute respiratory distress syndrome (ARDS), a feared complication of falciparum malaria. Whilst thrombocytopaenia can be caused by disseminated intravascular coagulation (DIC), it is also seen in many patients with uncomplicated malaria and hence would not automatically indicate severe malaria

Malaria: Falciparum

Feature of severe malaria
- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

Complications
- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria
- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- first choice is oral quinine for 5 days followed by sulfadoxine-pyrimethamine or doxycycline
- alternative regimes include atovaquone-proguanil or artemether-lumefantrine

Severe falciparum malaria
- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- options include intravenous quinine or artemisinins
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

Question 7 of 143

A 54-year-old female is admitted with a severe pneumonia following a holiday in Turkey. Bloods reveal both hyponatraemia and deranged liver function tests. A chest x-ray shows patchy alveolar infiltrates with consolidation in the right lower lobe. Which one of the following investigations is most likely to confirm the probable diagnosis?

- A. Sputum culture
- B. Urinary antigen
- C. Blood cultures
- D. Bone marrow aspirate
- E. Lumbar puncture

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Legionella

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophilia*. It is typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays. Person-to-person transmission is not seen

Features
- flu-like symptoms
- dry cough
- lymphopenia
- hyponatraemia
- deranged LFTs

Diagnosis
- urinary antigen

Management
- treat with erythromycin

Question 8 of 143

Which one of the following is a live attenuated vaccine?

- A. Yellow fever
- B. Rabies
- C. Pertussis
- D. Diphtheria
- E. Tetanus

Question 8 of 143

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Live attenuated vaccines
- BCG
- MMR
- oral polio
- yellow fever
- oral typhoid

Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients

Live attenuated vaccines
- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid

Whole killed organism*
- rabies
- pertussis

Fragment
- diphtheria
- tetanus
- meningococcus, pneumococcus, haemophilus

Others
- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of Vibrio cholerae together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

*injectable typhoid is no longer used in the UK

Question 9 of 143

A 22-year-old woman who is an immigrant from Malawi presents for review as she thinks she is pregnant. This is confirmed with a positive pregnancy test. She is known to be HIV positive. Which one of the following should not be part of the management plan to ensure an optimal outcome?

- A. Oral zidovudine for the newborn until 6 weeks of age
- B. Maternal antiretroviral therapy
- C. Encourage breast feeding
- D. Intrapartum zidovudine infusion
- E. Elective caesarean section

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Question 10 of 143

Which one of the following organisms causes erysipelas?

- A. *Staphylococcus aureus*
- B. *Streptococcus pneumoniae*
- C. *Staphylococcus epidermidis*
- D. *Streptococcus pyogenes*
- E. *Streptococcus viridans*

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Streptococci

Streptococci may be divided into alpha and beta haemolytic types

Alpha haemolytic streptococci

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

Beta haemolytic streptococci

These can be subdivided into group A and B

Group A
- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

Group B
- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

Question 11 of 143

A 38-year-old man presents to the genitourinary clinic with multiple, painless genital ulcers. A diagnosis of granuloma inguinale is made. What is the causative organism?

- A. *Klebsiella granulomatis*
- B. *Chlamydia*
- C. Herpes simplex virus
- D. *Treponema pallidum*
- E. *Haemophilus ducreyi*

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STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

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- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis**

*previously called *Calymmatobacterium granulomatis*

Question 12 of 143

A 24-year-old woman who is 18 weeks pregnant presents to the Emergency Department. Earlier on in the morning she came into contact with a child who has chickenpox. She is unsure if she had the condition herself as a child. What is the most appropriate action?

- A. Advise her to present within 24 hours of the rash developing for consideration of IV aciclovir
- B. Reassure her that there is no risk of fetal complications at this point in pregnancy
- C. Give varicella immunoglobulin
- D. Check varicella antibodies
- E. Prescribe oral aciclovir

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- E. Prescribe oral aciclovir

Chickenpox exposure in pregnancy - first step is to check antibodies

If there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies

Chickenpox exposure in pregnancy

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion. In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed fetal varicella syndrome

Fetal varicella syndrome (FVS)

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks
- features of FVS include skin scarring, eye defects (microphthalmia), limb hypoplasia, microcephaly and learning disabilities

Management of chickenpox exposure

- if there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies
- if the pregnant women is not immune to varicella she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure
- consensus guidelines suggest oral aciclovir should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

Question 13 of 143

A 27-year-old male presents with malaise, pyrexia, lymphadenopathy and a maculopapular rash. The Monospot test is negative. Given a history of high-risk sexual behaviour you are asked to exclude a HIV seroconversion illness. What is the most appropriate investigation?

- A. Antibodies to HIV-2
- B. gp120 polymerase chain reaction
- C. p24 antigen test
- D. CCR5 polymerase chain reaction
- E. Antibodies to HIV-1

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- C. p24 antigen test
- D. CCR5 polymerase chain reaction
- E. Antibodies to HIV-1

HIV: seroconversion

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

Features

- sore throat
- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningoencephalitis

Diagnosis

- antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis

Question 14 of 143

A 19-year-old man presents with dysuria associated with a watery discharge from his urethral meatus. A urethral swab shows non-specific urethritis and urine is sent for *Chlamydia*/gonococcus. What is the most appropriate antibiotic to use?

- A. Erythromycin
- B. Ciprofloxacin
- C. Metronidazole
- D. Cefixime
- E. Azithromycin

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Chlamydia - treat with azithromycin or doxycycline

Gonorrhoea would be demonstrated by the presence of Gram negative diplococci on the swab. As the swab showed non-specific urethritis a diagnosis of *Chlamydia* is most likely.

The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline.

Chlamydia

Chlamydia is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

Features
- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

Potential complications
- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

Investigation
- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice
- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

Screening
- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years

- relies heavily on opportunistic testing

Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

Question 15 of 143

A 25-year-old man returns from a gap-year in Central and South America and presents with a 2 month history of an ulcerating lesion on his lower lip. Examination of his nasal and oral mucosae reveals widespread involvement. What is the likely cause?

- A. *Leishmania brasiliensis*
- B. *Leishmania mexicana*
- C. *Trypanosoma cruzi*
- D. Basal cell carcinoma
- E. *Leishmania donovani*

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Mucocutaneous ulceration following travel? - *Leishmania brasiliensis*

This patient most likely has leishmaniasis. The pattern of a primary skin lesion with mucosal involvement is characteristic of *Leishmania brasiliensis*

Leishmaniasis

Leishmaniasis is caused by the intracellular protozoa Leishmania, usually being spread by sand flies. Cutaneous, mucocutaneous leishmaniasis and visceral forms are seen

Cutaneous leishmaniasis
- caused by Leishmania tropica or *Leishmania mexicana*
- crusted lesion at site of bite
- may be underlying ulcer

Mucocutaneous leishmaniasis
- caused by *Leishmania brasiliensis*
- skin lesions may spread to involve mucosae of nose, pharynx etc

Visceral leishmaniasis (kala-azar)
- mostly caused by *Leishmania donovani*
- occurs Mediterranean, Asia, South America, Africa
- fever, sweats, rigors
- massive splenomegaly. hepatomegaly
- poor appetite*, weight loss
- grey skin - 'kala-azar' means black sickness
- pancytopaenia secondary to hypersplenism

*occasionally patients may report increased appetite with paradoxical weight loss

Question 16 of 143

A 28-year-old man is admitted to the Emergency Department with dyspnoea and fever. Five days ago he developed an itchy, vesicular rash after coming into contact with a child who had chickenpox. On examination his temperature is 38.6ºC, respiratory rate 24 / min, pulse 120 / min and blood pressure 135/68 mmHg. Oxygen saturations are 95% on room air. Examination of chest reveals only occasional fine crackles bilaterally. What is the most important intervention?

- A. Elective intubation within the next 2 hours
- B. Prednisolone
- C. Varicella zoster immunoglobulin
- D. IV aciclovir
- E. Paracetamol

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- C. Varicella zoster immunoglobulin
- D. IV aciclovir
- E. Paracetamol

Varicella pneumonia is the most common and serious complication of chickenpox infection in adults. Auscultation of the chest is often unremarkable. Varicella zoster immunoglobulin is used for the prevention of varicella in at-risk groups (e.g. Immunocompromised, pregnant women), rather than for treatment

Chickenpox

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion

Chickenpox is highly infectious
- spread via the respiratory route
- can be caught from someone with shingles
- infectivity = 4 days before rash, until 5 days after the rash first appeared*
- incubation period = 10-21 days

Clinical features (tend to be more severe in older children/adults)
- fever initially
- itchy, rash starting on head/trunk before spreading. Initially macular then papular then vesicular
- systemic upset is usually mild

Management is supportive
- keep cool, trim nails
- calamine lotion
- school exclusion: current HPA advice is 5 days from start of skin eruption. They also state 'Traditionally children have been excluded until all lesions are crusted. However, transmission has never been reported beyond the fifth day of the rash.'
- immunocompromised patients and newborns with peripartum exposure should receive varicella zoster immunoglobulin (VZIG). If chickenpox develops then IV aciclovir should be considered

A common complication is secondary bacterial infection of the lesions. Rare complications include
- pneumonia
- encephalitis (cerebellar involvement may be seen)
- disseminated haemorrhagic chickenpox
- arthritis, nephritis and pancreatitis may very rarely be seen

*it was traditionally taught that patients were infective until all lesions had scabbed over

Question 17 of 143

A male child from a travelling community is diagnosed with measles. Which one of the following complications is he at risk from in the immediate aftermath of the initial infection?

- A. Arthritis
- B. Pancreatitis
- C. Infertility
- D. Subacute sclerosing panencephalitis
- E. Pneumonia

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- D. Subacute sclerosing panencephalitis
- E. Pneumonia

Subacute sclerosing panencephalitis is seen but develops 5-10 years following the illness. Pancreatitis and infertility may follow mumps infection

Measles

Overview
- RNA paramyxovirus
- spread by droplets
- infective from prodrome until 5 days after rash starts
- incubation period = 10-14 days

Features
- prodrome: irritable, conjunctivitis, fever
- Koplik spots (before rash): white spots ('grain of salt') on buccal mucosa
- rash: starts behind ears then to whole body, discrete maculopapular rash becoming blotchy & confluent

Complications
- encephalitis: typically occurs 1-2 weeks following the onset of the illness)
- subacute sclerosing panencephalitis: very rare, may present 5-10 years following the illness
- febrile convulsions
- pneumonia, tracheitis
- keratoconjunctivitis, corneal ulceration
- diarrhoea
- increased incidence of appendicitis
- myocarditis

Management of contacts
- if a child not immunized against measles comes into contact with measles then MMR should be offered (vaccine-induced measles antibody develops more rapidly than that following natural infection)
- this should be given within 72 hours

Question 18 of 143

Which one of the following best describes the action of aciclovir?

- A. Inhibits uncoating of virus in the cell
- B. Inhibits DNA polymerase
- C. Interferes with the capping of viral mRNA
- D. Inhibits RNA polymerase
- E. Protease inhibitor

Question 18 of 143

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Antiviral agents

Aciclovir
- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

Ribavirin
- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

Interferons
- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

Amantadine
- used to treat influenza
- inhibits uncoating of virus in cell

Anti-retroviral agent used in HIV

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

Protease inhibitors (PI)
- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz

Question 19 of 143

A 30-year-old man presents to the genito-urinary medicine clinic. He has been handed a slip from an ex-girlfriend stating she has tested positive for *Chlamydia*. He last slept with her 2 months ago. He has no symptoms of note, in particular no dysuria or discharge. What is the most appropriate management?

- A. Reassure symptoms would have presented by now
- B. Offer antibiotic therapy
- C. Offer *Chlamydia* testing and antibiotic treatment immediately without waiting for the results
- D. Offer *Chlamydia* testing and antibiotic treatment if positive
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Treatment is given on the basis of exposure to infection rather than proven infection

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Question 20 of 143

Which one of the following features is least likely to occur in a patient with visceral leishmaniasis?

- A. Massive splenomegaly
- B. Diarrhoea
- C. Pyrexia
- D. Pancytopaenia
- E. Grey skin

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The most common symptoms seen in patients with visceral leishmaniasis are pyrexia, splenomegaly (which is often massive), weight loss and night sweats. Pancytopaenia occurs secondary to hypersplenism. Diarrhoea is not a typical feature

Leishmaniasis

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Question 21 of 143

Which one of the following statements regarding scabies is false?

- A. All members of the household should be treated
- B. Typically affects the fingers, interdigital webs and flexor aspects of the wrist in adults
- C. Scabies causes a delayed type IV hypersensitivity reaction
- D. Patients who complain of pruritus 4 weeks following treatment should be retreated
- E. Malathion is suitable for the eradication of scabies

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- E. Malathion is suitable for the eradication of scabies

It is normal for pruritus to persist for up to 4-6 weeks post eradication

Scabies

Scabies is caused by the mite Sarcoptes scabiei and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features
- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management
- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)
- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:
- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8–12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Question 22 of 143

Which one of the following congenital infections is most characteristically associated with sensorineural deafness?

- A. Toxoplasma gondii
- B. Parvovirus B19
- C. Rubella
- D. *Treponema pallidum*
- E. Cytomegalovirus

Question 22 of 143

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- C. Rubella
- D. *Treponema pallidum*
- E. Cytomegalovirus

Congenital rubella
- sensorineural deafness
- congenital cataracts

Congenital infections

The major congenital infections encountered in examinations are rubella, toxoplasmosis and cytomegalovirus

Cytomegalovirus is the most common congenital infection in the UK. Maternal infection is usually asymptomatic

	Rubella	**Toxoplasmosis**	**Cytomegalovirus**
Characteristic features	Sensorineural deafness Congenital cataracts Congenital heart disease (e.g. patent ductus arteriosus) Glaucoma	Cerebral calcification Chorioretinitis Hydrocephalus	Growth retardation Purpuric skin lesions
Other features	Growth retardation Hepatosplenomegaly Purpuric skin lesions 'Salt and pepper' chorioretinitis Microphthalmia Cerebral palsy	Anaemia Hepatosplenomegaly Cerebral palsy	Sensorineural deafness Encephalitiis Pneumonitis Hepatosplenomegaly Anaemia Jaundice Cerebral palsy

Question 23 of 143

A 33-year-old man is admitted due to profuse diarrhoea. He has a history of HIV infection and Cryptosporidium diarrhoea is suspected. What investigation is most likely to confirm the diagnosis?

- A. Blood cultures
- B. Sigmoidoscopy with biopsy
- C. Abdominal x-ray
- D. Acid-fast staining of stool sample
- E. Cryptosporidium PCR of stool sample

Question 23 of 143

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- D. Acid-fast staining of stool sample
- E. Cryptosporidium PCR of stool sample

Cryptosporidium cysts turn red following acid-fast staining. Molecular methods are currently used mainly as a research tool

HIV: diarrhoea

Diarrhoea is common in patients with HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes

- Cryptosporidium + other protozoa (most common)
- Cytomegalovirus
- *Mycobacterium avium intracellulare*
- Giardia

Cryptosporidium is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of Cryptosporidium. Treatment is difficult, with the mainstay of management being supportive therapy*

Mycobacterium avium intracellulare is an atypical mycobacteria seen with the CD4 count is below 50. Typical features include fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with rifabutin, ethambutol and clarithromycin

*nitazozanide is licensed in the US for immunocompetent patients

Question 24 of 143

Which one of the following statements is true regarding *Listeria monocytogenes*?

- A. Multiples rapidly at high temperatures
- B. The organism is resistant to ampicillin
- C. It is a Gram negative bacillus
- D. It is diagnosed by the presence of urinary antigen
- E. May cause ataxia

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Listeria

Listeria monocytogenes is a Gram positive bacillus which has the unusual ability to multiply at low temperatures. It is typically spread via contaminated food, typically unpasteurised dairy products. Infection is particularly dangerous to the unborn child where it can lead to miscarriage

Features - can present in a variety of ways
- diarrhoea, flu-like illness
- pneumonia , meningoencephalitis
- ataxia and seizures

Suspected Listeria infection should be investigated by taking blood cultures. CSF may reveal a pleocytosis, with 'tumbling motility' on wet mounts

Management
- Listeria is sensitive to amoxicillin/ampicillin (cephalosporins usually inadequate)
- Listeria meningitis should be treated with IV amoxicillin/ampicillin and gentamicin

Question 25 of 143

A 19-year-old student is brought to the Emergency Department by friends due to a severe headache and drowsiness. On examination he has a widespread purpuric rash. Meningococcal infection is strongly suspected but he is known to be penicillin allergic (previous anaphylaxis). What is the antibiotic of choice?

- A. Chloramphenicol
- B. Meropenem
- C. Teicoplanin
- D. Erythromycin
- E. Ciprofloxacin

Question 25 of 143

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- A. Chloramphenicol
- B. Meropenem
- C. Teicoplanin
- D. Erythromycin
- E. Ciprofloxacin

If there is not a history of anaphylaxis then cefotaxime may be considered for penicillin allergic patients

Meningitis: management

Meningococcus
- if penicillin allergic then give chloramphenicol

Management of contacts
- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- rifampicin or ciprofloxacin may be used
- the risk is highest in the first 7 days but persists for at least 4 weeks
- meningococcal vaccination should be offered when serotype results are available, for close contacts who have not previously been vaccinated*

*no vaccine is available for meningococcal serogroup B

Question 26 of 143

A 72-year-old women is reviewed following a course of oral flucloxacillin for right lower limb cellulitis. The local protocol suggest oral clindamycin should be used next-line. Which one of the following side-effects is it most important to warn her about?

- A. Heartburn or indigestion
- B. Jaundice
- C. Sore throat, bruising or lethargy
- D. Avoid any food or drink containing alcohol
- E. Diarrhoea

Question 26 of 143

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Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading causes

Features
- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management
- oral metronidazole
- if severe or not responding to metronidazole then oral vancomycin may be used

Question 27 of 143

A 23-year-old woman comes for review. She has had recurrent genital warts for the past 4 years which have failed to respond to topical podophyllum. On one occasion she had cryotherapy but will not have it again due to local discomfort. On examination she has a large number of fleshy genital warts around her introitus. What is the most appropriate next step in treatment?

- A. Topical glutaraldehyde
- B. Oral podophyllum
- C. Topical imiquimod
- D. Oral aciclovir
- E. Topical salicylic acid

Question 27 of 143

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- E. Topical salicylic acid

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 28 of 143

A 57-year-old female presents with headache and fever to the Emergency Department. On examination neck stiffness is noted along with a positive Kernig's sign. A lumbar puncture is performed and reported as follows:

CSF culture Gram positive bacilli

What is the most likely causative organism?

- A. *Cryptococcus*
- B. *Haemophilus influenzae*
- C. *Streptococcus pneumoniae*
- D. *E. coli*
- E. *Listeria monocytogenes*

Question 28 of 143

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CSF culture Gram positive bacilli

What is the most likely causative organism?

- A. *Cryptococcus*
- B. *Haemophilus influenzae*
- C. *Streptococcus pneumoniae*
- D. *E. coli*
- E. *Listeria monocytogenes*

Classification of bacteria

Remember:

- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L

- *Actinomyces*
- *Bacillus antracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

Question 29 of 143

A 37-year-old immigrant from Bolivia is admitted to the Emergency Department following a collapse. He is known to have a history of Chagas' disease. Which one of the following complications of Chagas' disease accounts for the majority of mortality in affected patients?

- A. Large bowel perforation secondary to megacolon
- B. Myocarditis
- C. Perinephric abscess
- D. Meningoencephalitis
- E. Pulmonary haemorrhage

Question 29 of 143

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- B. Myocarditis
- C. Perinephric abscess
- D. Meningoencephalitis
- E. Pulmonary haemorrhage

Cardiac involvement is the leading cause of death in patients with Chagas' disease

Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - Trypanosoma gambiense in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

American trypanosomiasis, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaoesophagus and megacolon causing dysphagia and constipation

Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

Question 30 of 143

Which of the following vaccines uses a whole killed organism?

- A. Pneumococcus
- B. Meningococcus
- C. Pertussis
- D. Oral polio
- E. Diphtheria

Question 30 of 143

Which of the following vaccines uses a whole killed organism?

- A. Pneumococcus
- B. Meningococcus
- C. Pertussis
- D. Oral polio
- E. Diphtheria

Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients

Live attenuated vaccines
- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid

Whole killed organism*
- rabies
- pertussis

Fragment
- diphtheria
- tetanus
- meningococcus, pneumococcus, haemophilus

Others
- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of Vibrio cholerae together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

*injectable typhoid is no longer used in the UK

Question 31 of 143

Which one of the following is true regarding linezolid?

- A. Active against both MRSA and VRE (Vancomycin-Resistant Enterococcus)
- B. Bactericidal in action
- C. No activity against GISA (Glycopeptide Intermediate *Staphylococcus aureus*)
- D. Adverse effects include raised platelet count
- E. Inhibits RNA synthesis

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Linezolid

Linezolid is a type of oxazolidonone antibiotic which has been introduced in recent years. It inhibits bacterial protein synthesis by stopping formation of the 70s initiation complex and is bacteriostatic nature

Spectrum, highly active against Gram positive organisms including:

- MRSA (Methicillin-resistant *Staphylococcus aureus*)
- VRE (Vancomycin-resistant enterococcus)
- GISA (Glycopeptide Intermediate *Staphylococcus aureus*)

Adverse effects

- thrombocytopenia (reversible on stopping)
- monoamine oxidase inhibitor: avoid tyramine containing foods

Question 32 of 143

A 45-year-old man presents to the Emergency Department due to severe pain in the perineal area over the past 6 hours. On examination the skin is cellulitic, extremely tender and haemorrhagic bullae are seen. What is the most appropriate management?

- A. Surgical debridement
- B. IV cefuroxime and metronidazole
- C. IV flucloxacillin and benzylpenicillin
- D. Plasma exchange
- E. Urgent microscopy of wound swab

Question 32 of 143

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- D. Plasma exchange
- E. Urgent microscopy of wound swab

Surgical referral is the single most important step in the management of necrotising fasciitis. There has been little change in the mortality of necrotising fasciitis since the introduction of antibiotics

Necrotising fasciitis

Necrotising fasciitis is a medical emergency that is difficult to recognise in the early stages

It can be classified according to the causative organism:

- type 1 is caused by mixed anaerobes and aerobes (often occurs post-surgery in diabetics)
- type 2 is caused by *Streptococcus pyogenes*

Features

- acute onset
- painful, erythematous lesion develops
- extremely tender over infected tissue

Management

- urgent surgical referral debridement
- IV antibiotics

Question 33 of 143

A 44-year-old farmer presents with headache, fever and muscle aches. He initially thought he had a bad cold but his symptoms have got progressively worse over the past week. During the review of systems he reports nausea and a decreased urine output. On examination his temperature is 38.2ºC, pulse 102 / min and his chest is clear. Subconjunctival haemorrhages are noted but there is no evidence of jaundice. What is the most likely diagnosis?

- A. Mycoplasma pneumonia
- B. Lyme disease
- C. Legionella pneumonia
- D. Listeria
- E. Leptospirosis

Question 33 of 143

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- B. Lyme disease
- C. Legionella pneumonia
- D. Listeria
- E. Leptospirosis

The main clue in the question is the patients occupation. Mycoplasma and Legionella are less likely due to the absence of chest symptoms and signs. Liver failure is seen in only 10% of patients with leptospirosis.

Leptospirosis

Also known as Weil's disease*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete Leptospira interrogans (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

Features

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

Management

- high-dose benzylpenicillin or doxycycline

*the term Weil's disease is sometimes referred for the most severe 10% of cases of leptospirosis associated with jaundice

Question 34 of 143

A 62-year-old patient with type 2 diabetes mellitus presents with a 'rash' on his left shin. This has grown in size over the past two days and is now a painful, hot, erythematous area on his anterior left shin spreading around to the back of the leg. He is systemically well and a decision is made to give oral treatment. He has a past history of penicillin allergy. What is the most appropriate antibiotic to give?

- A. Clarithromycin
- B. Cefaclor
- C. Clindamycin
- D. Vancomycin
- E. Erythromycin

Question 34 of 143

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- B. Cefaclor
- C. Clindamycin
- D. Vancomycin
- E. Erythromycin

Cellulitis: management

The BNF recommends penicillin + flucloxacillin as first-line treatment for cellulitis. Erythromycin is recommend in patients allergic to penicillin. Treatment failure is now commonly treated with oral clindamycin.

Question 35 of 143

A 43-year-old Asian man presents with headache and neck stiffness. CT brain is normal and a lumbar puncture is performed with the following results

Serum glucose 4.7 mmol/l

Lumbar puncture reveals:

Opening pressure	15 cmCSF
Appearance	Cloudy
Glucose	3.3 mmol/l
Protein	0.7 g/l
White cells	100 / mm^3 (70% lymphocytes)

What is the most likely diagnosis?

- A. Bacterial meningitis
- B. Viral meningitis
- C. Tuberculous meningitis
- D. Normal CSF result
- E. Cryptococcal meningitis

Question 35 of 143

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What is the most likely diagnosis?

- A. Bacterial meningitis
- B. Viral meningitis
- C. Tuberculous meningitis
- D. Normal CSF result
- E. Cryptococcal meningitis

The CSF lymphocytosis combined with a glucose greater than half the serum level points towards a viral meningitis. TB meningitis is associated with a low CSF glucose

Meningitis: CSF analysis

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	Bacterial	**Viral**	**Tuberculous**
Appearance	Cloudy	Clear/cloudy	Fibrin web
Glucose	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
Protein	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
White cells	10 - 5,000 polymorphs/mm³	15 - 1,000 lymphocytes/mm³	10 - 1,000 lymphocytes/mm³

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Question 36 of 143

A 44-year-old farmer presents to the Emergency Department due to a high temperature and confusion. On examination his pulse is 124 bpm, blood pressure 84/56 mmHg and temperature 39.8ºC. He has a generalised erythematous rash which is starting to desquamate on his palms and is also noted to have a paronychial infection of a fingernail on the left hand. What is the most likely diagnosis?

- A. Paraquat overdose
- B. Leptospirosis
- C. Staphylococcal toxic shock syndrome
- D. Disseminated herpes simplex infection
- E. Organophosphate poisoning

Question 36 of 143

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Staphylococcal toxic shock syndrome

Staphylococcal toxic shock syndrome describes a severe systemic reaction to staphylococcal exotoxins. It came to prominence in the early 1980's following a series of cases related to infected tampons

Centers for Disease Control and Prevention diagnostic criteria

- fever: temperature > 38.9ºC
- hypotension: systolic blood pressure < 90 mmHg
- diffuse erythematous rash
- desquamation of rash, especially of the palms and soles
- involvement of three or more organ systems: e.g. gastrointestinal (diarrhoea and vomiting), mucous membrane erythema, renal failure, hepatitis, thrombocytopenia, CNS involvement (e.g. confusion)

Question 37 of 143

Following a diagnosis of tetanus, what is the most appropriate antibiotic therapy to give with human tetanus immunoglobulin?

- A. IV clarithromycin
- B. IV benzylpenicillin
- C. IV gentamicin
- D. IV metronidazole
- E. IV ciprofloxacin

Question 37 of 143

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Tetanus

Tetanus is caused by the tetanospasmin exotoxin released from *Clostridium tetani*. Tetanus spores are present in soil and may be introduced into the body from a wound, which is often unnoticed. Tetanospasmin prevents release of GABA

Features

- prodrome fever, lethargy, headache
- trismus (lockjaw)
- risus sardonicus
- opisthotonus (arched back, hyperextended neck)
- spasms (e.g. dysphagia)

Management

- supportive therapy including ventilatory support and muscle relaxants
- intramuscular human tetanus immunoglobulin for high-risk wounds (e.g. compound fractures, delayed surgical intervention, significant degree of devitalised tissue)
- metronidazole is now preferred to benzylpenicillin as the antibiotic of choice

Question 38 of 143

A 19-year-old man presents with a compound fracture of his leg following a fall from scaffolding. Examination reveals soiling of the wound with mud. He is sure he has had five previous tetanus vaccinations. What is the most appropriate course of action to prevent the development of tetanus?

- A. Clean wound + intramuscular human tetanus immunoglobulin
- B. Clean wound + tetanus vaccine
- C. Clean wound + tetanus vaccine + intramuscular human tetanus immunoglobulin
- D. Clean wound + tetanus vaccine + benzylpenicillin
- E. Clean wound

Question 38 of 143

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B. Clean wound + tetanus vaccine

C. Clean wound + tetanus vaccine + intramuscular human tetanus immunoglobulin

D. Clean wound + tetanus vaccine + benzylpenicillin

E. Clean wound

A soiled, compound fracture is regarded as high-risk for tetanus and intramuscular human tetanus immunoglobulin should be given. There is a role for antibiotics given the soiled wound although benzylpenicillin would not be the drug of choice.

Tetanus: vaccination

The tetanus vaccine is a cell-free purified toxin that is normally given as part of a combined vaccine.

Tetanus vaccine is currently given in the UK as part of the routine immunisation schedule at:

- 2 months
- 3 months
- 4 months
- 3-5 years
- 13-18 years

This therefore provides 5 doses of tetanus-containing vaccine. Five doses is now considered to provide adequate long-term protection against tetanus.

Intramuscular human tetanus immunoglobulin should be given to patients with high-risk wounds (e.g. Compound fractures, delayed surgical intervention, significant degree of devitalised tissue) irrespective of whether 5 doses of tetanus vaccine have previously been given

If vaccination history is incomplete or unknown then a dose of tetanus vaccine should be given combined with intramuscular human tetanus immunoglobulin for high-risk wounds

Question 39 of 143

You attend a meeting with the hospital management. There is currently an increased incidence of MRSA septicaemia in the hospital and a strategy is being drawn up to tackle this. What is the most effective single step to reduce the incidence of MRSA?

- A. The use of personal protective equipment for staff including gloves and aprons
- B. Hand hygiene
- C. Screening patients for MRSA on admission
- D. Cohort nursing
- E. Limiting the number of visitors

Question 39 of 143

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C. Screening patients for MRSA on admission

D. Cohort nursing

E. Limiting the number of visitors

Whilst tackling MRSA requires a multi-pronged approach the evidence base demonstrates that hand hygiene is the single most important step

MRSA

The following antibiotics are commonly used in the treatment of MRSA infections:

- vancomycin
- teicoplanin

Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:

- rifampicin
- macrolides
- tetracyclines
- aminoglycosides
- clindamycin

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases

Question 40 of 143

A 31-year-old woman presents as she has noted an offensive, fishy vaginal discharge. She describes a grey, watery discharge. What is the most likely diagnosis?

- A. *Trichomonas vaginalis*
- B. *Candida*
- C. *Chlamydia*
- D. Bacterial vaginosis
- E. Physiological discharge

Question 40 of 143

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- B. *Candida*
- C. *Chlamydia*
- D. Bacterial vaginosis
- E. Physiological discharge

Vaginal discharge

Vaginal discharge is a common presenting symptom and is not always pathological

Common causes
- physiological
- *Candida*
- *Trichomonas vaginalis*
- bacterial vaginosis

Less common causes
- whilst cervical infections such as *Chlamydia* and Gonorrhoea can cause a vaginal discharge this is rarely the presenting symptoms
- ectropion
- foreign body
- cervical cancer

Key features of the common causes are listed below

Condition	**Key features**
Candida	'Cottage cheese' discharge Vulvitis Itch
Trichomonas vaginalis	Offensive, yellow/green, frothy discharge Vulvovaginitis Strawberry cervix
Bacterial vaginosis	Offensive, thin, white/grey, 'fishy' discharge

Question 41 of 143

A 38-year-old homeless man is diagnosed as having pulmonary tuberculosis. It is decided that directly observed therapy should be used. How often will he need to take anti-tuberculosis medications?

- A. Once a week
- B. Twice a week
- C. Three times a week
- D. Five times a week
- E. Once every day

Question 41 of 143

A 38-year-old homeless man is diagnosed as having pulmonary tuberculosis. It is decided that directly observed therapy should be used. How often will he need to take anti-tuberculosis medications?

- A. Once a week
- B. Twice a week
- C. Three times a week
- D. Five times a week
- E. Once every day

Tuberculosis: drug therapy

The standard therapy for treating **active tuberculosis** is:

Initial phase - first 2 months (RIPE)
- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months
- Rifampicin
- Isoniazid

The treatment for **latent tuberculosis** is isoniazid alone for 6 months

Patients with **meningeal tuberculosis** are treated for a prolonged period (at least 12 months) with the addition of steroids

Directly observed therapy with a thrice weekly dosing regimen may be indicated in certain groups, including:
- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

Question 42 of 143

Which one of the following statements regarding toxoplasmosis is true?

- A. It is a type of flagellate
- B. Congenital toxoplasmosis results in optic nerve atrophy
- C. Ceftriaxone should be used initially in patients with HIV-associated toxoplasmosis
- D. The cat is the only known animal reservoir
- E. infection is usually self-limiting

Question 42 of 143

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- B. Congenital toxoplasmosis results in optic nerve atrophy
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- D. The cat is the only known animal reservoir
- E. infection is usually self-limiting

Toxoplasmosis

Toxoplasma gondii is a protozoa which infects the body via the GI tract, lung or broken skin. It's oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. The usual animal reservoir is the cat, although other animals such as rats carry the disease.

Most infections are asymptomatic. Symptomatic patients usually have a self-limiting infection, often having clinical features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Other less common manifestations include meningioencephalitis and myocarditis.

Investigation
- antibody test
- Sabin-Feldman dye test

Treatment is usually reserved for those with severe infections or patients who are immunosuppressed
- pyrimethamine plus sulphadiazine for at least 6 weeks

Congenital toxoplasmosis is due to transplacental spread from the mother. It causes a variety of effects to the unborn child including microcephaly, hydrocephalus, cerebral calcification and choroidoretinitis.

Question 43 of 143

A phlebotomist gives herself a needlestick injury whilst taking blood from a patient who is known to be hepatitis B positive. The phlebotomist has just started her job and is in the process of being immunised for hepatitis B but has only had one dose to date. What is the most appropriate action to minimise her risk of contracting hepatitis B from the needle?

- A. No action needed, complete hepatitis B vaccination course as normal
- B. Give oral ribavirin for 4 weeks
- C. Give an accelerated course of the hepatitis B vaccine + hepatitis B immune globulin
- D. Give hepatitis B immune globulin + oral ribavirin for 4 weeks
- E. Give hepatitis B immune globulin

Question 43 of 143

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C. Give an accelerated course of the hepatitis B vaccine + hepatitis B immune globulin

D. Give hepatitis B immune globulin + oral ribavirin for 4 weeks

E. Give hepatitis B immune globulin

Post-exposure prophylaxis

Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

HIV

- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

Question 44 of 143

Which of the following anti-retroviral drugs is most characteristically associated with nephrolithiasis?

- A. Zidovudine
- B. Didanosine
- C. Indinavir
- D. Ritonavir
- E. Nevirapine

Question 44 of 143

Which of the following anti-retroviral drugs is most characteristically associated with nephrolithiasis?

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- E. Nevirapine

HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Question 45 of 143

A 77-year-old female presents with a non-healing ulcer on her right foot. Blood cultures grow MRSA. Which antibiotic would you consider in addition to vancomycin?

- A. Flucloxacillin
- B. Ceftazidime
- C. Ciprofloxacin
- D. Metronidazole
- E. Rifampicin

Question 45 of 143

A 77-year-old female presents with a non-healing ulcer on her right foot. Blood cultures grow MRSA. Which antibiotic would you consider in addition to vancomycin?

- A. Flucloxacillin
- B. Ceftazidime
- C. Ciprofloxacin
- D. Metronidazole
- E. Rifampicin

MRSA

The following antibiotics are commonly used in the treatment of MRSA infections:

- vancomycin
- teicoplanin

Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:

- rifampicin
- macrolides
- tetracyclines
- aminoglycosides
- clindamycin

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases

Question 46 of 143

Which one of the following is the most common cause of visceral larva migrans?

- A. *Cryptococcus neoformans*
- B. Strongyloides stercoralis
- C. Visceral leishmaniasis
- D. Toxocara canis
- E. Giardiasis

Question 46 of 143

Which one of the following is the most common cause of visceral larva migrans?

- A. *Cryptococcus neoformans*
- B. Strongyloides stercoralis
- C. Visceral leishmaniasis
- D. Toxocara canis
- E. Giardiasis

Nematodes

Ancylostoma braziliense
- most common cause of cutaneous larva migrans
- common in Central and Southern America

Strongyloides stercoralis
- acquired percutaneously (e.g. walking barefoot)
- causes pruritus and larva currens - this has a similar appearance to cutaneous larva migrans but moves through the skin at a far greater rate
- abdo pain, diarrhoea, pneumonitis
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- eosinophilia sometimes seen
- management: thiabendazole, albendazole. Ivermectin also used, particularly in chronic infections

Toxocara canis
- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of visceral larva migrans
- other features: eye granulomas, liver/lung involvement

Question 47 of 143

A 23-year-old male presents with a purulent urethral discharge. A sample of the discharge is shown to be a Gram negative diplococcus. What is the most appropriate antimicrobial therapy?

- A. Ciprofloxacin 500mg BD PO for 7 days
- B. Penicillin V 500mg QDS PO for 7 days
- C. Doxycycline 100mg BD PO for 7 days
- D. Ciprofloxacin 500mg PO (single dose)
- E. Cefixime 400mg PO (single dose)

Question 47 of 143

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- D. Ciprofloxacin 500mg PO (single dose)
- E. Cefixime 400mg PO (single dose)

Cephalosporins are now the treatment of choice for Gonorrhoea

Ciprofloxacin should only be used if the organism is known to be sensitive due to increasing resistance. Penicillin, previously first-line treatment, is rarely used now due to widespread resistance

Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria* gonorrhoea. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

Features
- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

Management
- ciprofloxacin 500mg PO used to be the treatment of choice
- however, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- options include cefixime 400mg PO (single dose) or ceftriaxone 250mg IM

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthritis and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Key features of disseminated gonococcal infection
- tenosynovitis
- migratory polyarthritis
- dermatitis (lesions can be maculopapular or vesicular)

Question 48 of 143

A 31-year-old woman is admitted to hospital. As part of a liver screen the following results are obtained:

Anti-HBs	Positive
Anti-HBc	Positive
HBs antigen	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen

What is the patient's hepatitis B status?

- A. Previous immunisation to hepatitis B
- B. Chronic hepatitis B - highly infectious
- C. Previous hepatitis B infection, not a carrier
- D. Chronic hepatitis B - not infectious
- E. Acute hepatitis B infection

Question 48 of 143

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- D. Chronic hepatitis B - not infectious
- E. Acute hepatitis B infection

Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Question 49 of 143

A 33-year-old male nurse presents 6 weeks after visiting North Africa on business. He describes feeling lethargic and having episodic fever. A blood screen is sent which reveals the following:

Hb	15.9 g/dl
WBC	7.1 $*10^9$/l
Platelets	343 $*10^9$/l
Bilirubin	53 µmol/l
ALP	169 u/l
ALT	364 u/l
Hepatitis A IgM	Negative
Anti-HBs	Positive

What is the most likely diagnosis?

- A. Infectious mononucleosis
- B. Hepatitis B
- C. Hepatitis A
- D. HIV
- E. Hepatitis E

Question 49 of 143

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Platelets	343 *10^9/l
Bilirubin	53 µmol/l
ALP	169 u/l
ALT	364 u/l
Hepatitis A IgM	Negative
Anti-HBs	Positive

What is the most likely diagnosis?

- A. Infectious mononucleosis
- B. Hepatitis B
- C. Hepatitis A
- D. HIV
- E. Hepatitis E

The incubation period and negative Hepatitis A IgM points to a diagnosis of Hepatitis E

Hepatitis E

Overview

- RNA virus
- spread by the faecal-oral route, incubation period = 3-8 weeks
- common in Central and South-East Asia, North and West Africa, and in Mexico
- causes a similar disease to hepatitis A, but carries a significant mortality (about 20%) during pregnancy
- does not cause chronic disease
- a vaccine is currently in development*, but is not yet in widespread use

*New England Journal of Medicine 356:895, 2007

Question 50 of 143

A 34-year-old man presents with a widespread maculopapular rash and mouth ulcers. Two months ago he reports developing a painless penile ulcer. Which one of the following organisms is most likely to be responsible?

- A. Lymphogranuloma venereum
- B. Herpes simplex virus type 2
- C. *Mycoplasma genitalium*
- D. *Treponema pertenue*
- E. *Treponema pallidum*

Question 50 of 143

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- B. Herpes simplex virus type 2
- C. *Mycoplasma genitalium*
- D. *Treponema pertenue*
- E. *Treponema pallidum*

This patient has symptoms of secondary syphilis

Syphilis

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. The incubation period is between 9-90 days

Primary features
- chancre - painless ulcer at the site of sexual contact
- often not seen in women

Secondary features - occurs 4-10 weeks after primary infection
- systemic symptoms: fevers, lymphadenopathy
- rash on trunk, palms and soles
- buccal 'snail track' ulcers (30%)
- condylomata lata

Latent period

Tertiary features
- gummas
- aortic aneurysms
- general paralysis of the insane
- tabes dorsalis

Question 51 of 143

A 34-year-old abattoir worker presents to the Emergency Department following the development of black skin lesions. On examination a black eschar is noted with extensive surrounding oedema. A diagnosis of cutaneous anthrax is suspected. What is the most appropriate initial antibiotic therapy until sensitivities are known?

- A. Ciprofloxacin
- B. Metronidazole
- C. Erythromycin
- D. Benzylpenicillin
- E. Gentamicin

Question 51 of 143

A 34-year-old abattoir worker presents to the Emergency Department following the development of black skin lesions. On examination a black eschar is noted with extensive surrounding oedema. A diagnosis of cutaneous anthrax is suspected. What is the most appropriate initial antibiotic therapy until sensitivities are known?

- A. Ciprofloxacin
- B. Metronidazole
- C. Erythromycin
- D. Benzylpenicillin
- E. Gentamicin

The current Health Protection Agency advice for the initial management of cutaneous anthrax is ciprofloxacin

Anthrax

Anthrax is caused by Bacillus anthracis, a Gram positive rod. It is spread by infected carcasses

Features

- causes painless black eschar (cutaneous 'malignant pustule', but no pus)
- typically painless and non-tender
- may cause marked oedema
- anthrax can cause gastrointestinal bleeding

Management

- the current Health Protection Agency advice for the initial management of cutaneous anthrax is ciprofloxacin
- further treatment is based on microbiological investigations and expert advice

Question 52 of 143

Which one of the following is true regarding *Escherichia coli* infection?

- A. It is a Gram negative coccus
- B. E coli is an important cause of neonatal meningitis
- C. The O157:H7 strain is typically spread via shellfish
- D. Severe infection should be treated with teicoplanin
- E. It is an aerobic bacteria

Question 52 of 143

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- B. E coli is an important cause of neonatal meningitis
- C. The O157:H7 strain is typically spread via shellfish
- D. Severe infection should be treated with teicoplanin
- E. It is an aerobic bacteria

Escherichia coli is classified as a facultative anaerobe

Escherichia coli

Escherichia coli is a facultative anaerobic, lactose-fermenting, Gram negative rod which is a normal gut commensal.

E coli infections lead to a variety of diseases in humans including:

- diarrhoeal illnesses
- UTIs
- neonatal meningitis

E coli O157:H7 is a particular strain associated with severe, haemorrhagic, watery diarrhoea. It has a high mortality rate and can be complicated by haemolytic uraemic syndrome. It is often spread by contaminated ground beef.

Question 53 of 143

Each of the following organisms commonly cause respiratory tract infections in patients with cystic fibrosis, except:

A. Aspergillus

B. *Pseudomonas aeruginosa*

C. Burkholderia cepacia

D. Staphylococcal aureus

E. Strongyloides stercoralis

Question 53 of 143

Each of the following organisms commonly cause respiratory tract infections in patients with cystic fibrosis, except:

- A. Aspergillus
- B. *Pseudomonas aeruginosa*
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- D. Staphylococcal aureus
- E. Strongyloides stercoralis

Cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder causing increased viscosity of secretions (e.g. lungs and pancreas). It is due to a defect in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which codes a cAMP-regulated chloride channel

In the UK 80% of CF cases are due to a deletion at delta F508 on the long arm of chromosome 7. Cystic fibrosis affects 1 per 2500 births, and the carrier rate is c. 1 in 25

Organisms which may colonise CF patients

- Staph aureus
- *Pseudomonas aeruginosa*
- Burkholderia cepacia*
- Aspergillus

*previously known as *Pseudomonas* cepacia

Question 54 of 143

A 26-year-old man returns to the genito-urinary medicine clinic. He is a known intravenous drug user. Five days ago he was seen with a urethral discharge. A swab taken in the clinic showed a Gram-negative diplococcus and treatment with IM ceftriaxone was given. Unfortunately his symptoms have not resolved. What is the most likely explanation?

- A. Gonorrhoea-resistant to ceftriaxone
- B. Co-existent *Candida* infection
- C. HIV infection
- D. Co-existent syphilis infection
- E. Co-existent *Chlamydia* infection

Question 54 of 143

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- B. Co-existent *Candida* infection
- C. HIV infection
- D. Co-existent syphilis infection
- E. Co-existent *Chlamydia* infection

Co-existent infection with *Chlamydia* is extremely common in patients with gonorrhoea.

Chlamydia

Chlamydia is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

Features
- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

Potential complications
- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

Investigation
- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice
- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

Screening
- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

Question 55 of 143

A woman who is 14 weeks pregnant presents as she came into contact with a child who has chickenpox around 4 days ago. She is unsure if she had the condition herself as a child. Blood tests show the following:

Varicella IgM Negative

Varicella IgG Negative

What is the most appropriate management?

- A. Varicella zoster immunoglobulin
- B. No action required
- C. IV aciclovir
- D. Varicella zoster vaccination
- E. Varicella zoster vaccination + varicella zoster immunoglobulin

Question 55 of 143

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- C. IV aciclovir
- D. Varicella zoster vaccination
- E. Varicella zoster vaccination + varicella zoster immunoglobulin

Chickenpox exposure when pregnant - if not immune give VZIG

The negative IgG indicates no previous exposure to chickenpox

Chickenpox exposure in pregnancy

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion. In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed fetal varicella syndrome

Fetal varicella syndrome (FVS)

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks
- features of FVS include skin scarring, eye defects (microphthalmia), limb hypoplasia, microcephaly and learning disabilities

Management of chickenpox exposure

- if there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies
- if the pregnant women is not immune to varicella she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure
- consensus guidelines suggest oral aciclovir should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

Question 56 of 143

A 34-year-old HIV positive man is being treated for *Pneumocystis carinii* pneumonia with co-trimoxazole. Arterial blood gases show a pO2 of 8.2 kPa. What drug should be added to treatment?

- A. Meropenem
- B. Chloramphenicol
- C. Steroids
- D. Nebulised fluconazole
- E. Magnesium sulphate

Question 56 of 143

A 34-year-old HIV positive man is being treated for *Pneumocystis carinii* pneumonia with co-trimoxazole. Arterial blood gases show a pO2 of 8.2 kPa. What drug should be added to treatment?

- A. Meropenem
- B. Chloramphenicol
- C. Steroids
- D. Nebulised fluconazole
- E. Magnesium sulphate

HIV: *Pneumocystis carinii* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as Pneumocystis jiroveci, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- Pneumocystis jiroveci is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm^3 should receive PCP prophylaxis

Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if pO2 < 9.3kPa then steroids reduce risk of respiratory failure by 50% and death by a third)

Question 57 of 143

Which one of the following conditions is not associated with prior Epstein-Barr virus infection?

- A. Hodgkin's lymphoma
- B. Adult T-cell leukaemia
- C. Burkitt's lymphoma
- D. Nasopharyngeal carcinoma
- E. Hairy leukoplakia

Question 57 of 143

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- B. Adult T-cell leukaemia
- C. Burkitt's lymphoma
- D. Nasopharyngeal carcinoma
- E. Hairy leukoplakia

EBV: associated malignancies:
- Burkitt's lymphoma
- Hodgkin's lymphoma
- nasopharyngeal carcinoma

Adult T-cell leukaemia is associated with HTLV-1 infection

Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection
- Burkitt's lymphoma*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also assocaiated with EBV infection.

*EBV is currently thought to be associated with both African and sporadic Burkitt's

Question 58 of 143

Which one of the following antibiotics is most likely to cause pseudomembranous colitis?

- A. Cefuroxime
- B. Cefalexin
- C. Ciprofloxacin
- D. Co-amoxiclav
- E. Piperacillin-tazobactam

Question 58 of 143

Which one of the following antibiotics is most likely to cause pseudomembranous colitis?

- A. Cefuroxime
- B. Cefalexin
- C. Ciprofloxacin
- D. Co-amoxiclav
- E. Piperacillin-tazobactam

Cephalosporins, not just clindamycin, are strongly linked to *Clostridium difficile*

This is a difficult question as both co-amoxiclav and ciprofloxacin are known to cause *Clostridium difficile*. Studies looking at the relative risk (RR) of developing *Clostridium difficile* following antibiotic therapy give the following results (please see the link):

- clindamycin: RR = 31.8
- cephalosporins: RR = 14.9
- ciprofloxacin: RR = 5.0

Cefalexin is a first generation cephalosporin and less associated with *Clostridium difficile* than newer agents such as ceftriaxone

Clostridium difficile

Clostridium difficile is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading causes

Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

Management

- oral metronidazole
- if severe or not responding to metronidazole then oral vancomycin may be used

Question 59 of 143

Which of the following infections usually has the longest incubation period?

- A. Meningococcus
- B. Scarlet fever
- C. Typhoid
- D. Diphtheria
- E. Influenza

Question 59 of 143

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Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week
- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks
- malaria
- dengue fever
- typhoid
- measles

2 - 3 weeks
- mumps
- rubella
- chickenpox

Longer than 3 weeks
- infectious mononucleosis
- cytomegalovirus
- viral hepatitis
- HIV

Question 60 of 143

A pregnant 34-year-old female presents with uncomplicated Falciparum malaria following a trip to Kenya. Which one of the following is the most suitable treatment?

- A. Chloroquine
- B. Artemether-lumefantrine
- C. Doxycycline
- D. Quinine
- E. Atovaquone-proguanil

Question 60 of 143

A pregnant 34-year-old female presents with uncomplicated Falciparum malaria following a trip to Kenya. Which one of the following is the most suitable treatment?

- A. Chloroquine
- B. Artemether-lumefantrine
- C. Doxycycline
- D. Quinine
- E. Atovaquone-proguanil

Both artemether and atovaquone are not currently recommended in pregnancy

Malaria: Falciparum

Feature of severe malaria
- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

Complications
- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria
- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- first choice is oral quinine for 5 days followed by sulfadoxine-pyrimethamine or doxycycline
- alternative regimes include atovaquone-proguanil or artemether-lumefantrine

Severe falciparum malaria
- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- options include intravenous quinine or artemisinins
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

Question 61 of 143

A 43-year-old man from Sierra Leone presents with a flu-like illness. On examination he has very large posterior cervical lymph nodes. A diagnosis of African trypanosomiasis is confirmed on blood smear. What is the most appropriate treatment?

- A. Atovaquone-proguanil
- B. Sodium stibogluconate
- C. Benznidazole
- D. Metronidazole
- E. Pentamidine

Question 61 of 143

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- B. Sodium stibogluconate
- C. Benznidazole
- D. Metronidazole
- E. Pentamidine

Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - Trypanosoma gambiense in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

American trypanosomiasis, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaoesophagus and megacolon causing dysphagia and constipation

Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

Question 62 of 143

A 18-year-old male presents with generalised lymphadenopathy. Which one of the following is least likely to result in this presentation?

- A. Kawasaki disease
- B. Cytomegalovirus
- C. Acute lymphoblastic leukaemia
- D. Phenytoin therapy
- E. Infectious mononucleosis

Question 62 of 143

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- B. Cytomegalovirus
- C. Acute lymphoblastic leukaemia
- D. Phenytoin therapy
- E. Infectious mononucleosis

Kawasaki disease causes only cervical lymphadenopathy

Lymphadenopathy

There are many causes of generalised lymphadenopathy

Infective
- infectious mononucleosis
- HIV, including seroconversion illness
- eczema with secondary infection
- rubella
- toxoplasmosis
- CMV
- tuberculosis
- roseola infantum

Neoplastic
- leukaemia
- lymphoma

Others
- autoimmune conditions: SLE, rheumatoid arthritis
- graft versus host disease
- sarcoidosis
- drugs: phenytoin and to a lesser extent allopurinol, isoniazid

Question 63 of 143

A 55-year-old business man presents with a 15 day history of watery, non-bloody diarrhoea associated with anorexia and abdominal bloating. His symptoms started 4 days after returning from a trip to Pakistan. On examination he is apyrexial with dry mucous membranes but normal skin turgor. Given the likely organism, what is the most appropriate treatment?

- A. Hydroxychloroquine
- B. Aciclovir
- C. Benzylpenicillin
- D. Ciprofloxacin
- E. Metronidazole

Question 63 of 143

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- A. Hydroxychloroquine
- B. Aciclovir
- C. Benzylpenicillin
- D. Ciprofloxacin
- E. Metronidazole

Although *Escherichia coli* is the most common cause of travellers' diarrhoea, in this particular case the length of illness and nature of symptoms (bloating, watery diarrhoea) points to a diagnosis of Giardiasis.

Giardiasis

Giardiasis is caused by the flagellate protozoan *Giardia lamblia*. It is spread by the faeco-oral route

Features

- often asymptomatic
- lethargy, bloating, abdominal pain
- non-bloody diarrhoea
- chronic diarrhoea, malabsorption and lactose intolerance can occur
- stool microscopy for trophozoite and cysts are classically negative, therefore duodenal fluid aspirates or 'string tests' (fluid absorbed onto swallowed string) are sometimes needed

Treatment is with metronidazole

Question 64 of 143

Which one of the following features is not associated with Lyme disease?

- A. Jarisch-Herxheimer reaction
- B. Meningitis
- C. Prolonged PR interval on ECG
- D. Erythema marginatum
- E. Arthralgia

Question 64 of 143

Which one of the following features is not associated with Lyme disease?

- A. Jarisch-Herxheimer reaction
- B. Meningitis
- C. Prolonged PR interval on ECG
- D. Erythema marginatum
- E. Arthralgia

Lyme disease is associated with erythema chronicum migrans

Lyme disease: features

Early features
- erythema chronicum migrans (small papule often at site of the tick bite which develops into a larger annular lesion with central clearing, occurs in 70% of patients)
- systemic symptoms: malaise, fever, arthralgia

Later features
- CVS: heart block, myocarditis
- neurological: cranial nerve palsies, meningitis
- polyarthritis

Question 65 of 143

A 53-year-old woman is diagnosed with left leg cellulitis. A swab is taken and oral flucloxacillin is started. The following result is obtained:

Skin swab: Group A *Streptococcus*

How should the antibiotic therapy be changed?

- A. No change
- B. Add topical fusidic acid
- C. Add clindamycin
- D. Add penicillin
- E. Add erythromycin

Question 65 of 143

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How should the antibiotic therapy be changed?

- A. No change
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- C. Add clindamycin
- D. Add penicillin
- E. Add erythromycin

Penicillin is the antibiotic of choice for group A streptococcal infections. The BNF suggests stopping flucloxacillin if streptococcal infection is confirmed in patients with cellulitis, due to the high sensitivity. This should be balanced however with the variable absorption of phenoxymethylpenicillin

Streptococci

Streptococci may be divided into alpha and beta haemolytic types

Alpha haemolytic streptococci

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

Beta haemolytic streptococci

These can be subdivided into group A and B

Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

Question 66 of 143

A 14-year-old boy presents with pyrexia, myalgia and lethargy. Clinical examination reveals a temperature of 38.8ºC. He is haemodynamically stable and his chest is clear. Given the current pandemic a presumptive diagnosis of H1N1 influenza is made and oseltamivir is prescribed. What is the most likely side-effect he will experience?

- A. Dry mouth
- B. Headache
- C. Bronchospasm
- D. Nausea
- E. Rash

Question 66 of 143

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- A. Dry mouth
- B. Headache
- C. Bronchospasm
- D. Nausea
- E. Rash

Gastrointestinal symptoms are the most common side-effects of oseltamivir (Tamiflu).

H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

Features

The majority of symptoms are typical of those seen in a flu-like illness:

- fever greater than 38ºC
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

Treatment

There are two main treatments currently available:

Oseltamivir (Tamiflu)

- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

Zanamivir (Relenza)

- inhaled medication*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

*intravenous preparations are available for poorly patients

Question 67 of 143

Which one of the following is a Gram positive coccus?

- A. *Enterococcus faecalis*
- B. *Moraxella catarrhalis*
- C. *Haemophilus influenzae*
- D. *Neisseria meningitidis*
- E. Bacillus anthracis

Question 67 of 143

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- B. *Moraxella catarrhalis*
- C. *Haemophilus influenzae*
- D. *Neisseria meningitidis*
- E. Bacillus anthracis

Classification of bacteria

Remember:
- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L
- *Actinomyces*
- *Bacillus antracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

Question 68 of 143

Which of the following vaccines uses a fragment of the target organism?

- A. Pertussis
- B. Yellow fever
- C. Oral polio
- D. Measles
- E. Meningococcus

Question 68 of 143

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- A. Pertussis
- B. Yellow fever
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- D. Measles
- E. Meningococcus

Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients

Live attenuated vaccines
- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid

Whole killed organism*
- rabies
- pertussis

Fragment
- diphtheria
- tetanus
- meningococcus, pneumococcus, haemophilus

Others
- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of Vibrio cholerae together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

*injectable typhoid is no longer used in the UK

Question 69 of 143

You are reviewing test results. The urine sample from a 24-year-old woman who is 11 weeks pregnant shows a urine tract infection. On discussing the result with the patient she is asymptomatic and has no dysuria, frequency or fever. What is the most appropriate management?

- A. Ciprofloxacin for 7 days
- B. Amoxicillin for 7 days
- C. Repeat MSU to exclude contamination
- D. Trimethoprim for 3 days
- E. No treatment

Question 69 of 143

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- B. Amoxicillin for 7 days
- C. Repeat MSU to exclude contamination
- D. Trimethoprim for 3 days
- E. No treatment

Asymptomatic bacteruria in pregnant women - treat with amoxicillin or cephalosporin

Urinary tract infection in adults: management

Lower urinary tract infections in women (cystitis)
- local antibiotic guidelines should be followed if available
- Clinical Knowledge Summaries (CKS) recommend trimethoprim or nitrofurantoin for 3 days

Lower urinary tract infections in pregnancy
- asymptomatic bacteriuria is screened for on the booking visit and should be treated with an antibiotic for 7 days (sensitivities should already be available)
- for acute lower urinary tract infections consider amoxicillin or an oral cephalosporin for 7 days*

For patients with sign of acute pyelonephritis hospital admission should be considered
- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum cephalosporin or a quinolone for 10-14 days
- Clinical Knowledge Summaries recommend ciprofloxacin for 7 days or co-amoxiclav for 14 days

*CKS also mention the use of trimethoprim and nitrofurantoin. Trimethoprim is a folate antagonist and concerns have been raised regarding the potential risk of neural tube defects. Manufacturers advise to avoid. Whilst short-term trimethoprim use is unlikely to cause folate deficiency it would seem reasonable to use an antibiotic such as amoxicillin first-line. Nitrofurantoin should be avoided at term because of the risk of neonatal haemolysis

Question 70 of 143

Which of the following is true regarding the *Salmonella* species?

- A. Rose spots appear in all patients with typhoid
- B. They are normally present in the gut as commensals
- C. They are anaerobic organisms
- D. A relative bradycardia is often seen in typhoid fever
- E. *Salmonella typhi* can be categorised into type A, B and C

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Salmonella

The *Salmonella* group contains many members, most of which cause diarrhoeal diseases. They are aerobic, Gram negative rods which are not normally present as commensals in the gut.

Typhoid and paratyphoid are caused by *Salmonella typhi* and *Salmonella paratyphi* (types A, B & C) respectively. They are often termed enteric fevers, producing systemic symptoms such as headache, fever, arthralgia

Features

- initially systemic upset as above
- relative bradycardia
- abdominal pain, distension
- constipation: although *Salmonella* is a recognised cause of diarrhoea, constipation is more common in typhoid
- rose spots: present on the trunk in 40% of patients, and are more common in paratyphoid

Possible complications include

- osteomyelitis (especially in sickle cell disease where *Salmonella* is one of the most common pathogens)
- GI bleed/perforation
- meningitis
- cholecystitis
- chronic carriage (1%, more likely if adult females)

Question 71 of 143

What is the mechanism of action of macrolides?

- A. Causes misreading of mRNA
- B. Interferes with cell wall formation
- C. Inhibits DNA synthesis
- D. Inhibits RNA synthesis
- E. Inhibits protein synthesis

Question 71 of 143

What is the mechanism of action of macrolides?

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- D. Inhibits RNA synthesis
- E. Inhibits protein synthesis

Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation
- penicillins
- cephalosporins

Inhibit protein synthesis
- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis
- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis
- rifampicin

Question 72 of 143

What is the mechanism of action of the antiviral agent ribavirin?

- A. Inhibits DNA polymerase
- B. Inhibits uncoating of virus in the cell
- C. Protease inhibitor
- D. Nucleoside analogue reverse transcriptase inhibitor
- E. Interferes with the capping of viral mRNA

Question 72 of 143

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- E. Interferes with the capping of viral mRNA

Antiviral agents

Aciclovir
- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

Ribavirin
- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

Interferons
- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

Amantadine
- used to treat influenza
- inhibits uncoating of virus in cell

Anti-retroviral agent used in HIV

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

Protease inhibitors (PI)
- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz

Question 73 of 143

Which one of the following is least likely to cause a pyrexia of unknown origin?

- A. Hypernephroma
- B. Colorectal cancer
- C. Lymphoma
- D. Atrial myxoma
- E. Tuberculosis

Question 73 of 143

Which one of the following is least likely to cause a pyrexia of unknown origin?

- A. Hypernephroma
- B. Colorectal cancer
- C. Lymphoma
- D. Atrial myxoma
- E. Tuberculosis

Very rarely colorectal cancer may cause endocarditis secondary to *Streptococcus bovis*, but this is the least likely of the options

Pyrexia of unknown origin

Defined as a prolonged fever of > 3 weeks which resists diagnosis after a week in hospital

Neoplasia
- lymphoma
- hypernephroma
- preleukaemia
- atrial myxoma

Infections
- abscess
- TB

Connective tissue disorders

Question 74 of 143

A 28-year-old man who has recently emigrated from Nigeria presents with a penile ulcer. It initially started as a papule which later progressed to become a painful ulcer with an undermined ragged edge. Examination of the testes was unremarkable but tender inguinal lymphadenopathy was noted. What is the most likely diagnosis?

- A. Chancroid
- B. Lymphogranuloma venereum
- C. Syphilis
- D. Herpes simplex infection
- E. Granuloma inguinale

Question 74 of 143

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- A. Chancroid
- B. Lymphogranuloma venereum
- C. Syphilis
- D. Herpes simplex infection
- E. Granuloma inguinale

Genital ulcers
- painful: herpes >> chancroid
- painless: syphilis > lymphogranuloma venereum + granuloma inguinale

A diagnosis of chancroid is more likely than lymphogranuloma venereum as the ulcer is painful. Whilst herpes simplex is obviously more common the description of the ulcer is very characteristic of chancroid. Painful inguinal lymphadenopathy is present in around 50% of patients.

STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages
- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

Other causes of genital ulcers
- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis**

*previously called *Calymmatobacterium granulomatis*

Question 75 of 143

A 45-year-old man presents with pain and swelling of his left big toe. He has recently started treatment for active tuberculosis. Which one of the following medications is likely to be responsible?

- A. Streptomycin
- B. Rifampicin
- C. Ethambutol
- D. Isoniazid
- E. Pyrazinamide

Question 75 of 143

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- A. Streptomycin
- B. Rifampicin
- C. Ethambutol
- D. Isoniazid
- E. Pyrazinamide

There are case reports of ethambutol-induced gout but it is not listed as a side-effect in the BNF

Tuberculosis: drug side-effects

Common side effects:

Rifampicin
- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid
- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide
- hyperuricaemia causing gout
- hepatitis

Ethambutol
- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

Question 76 of 143

Which one of the following organisms causes lymphogranuloma venereum?

- A. *Haemophilus ducreyi*
- B. *Klebsiella granulomatis*
- C. Herpes simplex virus
- D. *Chlamydia*
- E. *Treponema pallidum*

Question 76 of 143

Which one of the following organisms causes lymphogranuloma venereum?

- A. *Haemophilus ducreyi*
- B. *Klebsiella granulomatis*
- C. Herpes simplex virus
- D. *Chlamydia*
- E. *Treponema pallidum*

STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages

- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

Other causes of genital ulcers

- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis**

*previously called *Calymmatobacterium granulomatis*

Question 77 of 143

A patient with HIV is reviewed. Which one of the following is an example of a nucleoside analogue reverse transcriptase inhibitors?

- A. Zidovudine
- B. indinavir
- C. Ritonavir
- D. Ribavirin
- E. Efavirenz

Question 77 of 143

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- A. Zidovudine
- B. indinavir
- C. Ritonavir
- D. Ribavirin
- E. Efavirenz

HIV drugs, rule of thumb:
- NRTIs end in 'ine'
- Pis: end in 'vir'
- NNRTIs: nevirapine, efavirenz

Zidovudine (AZT) was one of the first HIV drugs and remains important today.

HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)
- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Question 78 of 143

Which of the following antibiotics is predominately bactericidal?

- A. Trimethoprim
- B. Erythromycin
- C. Ciprofloxacin
- D. Chloramphenicol
- E. Minocycline

Question 78 of 143

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- D. Chloramphenicol
- E. Minocycline

Antibiotics: bactericidal vs. bacteriostatic

Bactericidal antibiotics
- penicillins
- cephalosporins
- aminoglycosides
- nitrofurantoin
- metronidazole
- quinolones
- rifampicin
- isoniazid

Bacteriostatic antibiotics
- chloramphenicol
- macrolides
- tetracyclines
- sulphonamides
- trimethoprim

Question 79 of 143

Which one of the following organisms causes West African sleeping sickness?

- A. Leishmania tropica
- B. Trypanosoma gambiense
- C. *Trypanosoma rhodesiense*
- D. *Leishmania mexicana*
- E. *Trypanosoma cruzi*

Question 79 of 143

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- C. *Trypanosoma rhodesiense*
- D. *Leishmania mexicana*
- E. *Trypanosoma cruzi*

Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - Trypanosoma gambiense in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

American trypanosomiasis, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaoesophagus and megacolon causing dysphagia and constipation

Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

Question 80 of 143

An 18-year-old man is bitten by a frantic dog whilst taking a gap year in Ecuador. He is worried about rabies and phones for advice. He was not immunised against prior to travelling to Ecuador. What is the most appropriate advice after thorough cleansing of the wound?

- A. Give human rabies immunoglobulin + full course of vaccination
- B. Give human rabies immunoglobulin + oral penicillin for the next 2 weeks
- C. Advise low risk but take oral co-amoxiclav for the dog bite
- D. Give human rabies immunoglobulin
- E. Give full course of vaccination

Question 80 of 143

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- D. Give human rabies immunoglobulin
- E. Give full course of vaccination

Rabies

Features
- prodrome: headache, fever, agitation
- hydrophobia: water-provoking muscle spasms
- hypersalivation

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries. Following an animal bite in at risk countries:
- if an individual is already immunised then 2 further doses of vaccine should be given
- if not previously immunised then human rabies immunoglobulin (HRIG) should be given along with a full course of vaccination

Question 81 of 143

A health care assistant sustains a needlestick injury whilst taking blood from a patient who is known to be HIV positive. Following thorough washing of the wound what is the most appropriate management?

- A. HIV test of health care worker in 3 months to determine treatment
- B. Immediate p24 HIV test of health care worker to determine treatment
- C. Oral antiretroviral therapy for 4 weeks
- D. Oral antiretroviral therapy for 3 months
- E. Intravenous zidovudine

Question 81 of 143

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Post-exposure prophylaxis for HIV: oral antiretroviral therapy for 4 weeks

Post-exposure prophylaxis

Hepatitis A
- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

Hepatitis B
- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

Hepatitis C
- monthly PCR - if seroconversion then interferon +/- ribavirin

HIV
- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster
- VZIG for IgG negative pregnant women/immunosuppressed

Question 82 of 143

A 37-year-old sewer worker presents to the Emergency Department with flu-like symptoms and pyrexia for the past 3 days. Since this morning he has started to develop a headache and signs of meningism are found on examination. Blood tests show:

Sodium	145 mmol/l
Potassium	4.7 mmol/l
Urea	10.3 mmol/l
Creatinine	133 µmol/l

What is the antibiotic treatment of choice?

- A. Co-trimoxazole
- B. Ciprofloxacin
- C. Metronidazole
- D. Benzylpenicillin
- E. Erythromycin

Question 82 of 143

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- D. Benzylpenicillin
- E. Erythromycin

Leptospirosis - give penicillin or doxycycline

This patient has leptospirosis. The treatment of choice is benzylpenicillin. A lumbar puncture should ideally be done first to confirm meningeal involvement.

Leptospirosis

Also known as Weil's disease*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete Leptospira interrogans (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

Features

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

Management

- high-dose benzylpenicillin or doxycycline

*the term Weil's disease is sometimes referred for the most severe 10% of cases of leptospirosis associated with jaundice

Question 83 of 143

A 24-year-old man presents with a three day history of painful ulcers on the shaft of his penis and dysuria. He has had no similar previous episodes. A clinical diagnosis of primary genital herpes is made. What is the most appropriate management?

- A. Topical famciclovir
- B. No treatment is indicated
- C. Topical podophyllotoxin
- D. Topical valaciclovir
- E. Oral aciclovir

Question 83 of 143

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- B. No treatment is indicated
- C. Topical podophyllotoxin
- D. Topical valaciclovir
- E. Oral aciclovir

Oral antiviral therapy is indicated for primary genital herpes infections, even if the presentation is delayed for up to 5 days

Herpes simplex virus

There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

Features

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

Question 84 of 143

A 34-year-old female presents with fever and lower abdominal pain. Over the past five days she has noticed deep dyspareunia and some post-coital bleeding. Her last period began 10 days ago. She is diffusely tender in the suprapubic area and vaginal examination reveals cervical excitation. Endocervical swabs are taken. A diagnosis of pelvic inflammatory disease is suspected. What is the most appropriate management?

- A. Oral doxycycline
- B. Await endocervical swab results
- C. Oral amoxicillin + ciprofloxacin
- D. Oral doxycycline + ciprofloxacin
- E. Oral ofloxacin + metronidazole

Question 84 of 143

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A. Oral doxycycline

B. Await endocervical swab results

C. Oral amoxicillin + ciprofloxacin

D. Oral doxycycline + ciprofloxacin

E. Oral ofloxacin + metronidazole

Consensus guidelines recommend treatment once a diagnosis of pelvic inflammatory disease is suspected, rather than waiting for the results of swabs

Pelvic inflammatory disease

Pelvic inflammatory disease (PID) is a term used to describe infection and inflammation of the female pelvic organs including the uterus, fallopian tubes, ovaries and the surrounding peritoneum. It is usually the result of ascending infection from the endocervix

Causative organisms
- *Chlamydia trachomatis* - the most common cause
- *Neisseria gonorrhoeae*
- *Mycoplasma genitalium*
- Mycoplasma hominis

Features
- lower abdominal pain
- fever
- deep dyspareunia
- dysuria and menstrual irregularities may occur
- vaginal or cervical discharge
- cervical excitation

Investigation
- screen for *Chlamydia* and Gonorrhoea

Management
- due to the difficulty in making an accurate diagnosis, and the potential complications of untreated PID, consensus guidelines recommend having a low threshold for treatment
- oral ofloxacin + oral metronidazole or intramuscular ceftriaxone + oral doxycycline + oral metronidazole
- RCOG guidelines suggest that in mild cases of PID intrauterine contraceptive devices may be left in

Complications
- infertility - the risk may be as high as 10-20% after a single episode
- chronic pelvic pain
- ectopic pregnancy

Question 85 of 143

Which of the following infections usually has the longest incubation period?

- A. Typhoid
- B. Diphtheria
- C. Dengue fever
- D. Measles
- E. Chickenpox

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- D. Measles
- E. Chickenpox

Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week
- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks
- malaria
- dengue fever
- typhoid
- measles

2 - 3 weeks
- mumps
- rubella
- chickenpox

Longer than 3 weeks
- infectious mononucleosis
- cytomegalovirus
- viral hepatitis
- HIV

Question 86 of 143

What is the mechanism of action of rifampicin?

- A. Inhibits DNA synthesis
- B. Interferes with cell wall formation
- C. Inhibits RNA synthesis
- D. Causes misreading of mRNA
- E. Inhibits protein synthesis

Question 86 of 143

What is the mechanism of action of rifampicin?

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- D. Causes misreading of mRNA
- E. Inhibits protein synthesis

Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation
- penicillins
- cephalosporins

Inhibit protein synthesis
- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis
- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis
- rifampicin

Question 87 of 143

Which one of the following is a Gram negative coccus?

- A. *Haemophilus influenzae*
- B. *Moraxella catarrhalis*
- C. *Enterococcus faecalis*
- D. *Listeria monocytogenes*
- E. *Campylobacter jejuni*

Question 87 of 143

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- C. *Enterococcus faecalis*
- D. *Listeria monocytogenes*
- E. *Campylobacter jejuni*

Classification of bacteria

Remember:
- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L
- *Actinomyces*
- *Bacillus antracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

Question 88 of 143

A 12-year-old boy who had a splenectomy following a road traffic accident is reviewed in clinic. He had his full immunisation course as a child and was given a repeat pneumococcal vaccination 5 days following surgery. What is the most appropriate ongoing management?

- A. Booster dose of Hib and MenC vaccine + lifelong penicillin V
- B. Booster dose of Hib and MenC vaccine + penicillin V for 2 years
- C. Lifelong penicillin V
- D. Booster dose of Hib and MenC vaccine + annual influenza vaccination + penicillin V for 2 years
- E. Booster dose of Hib and MenC vaccine + annual influenza vaccination + lifelong penicillin V

Question 88 of 143

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- E. Booster dose of Hib and MenC vaccine + annual influenza vaccination + lifelong penicillin V

Debate still exists regarding how long a patient should take penicillin prophylaxis for. The majority of doctors advocate lifelong penicillin. Consensus guidelines agree however that In this case prophylaxis should be continued until the patient is at least 16 years old, so of the available options E is the correct answer

Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus* infections

Vaccination
- if elective, should be done 2 weeks prior to operation
- pneumococcal, Hib, meningitis A & C and annual influenza vaccination

Antibiotic prophylaxis
- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

*usually from dog bites

Question 89 of 143

A man presents with severe vomiting. He reports not being able to keep fluids down for the past 12 hours. You suspect a diagnosis of gastroenteritis and on discussing possible causes he mentions reheating curry with rice the night before. What is the most likely causative organism?

- A. *Escherichia coli*
- B. *Campylobacter*
- C. *Salmonella*
- D. *Shigella*
- E. *Bacillus cereus*

Question 89 of 143

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- C. *Salmonella*
- D. *Shigella*
- E. *Bacillus cereus*

Bacillus cereus infection most commonly results from reheated rice.

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occuring after 6 hours

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 90 of 143

What is the mechanism of action of the antiviral agent amantadine?

- A. Inhibits DNA polymerase
- B. Protease inhibitor
- C. Nucleoside analogue reverse transcriptase inhibitor
- D. Inhibits uncoating of virus in the cell
- E. Interferes with the capping of viral mRNA

Question 90 of 143

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Antiviral agents

Aciclovir
- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

Ribavirin
- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

Interferons
- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

Amantadine
- used to treat influenza
- inhibits uncoating of virus in cell

Anti-retroviral agent used in HIV

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

Protease inhibitors (PI)
- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz

Question 91 of 143

Which one of the following is least associated with rabies?

- A. Hydrophobia
- B. Opisthotonus
- C. Pyrexia
- D. Headache
- E. Hypersalivation

Question 91 of 143

Which one of the following is least associated with rabies?

- A. Hydrophobia
- B. Opisthotonus
- C. Pyrexia
- D. Headache
- E. Hypersalivation

Opisthotonus is associated more with tetanus. It describes a state of a hyperextension and spasticity in which a patient's neck and spinal column enter into an arching position. It is an extrapyramidal effect and is caused by spasm of the axial muscles

Rabies

Features
- prodrome: headache, fever, agitation
- hydrophobia: water-provoking muscle spasms
- hypersalivation

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries. Following an animal bite in at risk countries:
- if an individual is already immunised then 2 further doses of vaccine should be given
- if not previously immunised then human rabies immunoglobulin (HRIG) should be given along with a full course of vaccination

Question 92 of 143

A 19-year-old man from a travelling community presents to the Emergency Department with breathing difficulties. On examination he has a temperature of 38.2ºC and stridor. A diagnosis of acute epiglottitis is suspected. Which one of the following organisms is most likely to be responsible?

- A. Epstein Barr Virus
- B. *Streptococcus pneumoniae*
- C. *Neisseria meningitidis*
- D. *Haemophilus influenzae*
- E. *Staphylococcus aureus*

Question 92 of 143

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- B. *Streptococcus pneumoniae*
- C. *Neisseria meningitidis*
- D. *Haemophilus influenzae*
- E. *Staphylococcus aureus*

Patients from travelling communities may not always receive a full course of immunisation.

Acute epiglottitis is of course much more common in young children

Acute epiglottitis

Acute epiglottitis is rare but serious infection caused by *Haemophilus influenzae* type B. Prompt recognition and treatment is essential as airway obstruction may develop. Epiglottitis generally occurs in children between the ages of 2 and 6 years. The incidence of epiglottitis has decreased since the introduction of the Hib vaccine

Features

- rapid onset
- unwell, toxic child
- stridor
- drooling of saliva

Question 93 of 143

Which one of the following tests is most likely to remain positive in a patient with syphilis despite treatment?

- A. Wassermann reaction
- B. Rapid plasma reagin (RPR)
- C. Venereal disease research laboratory (VDRL)
- D. Blood culture
- E. *Treponema pallidum* haemagglutination test (TPHA)

Question 93 of 143

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- D. Blood culture
- E. *Treponema pallidum* haemagglutination test (TPHA)

Syphilis: investigation

Treponema pallidum is a very sensitive organism and cannot be grown on artificial media. The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue

Serological tests can be divided into
- cardiolipin tests (not treponeme specific)
- treponemal specific antibody tests

Cardiolipin tests
- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin)
- insensitive in late syphilis
- becomes negative after treatment

Treponemal specific antibody tests
- example: TPHA (*Treponema pallidum* HaemAgglutination test)
- remains positive after treatment

Causes of false positive cardiolipin tests
- pregnancy
- SLE, anti-phospholipid syndrome
- TB
- leprosy
- malaria
- HIV

Question 94 of 143

A 23-year-old student returns from India and develops a febrile illness. Following investigation he is diagnosed as having *Plasmodium vivax* malaria. What is the most appropriate treatment?

- A. Chloroquine
- B. Atovaquone-proguanil
- C. Quinine
- D. Doxycycline
- E. Artemether-lumefantrine

Question 94 of 143

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- B. Atovaquone-proguanil
- C. Quinine
- D. Doxycycline
- E. Artemether-lumefantrine

Malaria: non-falciparum

The most common cause of non-falciparum malaria is *Plasmodium vivax*, with *Plasmodium ovale* and *Plasmodium malariae* accounting for the other cases. *Plasmodium vivax* is often found in Central America and the Indian Subcontinent whilst *Plasmodium ovale* typically comes from Africa

Benign malarias have a hypnozoite stage and may therefore relapse following treatment

Treatment

- non-falciparum malarias are almost always chloroquine sensitive
- primaquine should be used in *Plasmodium vivax* and *Plasmodium ovale* infection to destroy liver hypnozoites

Question 95 of 143

A nurse undergoes primary immunisation against hepatitis B. Levels of which one of the following should be checked four months later to ensure an adequate response to immunisation?

- A. Anti-HBs
- B. Anti-HBc
- C. Hepatitis B viral load
- D. HbeAg
- E. HBsAg

Question 95 of 143

A nurse undergoes primary immunisation against hepatitis B. Levels of which one of the following should be checked four months later to ensure an adequate response to immunisation?

- A. Anti-HBs
- B. Anti-HBc
- C. Hepatitis B viral load
- D. HbeAg
- E. HBsAg

It is preferable to achieve anti-HBs levels above 100 mIU/ml, although levels of 10 mIU/ml or more are generally accepted as enough to protect against infection

Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Question 96 of 143

A 31-year-old man from Russia who is known to be HIV positive presents with purple plaques on his skin. Which of the following viruses is thought to be the cause of Kaposi's sarcoma?

- A. HTLV-1
- B. HIV-2
- C. HHV-8
- D. CMV
- E. Alphavirus

Question 96 of 143

A 31-year-old man from Russia who is known to be HIV positive presents with purple plaques on his skin. Which of the following viruses is thought to be the cause of Kaposi's sarcoma?

- A. HTLV-1
- B. HIV-2
- C. HHV-8
- D. CMV
- E. Alphavirus

HIV: Kaposi's sarcoma

Kaposi's sarcoma

- caused by HHV-8 (human herpes virus 8)
- presents as purple papules or plaques on the skin or mucosa (e.g. gastrointestinal and respiratory tract)
- skin lesions may later ulcerate
- respiratory involvement may cause massive haemoptysis and pleural effusion
- radiotherapy + resection

Question 97 of 143

A 17-year-old girl presents with a sore throat. On examination she has inflamed tonsils covered in white patches. Tender cervical lymphadenopathy and a low grade pyrexia are also present. Which one of the following organisms is most likely to be responsible?

- A. *Streptococcus viridans*
- B. *Streptococcus agalactiae*
- C. *Streptococcus pneumoniae*
- D. *Staphylococcus aureus*
- E. *Streptococcus pyogenes*

Question 97 of 143

A 17-year-old girl presents with a sore throat. On examination she has inflamed tonsils covered in white patches. Tender cervical lymphadenopathy and a low grade pyrexia are also present. Which one of the following organisms is most likely to be responsible?

- A. *Streptococcus viridans*
- B. *Streptococcus agalactiae*
- C. *Streptococcus pneumoniae*
- D. *Staphylococcus aureus*
- E. *Streptococcus pyogenes*

Streptococci

Streptococci may be divided into alpha and beta haemolytic types

Alpha haemolytic streptococci

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

Beta haemolytic streptococci

These can be subdivided into group A and B

Group A
- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

Group B
- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

Question 98 of 143

A 31-year-old female presents to the genitourinary medicine clinic due to four fleshy, protuberant lesions on her vulva which are slightly pigmented. She has recently started a relationship with a new partner. What is the most appropriate initial management?

- A. Oral aciclovir
- B. Topical podophyllum
- C. Topical salicylic acid
- D. Topical aciclovir
- E. Electrocautery

Question 98 of 143

A 31-year-old female presents to the genitourinary medicine clinic due to four fleshy, protuberant lesions on her vulva which are slightly pigmented. She has recently started a relationship with a new partner. What is the most appropriate initial management?

- A. Oral aciclovir
- B. Topical podophyllum
- C. Topical salicylic acid
- D. Topical aciclovir
- E. Electrocautery

Genital wart treatment
- multiple, non-keratinised warts: topical podophyllum
- solitary, keratinised warts: cryotherapy

Cryotherapy is also acceptable as an initial treatment for genital warts

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 99 of 143

Which of the following types of viral meningitis may be characteristically associated with a low cerebrospinal fluid glucose level?

- A. Mumps
- B. Cytomegalovirus
- C. Measles
- D. HIV
- E. Echovirus

Question 99 of 143

Which of the following types of viral meningitis may be characteristically associated with a low cerebrospinal fluid glucose level?

- A. Mumps
- B. Cytomegalovirus
- C. Measles
- D. HIV
- E. Echovirus

Mumps meningitis is associated with a low CSF glucose

Mumps meningitis is associated with a low glucose in up to a third of patients

Meningitis: CSF analysis

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	Bacterial	**Viral**	**Tuberculous**
Appearance	Cloudy	Clear/cloudy	Fibrin web
Glucose	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
Protein	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
White cells	10 - 5,000 polymorphs/mm^3	15 - 1,000 lymphocytes/mm^3	10 - 1,000 lymphocytes/mm^3

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Question 100 of 143

A 45-year-old female presents to the Emergency Department three days after returning from Thailand complaining of severe muscle ache and headache. On examination she has a widespread maculopapular rash. Results show:

Malaria film:	negative
Hb	16.2 *10^9 g/dl
Plt	96 *10^9/l
WBC	2.4 *10^9/l
ALT	146 iu/l

What is the most likely diagnosis?

- A. Hepatitis A
- B. Japanese encephalitis
- C. Rheumatic fever
- D. Malaria
- E. Dengue fever

Question 100 of 143

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ALT 146 iu/l

What is the most likely diagnosis?

- A. Hepatitis A
- B. Japanese encephalitis
- C. Rheumatic fever
- D. Malaria
- E. Dengue fever

The low platelet count and raised transaminase level is typical of dengue fever

Dengue fever

Dengue fever is a type of viral haemorrhagic fever (also yellow fever, Lassa fever, Ebola)

Basics

- transmitted by the Aedes aegyti mosquito
- incubation period of 7 days
- a form of disseminated intravascular coagulation (DIC) known as dengue haemorrhagic fever (DHF) may develop. Around 20-30% of these patients go on to develop dengue shock syndrome (DSS)

Features

- causes headache (often retro-orbital)
- myalgia
- pleuritic pain
- facial flushing (dengue)
- maculopapular rash
- pyrexia

Treatment is entirely symptomatic e.g. fluid resuscitation, blood transfusion etc

Question 101 of 143

A 43-year-old man from South Africa is reviewed in clinic. He has recently started treatment for tuberculosis but is complaining of a deterioration in his vision. Which one of the following drugs is most likely to cause decreased visual acuity?

- A. Rifampicin
- B. Streptomycin
- C. Isoniazid
- D. Ethambutol
- E. Pyrazinamide

Question 101 of 143

A 43-year-old man from South Africa is reviewed in clinic. He has recently started treatment for tuberculosis but is complaining of a deterioration in his vision. Which one of the following drugs is most likely to cause decreased visual acuity?

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- B. Streptomycin
- C. Isoniazid
- D. Ethambutol
- E. Pyrazinamide

Optic neuritis is common in patients taking ethambutol

Tuberculosis: drug side-effects

Common side effects:

Rifampicin
- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid
- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide
- hyperuricaemia causing gout
- hepatitis

Ethambutol
- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

Question 102 of 143

A 31-year-old man who is known to be HIV positive presents with dyspnoea and a dry cough. He is currently homeless and has not been attending his outpatient appointments or taking antiretroviral medication.
Clinical examination reveals a respiratory rate of 24 / min. Chest auscultation is unremarkable with only scattered crackles. His oxygen saturation is 96% on room air but this falls rapidly after walking the length of the ward. Given the likely diagnosis, what is the most appropriate first-line treatment?

- A. Fluconazole
- B. Co-trimoxazole
- C. Erythromycin
- D. Ganciclovir
- E. Sulfadiazine and pyrimethamine

Question 102 of 143

A 31-year-old man who is known to be HIV positive presents with dyspnoea and a dry cough. He is currently homeless and has not been attending his outpatient appointments or taking antiretroviral medication.
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- B. Co-trimoxazole
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- D. Ganciclovir
- E. Sulfadiazine and pyrimethamine

HIV: Pneumocystis jiroveci pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as Pneumocystis jiroveci, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- Pneumocystis jiroveci is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm³ should receive PCP prophylaxis

Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if pO2 < 9.3kPa then steroids reduce risk of respiratory failure by 50% and death by a third)

Question 103 of 143

A 30-year-old man comes for review. He returned from a holiday in Egypt yesterday. For the past two days he has been passing frequent bloody diarrhoea associated with crampy abdominal pain. Abdominal examination demonstrates diffuse lower abdominal tenderness but there is no guarding or rigidity. His temperature is 37.5ºC. What is the most likely causative organism?

- A. Giardiasis
- B. Enterotoxigenic *Escherichia coli*
- C. *Staphylococcus aureus*
- D. *Salmonella*
- E. *Shigella*

Question 103 of 143

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- B. Enterotoxigenic *Escherichia coli*
- C. *Staphylococcus aureus*
- D. *Salmonella*
- E. *Shigella*

Enterotoxigenic *Escherichia coli* infections do not usually cause bloody diarrhoea. A differential diagnosis would be amoebic dysentry, enterohemorrhagic *Escherichia coli* and possibly *Campylobacter*.

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea) Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occuring after 6 hours

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 104 of 143

A 22-year-old woman presents with lethargy, pyrexia and headaches. She is a student and returned from a holiday in Ibiza ten days ago. These symptoms have been present for the past six days and she is wondering whether she may need an antibiotic. She also has a history of menorrhagia and is concerned that she may be anaemic. Clinical examination reveals a temperature of 37.9ºC and marked cervical lymphadenopathy. You order a full blood count which is reported as follows:

Hb 12.1 g/dl

Platelets 189 * 10^9/l

WCC 13.1 * 10^9/l

Neut 5.2 * 10^9/l

Lymp 6.2 * 10^9/l

Film Atypical lymphocytes seen

What is the most likely diagnosis?

- A. Acute lymphoblasic leukaemia
- B. Hashimoto's thyroiditis
- C. Infectious mononucleosis
- D. HIV seroconversion
- E. Septicaemia seconadary to streptococcal throat infection

Question 104 of 143

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- C. Infectious mononucleosis
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- E. Septicaemia seconadary to streptococcal throat infection

Atypical lymphocytes - ?glandular fever

Infectious mononucleosis

Infectious mononucleosis (glandular fever) is caused by the Epstein-Barr virus (also known as human herpesvirus 4, HHV-4). It is most common in adolescents and young adults.

Features

- sore throat
- lymphadenopathy
- pyrexia
- malaise, anorexia, headache
- palatal petechiae
- splenomegaly - occurs in around 50% of patients and may rarely predispose to splenic rupture
- hepatitis
- presence of 50% lymphocytes with at least 10% atypical lymphocytes
- haemolytic anaemia

Management is supportive and includes:

- rest during the early stages, drink plenty of fluid, avoid alcohol
- simple analgesia for any aches or pains
- consensus guidance in the UK is to avoid playing contact sports for 8 weeks after having glandular fever to reduce the risk of splenic rupture

Question 105 of 143

A 27-year-old woman develops fever and lymph node swelling after being scratched by her cat. Which one of the organisms is responsible for cat scratch disease?

- A. *Bordetella pertussis*
- B. *Moraxella catarrhalis*
- C. *Bartonella henselae*
- D. *Francisella tularensis*
- E. *Yersinia enterocolitica*

Question 105 of 143

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- C. *Bartonella henselae*
- D. *Francisella tularensis*
- E. *Yersinia enterocolitica*

Cat scratch disease - caused by *Bartonella henselae*

Cat scratch disease

Cat scratch disease is generally caused by the Gram negative rod *Bartonella henselae*

Features

- fever
- history of a cat scratch
- regional lymphadenopathy
- headache, malaise

Question 106 of 143

Which of the following anti-retroviral drugs is most characteristically associated with pancreatitis?

- A. Zidovudine
- B. Didanosine
- C. Indinavir
- D. Ritonavir
- E. Nevirapine

Question 106 of 143

Which of the following anti-retroviral drugs is most characteristically associated with pancreatitis?

- A. Zidovudine
- B. Didanosine
- C. Indinavir
- D. Ritonavir
- E. Nevirapine

Ritonavir may cause acute pancreatitis but this is not as common as with didanosine therapy

HIV: biliary and pancreatic disease

The most common cause of biliary disease in patients with HIV is sclerosing cholangitis due to infections such as CMV, Cryptosporidium and Microsporidia

Pancreatitis in the context of HIV infection may be secondary to anti-retroviral treatment (especially didanosine) or by opportunistic infections e.g. CMV

Question 107 of 143

A 74-year-old female presents with headache and neck stiffness to the Emergency Department. Following a lumbar puncture the patient was started on IV ceftriaxone. CSF culture grows *Listeria monocytogenes*. What is the most appropriate treatment?

- A. Add IV amoxicillin
- B. Change to IV amoxicillin + gentamicin
- C. Add IV ciprofloxacin
- D. Add IV co-amoxiclav
- E. Continue IV ceftriaxone as monotherapy

Question 107 of 143

A 74-year-old female presents with headache and neck stiffness to the Emergency Department. Following a lumbar puncture the patient was started on IV ceftriaxone. CSF culture grows *Listeria monocytogenes*. What is the most appropriate treatment?

- A. Add IV amoxicillin
- B. Change to IV amoxicillin + gentamicin
- C. Add IV ciprofloxacin
- D. Add IV co-amoxiclav
- E. Continue IV ceftriaxone as monotherapy

The current BNF suggests treatment with amoxicillin/ampicillin + gentamicin. Treatment should be for at least 10-14 days

Listeria

Listeria monocytogenes is a Gram positive bacillus which has the unusual ability to multiply at low temperatures. It is typically spread via contaminated food, typically unpasteurised dairy products. Infection is particularly dangerous to the unborn child where it can lead to miscarriage

Features - can present in a variety of ways
- diarrhoea, flu-like illness
- pneumonia , meningoencephalitis
- ataxia and seizures

Suspected Listeria infection should be investigated by taking blood cultures. CSF may reveal a pleocytosis, with 'tumbling motility' on wet mounts

Management
- Listeria is sensitive to amoxicillin/ampicillin (cephalosporins usually inadequate)
- Listeria meningitis should be treated with IV amoxicillin/ampicillin and gentamicin

Question 108 of 143

A 39-year-old female who has recently emigrated from sub-Saharan Africa is screened for tuberculosis. She reports being fit and well with no past medical history and has never had a BCG vaccination. Her chest x-ray is normal so she has a Mantoux test which is positive. An interferon gamma test is also performed which is positive. A HIV test is requested which is negative. What treatment would you recommend?

- A. Isoniazid for 6 months
- B. Rifampicin, isoniazid, pyrazinamide and ethambutol for 6 months
- C. Observe
- D. Rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months then step down to rifampicin and isoniazid for 4 months
- E. Rifampicin and isoniazid for 6 months

Question 108 of 143

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C. Observe

D. Rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months then step down to rifampicin and isoniazid for 4 months

E. Rifampicin and isoniazid for 6 months

This patient has latent tuberculosis

Tuberculosis: drug therapy

The standard therapy for treating **active tuberculosis** is:

Initial phase - first 2 months (RIPE)
- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months
- Rifampicin
- Isoniazid

The treatment for **latent tuberculosis** is isoniazid alone for 6 months

Patients with **meningeal tuberculosis** are treated for a prolonged period (at least 12 months) with the addition of steroids

Directly observed therapy with a thrice weekly dosing regimen may be indicated in certain groups, including:
- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

Question 109 of 143

A 23-year-old man is admitted to the Emergency Department with an evolving purpuric rash, pyrexia and confusion. His GP had given him intramuscular benzylpenicillin in the surgery and dialled 999. Which one of the following investigations is most likely to reveal the diagnosis?

- A. Urinary antigen
- B. Blood PCR for meningococcus
- C. Blood culture
- D. CT head
- E. Lumbar puncture

Question 109 of 143

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- A. Urinary antigen
- B. Blood PCR for meningococcus
- C. Blood culture
- D. CT head
- E. Lumbar puncture

The blood cultures are likely to be negative as antibiotics have already been given. PCR has a sensitivity of over 90%.

Meningococcal septicaemia: investigation

Investigations
- blood cultures
- blood PCR
- lumbar puncture is usually contraindicated
- full blood count and clotting to assess for disseminated intravascular coagulation

Question 110 of 143

A 62-year-old female with chronic renal failure (GFR = 35 ml/min) is diagnosed as having pulmonary tuberculosis. What changes need to be made to her anti-tuberculosis regime given her renal impairment?

- A. Reduction in isoniazid dose
- B. Reduction in rifampicin dose
- C. Reduction in pyrazinamide dose
- D. Reduction in ethambutol dose
- E. No changes

Question 110 of 143

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- C. Reduction in pyrazinamide dose
- D. Reduction in ethambutol dose
- E. No changes

Tuberculosis: drug side-effects

Common side effects:

Rifampicin
- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid
- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide
- hyperuricaemia causing gout
- hepatitis

Ethambutol
- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

Question 111 of 143

A 63-year-old man who migrated from India 7 months ago is referred to the acute medical unit with a history of headache and pyrexia. A lumbar puncture suggests a diagnosis of meningeal tuberculosis. What treatment should he be started on?

- A. Rifampicin, isoniazid, pyrazinamide and ethambutol
- B. Rifampicin and streptomycin
- C. Rifampicin, isoniazid, pyrazinamide, ethambutol and streptomycin
- D. Rifampicin and isoniazid with prednisolone
- E. Rifampicin, isoniazid, pyrazinamide and ethambutol with prednisolone

Question 111 of 143

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- B. Rifampicin and streptomycin
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- D. Rifampicin and isoniazid with prednisolone
- E. Rifampicin, isoniazid, pyrazinamide and ethambutol with prednisolone

The use of steroids in patients with tuberculous meningitis is supported by a Cochrane review in 2008

Tuberculosis: drug therapy

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- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months
- Rifampicin
- Isoniazid

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- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

Question 112 of 143

A 22-year-old female presents with an offensive vaginal discharge. History and examination findings are consistent with a diagnosis of bacterial vaginosis. What is the most appropriate initial management?

- A. Oral azithromycin
- B. Topical hydrocortisone
- C. Oral metronidazole
- D. Clotrimazole pessary
- E. Advice regarding hygiene and cotton underwear

Question 112 of 143

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- B. Topical hydrocortisone
- C. Oral metronidazole
- D. Clotrimazole pessary
- E. Advice regarding hygiene and cotton underwear

Bacterial vaginosis: oral metronidazole

Bacterial vaginosis

Bacterial vaginosis (BV) describes an overgrowth of predominately anaerobic organisms such as Gardnerella vaginalis. This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH.

Whilst BV is not a sexually transmitted infection it is seen almost exclusively in sexually active women.

Features
- vaginal discharge: 'fishy', offensive
- asymptomatic in 50%

Amsel's criteria for diagnosis of BV - 3 of the following 4 points should be present
- thin, white homogenous discharge
- clue cells on microscopy
- vaginal pH > 4.5
- positive whiff test (addition of potassium hydroxide results in fishy odour)

Management
- oral metronidazole for 5-7 days
- 70-80% initial cure rate
- relapse rate > 50% within 3 months

Bacterial vaginosis in pregnancy
- results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage
- it was previously taught that oral metronidazole should be avoided in the first trimester and topical clindamycin used instead. Recent guidelines however recommend that oral metronidazole is used throughout pregnancy. The BNF still advises against the use of high dose metronidazole regimes

Question 113 of 143

A 31-year-old woman who is known to be HIV positive presents following a positive pregnancy test. Her last menstrual period was 6 weeks ago. The last CD4 count was 420 * 10^6/l and she does not take any antiretroviral therapy. What is the most appropriate management with regards to antiretroviral therapy?

- A. Check CD4 at 12 weeks and initiate antiretroviral therapy if CD4 count is less than 350 * 10^6/l
- B. Do not give antiretroviral therapy
- C. Start antiretroviral therapy at 20-30 weeks
- D. Start antiretroviral therapy at 10-12 weeks
- E. Start antiretroviral therapy immediately

Question 113 of 143

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- E. Start antiretroviral therapy immediately

HIV and pregnancy

With the increased incidence of HIV infection amongst the heterosexual population there are an increasing number of HIV positive women giving birth in the UK. In London the incidence may be as high as 0.4% of pregnant women. The aim of treating HIV positive women during pregnancy is to minimise harm to both the mother and fetus, and to reduce the chance of vertical transmission.

Factors which reduce vertical transmission (from 25-30% to 2%)
- maternal antiretroviral therapy
- mode of delivery (caesarean section)
- neonatal antiretroviral therapy
- infant feeding (bottle feeding)

Screening
- NICE guidelines recommend offering HIV screening to all pregnant women

Antiretroviral therapy
- all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously
- if women are not currently taking antiretroviral therapy it is usually commenced between 28 and 32 weeks of gestation and should be continued intrapartum

Mode of delivery
- elective caesarean section*
- a zidovudine infusion should be started four hours before beginning the caesarean section

Neonatal antiretroviral therapy
- zidovudine is usually administered orally to the neonate for four to six weeks

Infant feeding
- in the UK all women should be advised not to breast feed

*the 2008 BHIVA guidelines suggest vaginal delivery may be an option for women on HAART who have an undetectable viral load but whether this will translate into clinical practice remains to be seen

Question 114 of 143

A 43-year-old sheep farmer presents with a lesion on his right hand. It initially started as a small, raised, red papule but has now become larger. On examination a 2cm, flat-topped haemorrhagic lesion is seen. What is the most likely diagnosis?

- A. Orf
- B. Tetanus
- C. Hand, foot and mouth disease
- D. Paronychia
- E. Anthrax

Question 114 of 143

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- A. Orf
- B. Tetanus
- C. Hand, foot and mouth disease
- D. Paronychia
- E. Anthrax

Orf

Orf is generally a condition found in sheep and goats although it can be transmitted to humans. It is caused by the parapox virus.

In animals
- 'scabby' lesions around the mouth and nose

In humans
- generally affects the hands and arms
- initially small, raised, red-blue papules
- later may increase in size to 2-3 cm and become flat-topped and haemorrhagic

Question 115 of 143

A 12-year-old girl is prescribed oseltamivir for suspected influenza. What is the mechanism of action of oseltamivir?

- A. Inhibits RNA polymerase
- B. Interferes with the capping of viral mRNA
- C. Neuraminidase inhibitor
- D. Inhibits DNA polymerase
- E. Protease inhibitor

Question 115 of 143

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H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:
- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

Features
The majority of symptoms are typical of those seen in a flu-like illness:
- fever greater than 38ºC
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

Treatment
There are two main treatments currently available:
Oseltamivir (Tamiflu)
- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

Zanamivir (Relenza)
- inhaled medication*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

*intravenous preparations are available for patients who are acutely unwell

Question 116 of 143

A 39-year-old man returns from a two week business trip to Kenya. Four weeks after his return he presents complaining of malaise, headaches and night sweats. On examination there is a symmetrical erythematous macular rash over his trunk and limbs associated with cervical and inguinal lymphadenopathy. What is the most likely diagnosis?

- A. Typhoid fever
- B. Tuberculosis
- C. Dengue fever
- D. Schistosomiasis
- E. Acute HIV infection

Question 116 of 143

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- C. Dengue fever
- D. Schistosomiasis
- E. Acute HIV infection

Man returns from trip abroad with maculopapular rash and flu-like illness - think HIV seroconversion

Stereotypes are alive and well in the MRCP exam. For questions involving businessmen always consider sexually transmitted infections

HIV: seroconversion

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

Features

- sore throat
- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningoencephalitis

Diagnosis

- antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis

Question 117 of 143

Which one of the following is least associated with a false negative tuberculin skin test?

- A. Lymphoma
- B. Miliary tuberculosis
- C. Sarcoidosis
- D. Chronic kidney disease stage 3
- E. HIV

Question 117 of 143

Which one of the following is least associated with a false negative tuberculin skin test?

- A. Lymphoma
- B. Miliary tuberculosis
- C. Sarcoidosis
- D. Chronic kidney disease stage 3
- E. HIV

Severe renal failure may cause a false negative test but CKD stage 3 would not.

Tuberculosis: skin tests

Overview
- Heaf test is done in UK to see if BCG is needed, used for screening
- Mantoux test is considered more accurate

Mantoux test
- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later
- erythema & induration > 10mm = positive result - this implies previous exposure including BCG

Heaf test

The Heaf test classically involves injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It is then read 3-10 days later

Negative	No induration, maybe 6 minute puncture scars
Grade 1	4-6 puncture sites are indurated
Grade 2	Confluent puncture sites form indurated ring
Grade 3	Extensive induration to form disc (5-10 mm)
Grade 4	Severe induration > 10 mm with or without blistering

Grades 1 and 2 may be the result of previous BCG or avian tuberculosis whilst grades 3 or 4 require a CXR and follow-up

False negative tests may be caused by:
- miliary TB
- sarcoidosis
- HIV
- lymphoma
- very young age (e.g. < 6 months)

Question 118 of 143

A 62-year-old woman who has recently been treated for ascending cholangitis is referred to hospital due to persistent fever and anorexia. An ultrasound scan reveals the presence of a liver abscess. What is the most appropriate antibiotic therapy to accompany drainage of the abscess?

- A. Vancomycin + meropenem
- B. Co-amoxiclav + metronidazole
- C. Amoxicillin + ciprofloxacin + metronidazole
- D. Clindamycin + metronidazole
- E. Metronidazole + vancomycin

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- B. Co-amoxiclav + metronidazole
- C. Amoxicillin + ciprofloxacin + metronidazole
- D. Clindamycin + metronidazole
- E. Metronidazole + vancomycin

Pyogenic liver abscess

Management
- drainage (needle aspiration or catheter) should always be performed
- amoxicillin + ciprofloxacin + metronidazole
- if penicillin allergic: ciprofloxacin + clindamycin

Question 119 of 143

A prison GP is bitten by a patient who is known to have hepatitis B. The GP has a documented full history of hepatitis B vaccination and was known to be a responder. What is the most appropriate action to reduce the chance of contracting hepatitis B?

- A. Admit for intravenous interferon
- B. Give hepatitis B immune globulin
- C. Give hepatitis B immune globulin + hepatitis B vaccine booster
- D. Give hepatitis B vaccine booster
- E. Give oral ribavirin for 4 weeks

Question 119 of 143

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- C. Give hepatitis B immune globulin + hepatitis B vaccine booster
- D. Give hepatitis B vaccine booster
- E. Give oral ribavirin for 4 weeks

Post-exposure prophylaxis

Hepatitis A
- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

Hepatitis B
- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

Hepatitis C
- monthly PCR - if seroconversion then interferon +/- ribavirin

HIV
- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster
- VZIG for IgG negative pregnant women/immunosuppressed

Question 120 of 143

A man develops vomiting and abdominal pain 2 hours after leaving a Chinese restaurant. What is the most likely causative organism?

- A. *Escherichia coli*
- B. *Shigella*
- C. *Staphylococcus aureus*
- D. *Bacillus cereus*
- E. *Clostridium perfringens*

Question 120 of 143

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- A. *Escherichia coli*
- B. *Shigella*
- C. *Staphylococcus aureus*
- D. *Bacillus cereus*
- E. *Clostridium perfringens*

The obvious clue in this question is the short incubation period - this points to a diagnosis of *Staphylococcus aureus* or *Bacillus cereus*. *Bacillus cereus* infection is often associated with Chinese restaurants due to the link with rice

There are two recognised types of *Bacillus cereus* infection. The first type produces a vomiting illness and has an incubation period of 1-6 hours. The second type produces a diarrhoeal illness with an incubation period of 6-14 hours.

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occuring after 6 hours

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 121 of 143

A 29-year-old HIV positive man is admitted with right-sided hemiplegia. For the past four days he has been complaining of headache and flu-like symptoms. CT scan shows multiple ring enhancing lesions. A diagnosis of cerebral toxoplasmosis is suspected. What is the most suitable management?

- A. Artemether and lumefantrine
- B. Co-trimoxazole
- C. Supportive treatment
- D. Pyrimethamine and sulphadiazine
- E. Metronidazole and gentamicin

Question 121 of 143

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- E. Metronidazole and gentamicin

Toxoplasmosis

Toxoplasma gondii is a protozoa which infects the body via the GI tract, lung or broken skin. It's oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. The usual animal reservoir is the cat, although other animals such as rats carry the disease.

Most infections are asymptomatic. Symptomatic patients usually have a self-limiting infection, often having clinical features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Other less common manifestations include meningioencephalitis and myocarditis.

Investigation
- antibody test
- Sabin-Feldman dye test

Treatment is usually reserved for those with severe infections or patients who are immunosuppressed
- pyrimethamine plus sulphadiazine for at least 6 weeks

Congenital toxoplasmosis is due to transplacental spread from the mother. It causes a variety of effects to the unborn child including microcephaly, hydrocephalus, cerebral calcification and choroidoretinitis.

Question 122 of 143

A 29-year-old woman presents to the genitourinary medicine clinic for treatment of recurrent genital warts. Which one the following viruses are most likely to be responsible?

- A. Human papilloma virus 16 & 18
- B. Human papilloma virus 13 & 17
- C. Human papilloma virus 6 & 11
- D. Human papilloma virus 12 & 14
- E. Human papilloma virus 15 & 2

Question 122 of 143

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- B. Human papilloma virus 13 & 17
- C. Human papilloma virus 6 & 11
- D. Human papilloma virus 12 & 14
- E. Human papilloma virus 15 & 21

Genital warts - 90% are caused by HPV 6 & 11

Types 6 and 11 are responsible for 90% of genital warts cases

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 123 of 143

The most appropriate treatment for cutaneous larva migrans is:

- A. Thiabendazole
- B. Sulfadoxine
- C. Pyrimethamine
- D. Metronidazole
- E. Dapsone

Question 123 of 143

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- A. Thiabendazole
- B. Sulfadoxine
- C. Pyrimethamine
- D. Metronidazole
- E. Dapsone

Nematodes

Ancylostoma braziliense
- most common cause of cutaneous larva migrans
- common in Central and Southern America

Strongyloides stercoralis
- acquired percutaneously (e.g. walking barefoot)
- causes pruritus and larva currens - this has a similar appearance to cutaneous larva migrans but moves through the skin at a far greater rate
- abdo pain, diarrhoea, pneumonitis
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- eosinophilia sometimes seen
- management: thiabendazole, albendazole. Ivermectin also used, particularly in chronic infections

Toxocara canis
- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of visceral larva migrans
- other features: eye granulomas, liver/lung involvement

Question 124 of 143

A 35-year-old woman is referred to hospital. As part of a liver screen the following results are obtained:

Anti-HBs	Negative
Anti-HBc	Positive
HBs antigen	Positive
IgM anti-HBc	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen
What is the patient's hepatitis B status?

- A. Probable hepatitis D infection
- B. Acute hepatitis B infection
- C. Previous immunisation to hepatitis B
- D. Chronic hepatitis B
- E. Previous hepatitis B infection, not a carrier

Question 124 of 143

A 35-year-old woman is referred to hospital. As part of a liver screen the following results are obtained:

Anti-HBs	Negative
Anti-HBc	Positive
HBs antigen	Positive
IgM anti-HBc	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen
What is the patient's hepatitis B status?

- A. Probable hepatitis D infection
- B. Acute hepatitis B infection
- C. Previous immunisation to hepatitis B
- D. Chronic hepatitis B
- E. Previous hepatitis B infection, not a carrier

The negative IgM anti-HBc points to a chronic rather than acute infection.

Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Question 125 of 143

A 24-year-old woman presents due to an itchy vulva and pain during sex. She also mentions a green, offensive vaginal discharge for the past 2 weeks. What is the most likely diagnosis?

- A. *Candida*
- B. Bacterial vaginosis
- C. Gonorrhoea
- D. *Trichomonas vaginalis*
- E. *Chlamydia*

Question 125 of 143

A 24-year-old woman presents due to an itchy vulva and pain during sex. She also mentions a green, offensive vaginal discharge for the past 2 weeks. What is the most likely diagnosis?

- A. *Candida*
- B. Bacterial vaginosis
- C. Gonorrhoea
- D. *Trichomonas vaginalis*
- E. *Chlamydia*

Vaginal discharge

Vaginal discharge is a common presenting symptom and is not always pathological

Common causes
- physiological
- *Candida*
- *Trichomonas vaginalis*
- bacterial vaginosis

Less common causes
- whilst cervical infections such as *Chlamydia* and Gonorrhoea can cause a vaginal discharge this is rarely the presenting symptoms
- ectropion
- foreign body
- cervical cancer

Key features of the common causes are listed below

Condition	**Key features**
Candida	'Cottage cheese' discharge Vulvitis Itch
Trichomonas vaginalis	Offensive, yellow/green, frothy discharge Vulvovaginitis Strawberry cervix
Bacterial vaginosis	Offensive, thin, white/grey, 'fishy' discharge

Question 126 of 143

A 27-year-old pregnant woman is found to have *Chlamydia*. What is the most appropriate treatment?

- A. No antibiotic therapy is indicated
- B. Cefixime
- C. Erythromycin
- D. Doxycycline
- E. Ciprofloxacin

Question 126 of 143

A 27-year-old pregnant woman is found to have *Chlamydia*. What is the most appropriate treatment?

- A. No antibiotic therapy is indicated
- B. Cefixime
- C. Erythromycin
- D. Doxycycline
- E. Ciprofloxacin

Erythromycin or amoxicillin is currently recommended for pregnant or breast feeding women. The efficacy of amoxicillin, often assumed to be ineffective against *Chlamydia*, was supported in a recent Cochrane review. A test of cure should be carried out following treatment

Chlamydia

Chlamydia is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

Features
- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

Potential complications
- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

Investigation
- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice
- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

Screening
- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

Management
- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline

- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

Question 127 of 143

Which of the following vaccines uses a whole killed organism?

- A. Tetanus
- B. Meningococcus
- C. Oral polio
- D. Rabies
- E. Diphtheria

uestion 127 of 143

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- C. Oral polio
- D. Rabies
- E. Diphtheria

Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients

Live attenuated vaccines
- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid

Whole killed organism*
- rabies
- pertussis

Fragment
- diphtheria
- tetanus
- meningococcus, pneumococcus, haemophilus

Others
- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of Vibrio cholerae together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

*whole cell typhoid vaccine is no longer used in the UK

Question 128 of 143

A 60-year-old man with a past medical history of osteoarthritis presents with a swollen, red and hot left knee joint. He is unable to move it due to the pain. On examination he is pyrexial with a temperature of 38.7 C and a blood sample shows a white cell count of 22.8 $*10^9$/l. Following joint aspiration, what is the most appropriate antibiotic therapy?

- A. IV flucloxacillin + benzylpenicillin
- B. IV gentamicin + benzylpenicillin
- C. IV flucloxacillin + fusidic acid
- D. IV flucloxacillin + cefotaxime
- E. IV gentamicin + rifampicin + benzylpenicillin

Question 128 of 143

A 60-year-old man with a past medical history of osteoarthritis presents with a swollen, red and hot left knee joint. He is unable to move it due to the pain. On examination he is pyrexial with a temperature of 38.7 C and a blood sample shows a white cell count of 22.8 $*10^9$/l. Following joint aspiration, what is the most appropriate antibiotic therapy?

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- B. IV gentamicin + benzylpenicillin
- C. IV flucloxacillin + fusidic acid
- D. IV flucloxacillin + cefotaxime
- E. IV gentamicin + rifampicin + benzylpenicillin

Septic arthritis: IV flucloxacillin + fusidic acid

Septic arthritis

Overview
- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

Management
- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin + fusidic acid or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

Question 129 of 143

You are counselling a 26-year-old man who has recently had a positive HIV test. His most recent CD4 count is 650 cells/mm^3. Which one of the following vaccinations is contraindicated?

- A. Oral poliomyelitis
- B. Yellow fever
- C. Pneumococcus
- D. Parenteral poliomyelitis
- E. Measles, Mumps, Rubella

Question 129 of 143

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- E. Measles, Mumps, Rubella

HIV: immunisation

The Department of Health 'Greenbook' on immunisation defers to the British HIV Association for guidelines relating to immunisation of HIV-infected adults

Vaccines that can be used in all HIV-infected adults	**Vaccines that can be used if CD4 > 200**	**Contraindicated in HIV-infected adults**
Hepatitis A Hepatitis B *Haemophilus influenzae* B (Hib) Influenza-parenteral Japanese encephalitis Meningococcus-MenC Meningococcus-ACWY I Pneumococcus-PPV23 Poliomyelitis-parenteral (IPV) Rabies Tetanus-Diphtheria (Td)	Measles, Mumps, Rubella (MMR) Varicella Yellow Fever	Cholera CVD103-HgR Influenza-intranasal Poliomyelitis-oral (OPV) Tuberculosis (BCG)

Question 130 of 143

A 34-year-old man is diagnosed as being HIV positive. He was born and brought up in the United Kingdom and is currently fit and well with no past medical history. At what point should anti-retroviral therapy be started?

- A. At the time of diagnosis
- B. CD4 < 200 * 10^6/l
- C. CD4 < 250 * 10^6/l
- D. CD4 < 300 * 10^6/l
- E. CD4 < 350 * 10^6/l

Question 130 of 143

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- B. CD4 < 200 * 10^6/l
- C. CD4 < 250 * 10^6/l
- D. CD4 < 300 * 10^6/l
- E. CD4 < 350 * 10^6/l

Start anti-retrovirals in HIV when CD4 < 350 * 10^6/l

Anti-retroviral therapy has previously been delayed until CD4 counts were below 200 * 10^6/l. This was largely due to the toxicity of drugs and fear of resistance developing. Recent guidelines now suggest starting treatment when counts drop below 350 * 10^6/l

HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)
- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Question 131 of 143

What is the most appropriate antibiotic to use in cholera?

- A. Erythromycin
- B. Metronidazole
- C. Doxycycline
- D. Penicillin V
- E. Trimethoprim

Question 131 of 143

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Cholera

Overview
- caused by Vibro cholerae - Gram negative bacteria

Features
- profuse 'rice water' diarrhoea
- dehydration
- hypoglycaemia

Management
- oral rehydration therapy
- antibiotics: doxycycline, ciprofloxacin

Question 132 of 143

A 35-year-old man returns from a two week holiday in Italy. He has a 10 day history of rectal bleeding associated with lower back pain. On examination there is a painful swelling of his right knee. What is the most likely diagnosis?

- A. Gonococcal septicaemia
- B. Amoebiasis
- C. Crohn's disease
- D. Tuberculosis
- E. Ulcerative colitis

Question 132 of 143

A 35-year-old man returns from a two week holiday in Italy. He has a 10 day history of rectal bleeding associated with lower back pain. On examination there is a painful swelling of his right knee. What is the most likely diagnosis?

- A. Gonococcal septicaemia
- B. Amoebiasis
- C. Crohn's disease
- D. Tuberculosis
- E. Ulcerative colitis

Gonococcus contracted via anal sex may cause proctitis. The knee swelling seen in this patient is septic arthritis, which is characteristic of the second stage of disseminated gonococcal infection. Proctitis may present with either lower back or rectal pain

Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria* gonorrhoea. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

Features
- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

Management
- ciprofloxacin 500mg PO used to be the treatment of choice
- however, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- options include cefixime 400mg PO (single dose) or ceftriaxone 250mg IM

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthritis and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Key features of disseminated gonococcal infection
- tenosynovitis
- migratory polyarthritis
- dermatitis (lesions can be maculopapular or vesicular)

Question 133 of 143

A 48-year-old salesman presents with a 5 day history of cough and pleuritic chest pain. He has no past medical history of note. On examination his temperature is 38.2ºC, blood pressure is 120/80 mmHg, respiratory rate 18/min and pulse 84/min. Auscultation of the chest reveals bronchial breathing in the left base and the same area is dull to percussion. What is the most suitable management?

- A. Oral amoxicillin
- B. Oral co-amoxiclav
- C. Oral amoxicillin + erythromycin
- D. Oral erythromycin
- E. Admit

Question 133 of 143

A 48-year-old salesman presents with a 5 day history of cough and pleuritic chest pain. He has no past medical history of note. On examination his temperature is 38.2ºC, blood pressure is 120/80 mmHg, respiratory rate 18/min and pulse 84/min. Auscultation of the chest reveals bronchial breathing in the left base and the same area is dull to percussion. What is the most suitable management?

- A. Oral amoxicillin
- B. Oral co-amoxiclav
- C. Oral amoxicillin + erythromycin
- D. Oral erythromycin
- E. Admit

Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- Staphylococcal aureus
- atypical pneumonias (e.g. Due to Mycoplasma pneumoniae)
- viruses

Klebsiella pneumoniae is classically in alcoholics

Streptococcus pneumoniae **(pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Antibiotic choices

- home-treated uncomplicated CAP: first line - oral amoxicillin
- hospitalized uncomplicated CAP: if admitted for non-clinical reasons or not previously treated in the community for this episode then oral amoxicillin, otherwise amoxicillin + macrolide

Question 134 of 143

Which of the following is least recognised as a cause of a false positive VDRL test?

- A. Pregnancy
- B. SLE
- C. Oral contraceptive pill
- D. Tuberculosis
- E. HIV

Question 134 of 143

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- D. Tuberculosis
- E. HIV

Syphilis: investigation

Treponema pallidum is a very sensitive organism and cannot be grown on artificial media. The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue

Serological tests can be divided into
- cardiolipin tests (not treponeme specific)
- treponemal specific antibody tests

Cardiolipin tests
- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin)
- insensitive in late syphilis
- becomes negative after treatment

Treponemal specific antibody tests
- example: TPHA (*Treponema pallidum* HaemAgglutination test)
- remains positive after treatment

Causes of false positive cardiolipin tests
- pregnancy
- SLE, anti-phospholipid syndrome
- TB
- leprosy
- malaria
- HIV

Question 135 of 143

A 34-year-old man from Venezuela presents with a flu-like illness and periorbital oedema. Generalised lymphadenopathy is noted. A diagnosis of Chagas' disease is confirmed on blood smear. What is the most appropriate treatment?

- A. Benznidazole
- B. Sodium stibogluconate
- C. Metronidazole
- D. Pentamidine
- E. Atovaquone-proguanil

Question 135 of 143

A 34-year-old man from Venezuela presents with a flu-like illness and periorbital oedema. Generalised lymphadenopathy is noted. A diagnosis of Chagas' disease is confirmed on blood smear. What is the most appropriate treatment?

- A. Benznidazole
- B. Sodium stibogluconate
- C. Metronidazole
- D. Pentamidine
- E. Atovaquone-proguanil

Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - Trypanosoma gambiense in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

American trypanosomiasis, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaoesophagus and megacolon causing dysphagia and constipation

Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

Question 136 of 143

A 50-year-old sewage worker presents with a one week history of fever and feeling generally unwell. Which one of the following features would be least consistent with a diagnosis of leptospirosis?

- A. Meningism
- B. Conjunctival erythema
- C. Productive cough
- D. Decreased urine output
- E. Severe myalgia

Question 136 of 143

A 50-year-old sewage worker presents with a one week history of fever and feeling generally unwell. Which one of the following features would be least consistent with a diagnosis of leptospirosis?

- A. Meningism
- B. Conjunctival erythema
- C. Productive cough
- D. Decreased urine output
- E. Severe myalgia

Pulmonary complications can occur in leptospirosis but generally happen in severe and late-stage disease. Severe disease may result in acute respiratory distress syndrome or pulmonary haemorrhage.

Leptospirosis

Also known as Weil's disease*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete Leptospira interrogans (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

Features
- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

Management
- high-dose benzylpenicillin or doxycycline

*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice

Question 137 of 143

A 17-year-old man attends the local sexual health clinic. He has developed a large, keratinised genital wart on the shaft of his penis. This has been present for around three months but he has been too embarrassed to present before now. What is the most appropriate initial management?

- A. Topical aciclovir
- B. Cryotherapy
- C. Topical salicylic acid
- D. Electrocautery
- E. Topical podophyllum

Question 137 of 143

A 17-year-old man attends the local sexual health clinic. He has developed a large, keratinised genital wart on the shaft of his penis. This has been present for around three months but he has been too embarrassed to present before now. What is the most appropriate initial management?

- A. Topical aciclovir
- B. Cryotherapy
- C. Topical salicylic acid
- D. Electrocautery
- E. Topical podophyllum

Genital wart treatment
- multiple, non-keratinised warts: topical podophyllum
- solitary, keratinised warts: cryotherapy

As the wart is keratinised cryotherapy should be used initially

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 138 of 143

Which one of the following congenital infections is most characteristically associated with chorioretinitis?

- A. Cytomegalovirus
- B. *Treponema pallidum*
- C. Rubella
- D. Toxoplasma gondii
- E. Parvovirus B19

Question 138 of 143

Which one of the following congenital infections is most characteristically associated with chorioretinitis?

- A. Cytomegalovirus
- B. *Treponema pallidum*
- C. Rubella
- D. Toxoplasma gondii
- E. Parvovirus B19

Congenital toxoplasmosis
- cerebral calcification
- chorioretinitis

A form of 'salt and pepper' chorioretinitis is also seen in congenital rubella but this is not a common feature

Congenital infections

The major congenital infections encountered in examinations are rubella, toxoplasmosis and cytomegalovirus

Cytomegalovirus is the most common congenital infection in the UK. Maternal infection is usually asymptomatic

	Rubella	**Toxoplasmosis**	**Cytomegalovirus**
Characteristic features	Sensorineural deafness Congenital cataracts Congenital heart disease (e.g. patent ductus arteriosus) Glaucoma	Cerebral calcification Chorioretinitis Hydrocephalus	Growth retardation Purpuric skin lesions
Other features	Growth retardation Hepatosplenomegaly Purpuric skin lesions 'Salt and pepper' chorioretinitis Microphthalmia Cerebral palsy	Anaemia Hepatosplenomegaly Cerebral palsy	Sensorineural deafness Encephalitiis Pneumonitis Hepatosplenomegaly Anaemia Jaundice Cerebral palsy

Question 139 of 143

Which one of the following organisms is most contagious?

- A. Varicella zoster virus
- B. Epstein Barr virus
- C. Rotavirus
- D. Herpes simplex virus
- E. *Haemophilus influenzae*

Question 139 of 143

Which one of the following organisms is most contagious?

- A. Varicella zoster virus
- B. Epstein Barr virus
- C. Rotavirus
- D. Herpes simplex virus
- E. *Haemophilus influenzae*

Chickenpox

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion

Chickenpox is highly infectious
- spread via the respiratory route
- can be caught from someone with shingles
- infectivity = 4 days before rash, until 5 days after the rash first appeared*
- incubation period = 10-21 days

Clinical features (tend to be more severe in older children/adults)
- fever initially
- itchy, rash starting on head/trunk before spreading. Initially macular then papular then vesicular
- systemic upset is usually mild

Management is supportive
- keep cool, trim nails
- calamine lotion
- school exclusion: current HPA advice is 5 days from start of skin eruption. They also state 'Traditionally children have been excluded until all lesions are crusted. However, transmission has never been reported beyond the fifth day of the rash.'
- immunocompromised patients and newborns with peripartum exposure should receive varicella zoster immunoglobulin (VZIG). If chickenpox develops then IV aciclovir should be considered

A common complication is secondary bacterial infection of the lesions. Rare complications include
- pneumonia
- encephalitis (cerebellar involvement may be seen)
- disseminated haemorrhagic chickenpox
- arthritis, nephritis and pancreatitis may very rarely be seen

*it was traditionally taught that patients were infective until all lesions had scabbed over

Question 140 of 143

Which one of the following is least likely to result from *Streptococcus pyogenes* infection?

- A. Rheumatic fever
- B. Scarlet fever
- C. Cellulitis
- D. Type 2 necrotizing fasciitis
- E. Pneumonia

Question 140 of 143

Which one of the following is least likely to result from *Streptococcus pyogenes* infection?

- A. Rheumatic fever
- B. Scarlet fever
- C. Cellulitis
- D. Type 2 necrotizing fasciitis
- E. Pneumonia

Streptococcus pyogenes rarely causes pneumonia

Streptococci

Streptococci may be divided into alpha and beta haemolytic types

Alpha haemolytic streptococci

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

Beta haemolytic streptococci

These can be subdivided into group A and B

Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

Question1 41 of 143

What is the first line treatment in hydatid disease?

- A. Metronidazole
- B. Ciprofloxacin
- C. Itraconazole
- D. Albendazole
- E. Sodium stibogluconate

Question 141 of 143

What is the first line treatment in hydatid disease?

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Tape worms

Tape worms are made up of repeated segments called proglottids. These are often present in faeces and are useful diagnostically

Cysticercosis
- caused by Taenia solium (from pork) and Taenia saginata (from beef)
- management: niclosamide

Hydatid disease
- caused by the dog tapeworm Echinococcus granulosus
- life-cycle involves dogs ingesting hydatid cysts from sheep liver
- often seen in farmers
- may cause liver cysts
- management: albendazole

Question 142 of 143

Infection with Schistosoma haematobium is most strongly associated with:

- A. Transitional cell bladder cancer
- B. Lung cancer
- C. Hepatoma
- D. Vulval carcinoma
- E. Squamous cell bladder cancer

Question 142 of 143

Infection with Schistosoma haematobium is most strongly associated with:

- A. Transitional cell bladder cancer
- B. Lung cancer
- C. Hepatoma
- D. Vulval carcinoma
- E. Squamous cell bladder cancer

Schistosomiasis is a risk factor for **S**quamous cell bladder cancer

Schistosomiasis

Schistosomiasis, or bilharzia, is a parasitic flatworm infection. The following types of schistosomiasis are recognised:

- Schistosoma mansoni and Schistosoma intercalatum: intestinal schistosomiasis
- Schistosoma haematobium: urinary schistosomiasis

Schistosoma haematobium

This typically presents as a 'swimmer's itch' in patients who have recently returned from Africa. Schistosoma haematobium is a risk factor for squamous cell bladder cancer

Features

- frequency
- haematuria
- bladder calcification

Management

- single oral dose of praziquantel

Question 143 of 143

A 24-year-old man is admitted to the Emergency Department with breathing difficulties and confusion three weeks after returning from a holiday in Cambodia. His partner says he has had 'the flu' for the past two weeks. A blood film is positive for malarial parasites and a chest x-ray and arterial blood gases suggest acute respiratory distress syndrome. A diagnosis of severe falciparum malaria is suspected. What is the treatment of choice?

- A. Oral artemether-lumefantrine
- B. Intravenous clindamycin + oral artemether-lumefantrine
- C. Intravenous artemether-lumefantrine
- D. Oral atovaquone-proguanil
- E. Intravenous quinine

Question 143 of 143

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- C. Intravenous artemether-lumefantrine
- D. Oral atovaquone-proguanil
- E. Intravenous quinine

Severe falciparum malaria - intravenous quinine

Malaria: Falciparum

Feature of severe malaria
- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

Complications
- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria
- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- first choice is oral quinine for 5 days followed by sulfadoxine-pyrimethamine or doxycycline
- alternative regimes include atovaquone-proguanil or artemether-lumefantrine

Severe falciparum malaria
- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- intravenous quinine is the treatment of choice
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

Question 1 of 45

A 65-year-old man with a known history of Paget's disease is noted to have irregular dark red lines radiating from the optic nerve. What is the likely diagnosis?

- A. Retinitis pigmentosa
- B. Optic neuritis
- C. Angioid retinal streaks
- D. Choroidoretinitis
- E. Malignant hypertension

Question 1 of 45

A 65-year-old man with a known history of Paget's disease is noted to have irregular dark red lines radiating from the optic nerve. What is the likely diagnosis?

- A. Retinitis pigmentosa
- B. Optic neuritis
- ✓ C. Angioid retinal streaks
- D. Choroidoretinitis
- E. Malignant hypertension

This is a typical description of angioid retinal streaks which are associated with Paget's disease

Angioid retinal streaks

Angioid retinal streaks are seen on fundoscopy as irregular dark red streaks radiating from the optic nerve head. The elastic layer of Bruch's membrane is characteristically thickened and calcified

Causes

- pseudoxanthoma elasticum
- Ehler-Danlos syndrome
- Paget's disease
- sickle-cell anaemia
- acromegaly

Question 2 of 45

Each one of the following is a cause of a mydriatic pupil, except:

- A. Third nerve palsy
- B. Atropine
- C. Holmes-Adie pupil
- D. Argyll-Robertson pupil
- E. Traumatic iridoplegia

Question 2 of 45

Each one of the following is a cause of a mydriatic pupil, except:

- A. Third nerve palsy
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- C. Holmes-Adie pupil
- ✓ D. Argyll-Robertson pupil
- E. Traumatic iridoplegia

Mydriasis

Causes of mydriasis (large pupil)
- third nerve palsy
- Holmes-Adie pupil
- traumatic iridoplegia
- phaeochromocytoma
- congenital

Drug causes of mydriasis
- topical mydriatics: tropicamide, atropine
- sympathomimetic drugs: amphetamines
- anticholinergic drugs: tricyclic antidepressants

Question 3 of 45

A 34-year-old woman presents complaining of headaches. Examination of her pupils using a light shone alternately in each eye reveals that when the light is shone in the right eye both pupils constrict but when the light source immediately moves to the left eye both eyes appear to dilate.

What is the most likely diagnosis?

- A. Right optic neuritis
- B. Left sided Horner's syndrome
- C. Craniopharyngioma
- D. Left optic neuritis
- E. Right Holmes-Adie pupil

Question 3 of 45

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What is the most likely diagnosis?

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- B. Left sided Horner's syndrome
- C. Craniopharyngioma
- ✓ D. Left optic neuritis
- E. Right Holmes-Adie pupil

This is the 'swinging light test' and reveals a relative afferent pupillary defect. As there is a defect in the afferent nerve on the left side the pupils constrict less than normal, giving the impression of dilation.

Given her age, multiple sclerosis causing optic neuritis is the likely underlying diagnosis. Optic neuritis typically causes a dull ache in the region of the eye which is aggravated by movement

Relative afferent pupillary defect

Also known as the Marcus-Gunn pupil, a relative afferent pupillary defect is found by the 'swinging light test'. It is caused by a lesion anterior to the optic chiasm i.e. optic nerve or retina

Causes

- retina: detachment
- optic nerve: optic neuritis e.g. multiple sclerosis

Pathway of pupillary light reflex

- afferent: retina --> optic nerve --> lateral geniculate body --> midbrain
- efferent: Edinger-Westphal nucleus (midbrain) --> oculomotor nerve

Question 4 of 45

A 65-year-old man with a 16 year history of type 2 diabetes mellitus presents complaining of poor eye sight and blurred vision. Visual acuity measured using a Snellen chart is reduced to 6/12 in the right eye and 6/18 in the left eye. Fundoscopy reveals a number of yellow deposits in the left eye consistent with drusen formation. Similar changes but to a lesser extent are seen in the right eye. What is the most likely diagnosis?

- A. Wet age-related macular degeneration
- B. Pre-proliferative diabetic retinopathy
- C. Chronic open angle glaucoma
- D. Proliferative diabetic retinopathy
- E. Dry age-related macular degeneration

Question 4 of 45

A 65-year-old man with a 16 year history of type 2 diabetes mellitus presents complaining of poor eye sight and blurred vision. Visual acuity measured using a Snellen chart is reduced to 6/12 in the right eye and 6/18 in the left eye. Fundoscopy reveals a number of yellow deposits in the left eye consistent with drusen formation. Similar changes but to a lesser extent are seen in the right eye. What is the most likely diagnosis?

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- B. Pre-proliferative diabetic retinopathy
- C. Chronic open angle glaucoma
- D. Proliferative diabetic retinopathy
- ✓ E. Dry age-related macular degeneration

Drusen = **D**ry macular degeneration

Macular degeneration

Macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral. Two forms of macular degeneration are seen:

- dry macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Risk factors

- age: most patients are over 60 years of age
- family history
- smoking
- more common in Caucasians
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
- high does of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Should be avoided in smokers due to an increased risk of lung cancer

Dry macular degeneration - no current medical treatments

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Question 5 of 45

Which one of the following is associated with the Holmes-Adie pupil?

- A. Decreased ankle reflexes
- B. Pupillary constriction
- C. Ptosis in 10-20% of cases
- D. An increased of developing multiple sclerosis
- E. Neurosyphilis

Question 5 of 45

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✓ A. Decreased ankle reflexes

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C. Ptosis in 10-20% of cases

D. An increased of developing multiple sclerosis

E. Neurosyphilis

Holmes ADIe = DIlated pupil, females, absent leg reflexes

Holmes-Adie pupil

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

Overview
- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

Holmes-Adie syndrome
- association of Holmes-Adie pupil with absent ankle/knee reflexes

Question 6 of 45

Which one of the following is least associated with the development of optic atrophy?

- A. Ataxic telangiectasia
- B. Longstanding papilloedema
- C. Multiple sclerosis
- D. Glaucoma
- E. Retinitis pigmentosa

Question 6 of 45

Which one of the following is least associated with the development of optic atrophy?

- ✓ A. Ataxic telangiectasia
- B. Longstanding papilloedema
- C. Multiple sclerosis
- D. Glaucoma
- E. Retinitis pigmentosa

Optic atrophy

Optic atrophy is seen as pale, well demarcated disc on fundoscopy. It is usually bilateral and causes a gradual loss of vision. Causes may be acquired or congenital

Acquired causes

- multiple sclerosis
- papilloedema (longstanding)
- raised intraocular pressure (e.g. glaucoma, tumour)
- retinal damage (e.g. choroiditis, retinitis pigmentosa)
- ischaemia
- toxins: tobacco amblyopia, quinine, methanol, arsenic, lead
- nutritional: vitamin B1, B2, B6 and B12 deficiency

Congenital causes

- Friedreich's ataxia
- mitochondrial disorders e.g. Leber's optic atrophy
- DIDMOAD - the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Question 7 of 45

A 64-year-old woman presents with bilateral sore eyelids. She also complains of her eyes being dry all the time. On examination her eyelid margins are erythematous at the margins but are not swollen. Of the given options, what is the most appropriate initial management?

- A. Topical chloramphenicol + mechanical removal of lid debris
- B. Hot compresses + topical steroids
- C. Topical chloramphenicol + topical steroids
- D. Hot compresses + mechanical removal of lid debris
- E. Topical chloramphenicol + hot compresses

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- E. Topical chloramphenicol + hot compresses

Artificial tears may also be given for symptom relief of blepharitis

Blepharitis

Blepharitis is inflammation of the eyelid margins. It may due to either meibomian gland dysfunction (common, posterior blepharitis) or seborrhoeic dermatitis/staphylococcal infection (less common, anterior blepharitis). Blepharitis is also more common in patients with rosacea

The meibomian glands secrete oil on to the eye surface to prevent rapid evaporation of the tear film. Any problem affecting the meibomian glands (as in blepharitis) can hence cause drying of the eyes which in turns leads to irritation

Features

- symptoms are usually bilateral
- grittiness and discomfort, particularly around the eyelid margins
- eyes may be sticky in the morning
- eyelid margins may be red. Swollen eyelids may be seen in staphylococcal blepharitis
- styes and chalazions are more common in patients with blepharitis
- secondary conjunctivitis may occur

Management

- softening of the lid margin using hot compresses twice a day
- mechanical removal of the debris from lid margins - cotton wool buds dipped in a mixture of cooled boiled water and baby shampoo is often used*
- artificial tears may be given for symptom relief in people with dry eyes or an abnormal tear film

*an alternative is sodium bicarbonate, a teaspoonful in a cup of cooled water that has recently been boiled

Question 8 of 45

A 54-year-old woman presents with a persistent watery left eye for the past 4 days. On examination there is erythema and swelling of the inner canthus of the left eye. What is the most likely diagnosis?

- A. Blepharitis
- B. Acute angle closure glaucoma
- C. Meibomian cyst
- D. Dacryocystitis
- E. Pinguecula

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Lacrimal duct problems

Dacryocystitis is infection of the lacrimal sac

Features
- watering eye (epiphora)
- swelling and erythema at the inner canthus of the eye

Management is with systemic antibiotics. Intravenous antibiotics are indicated if there is associated periorbital cellulitis

Congenital lacrimal duct obstruction affects around 5-10% of newborns. It is bilateral in around 20% of cases

Features
- watering eye (even if not crying)
- secondary infection may occur

Symptoms resolve in 99% of cases by 12 months of age

Question 9 of 45

A 67-year-old woman presents for review. She has recently been diagnosed with dry age-related macular degeneration. Which one of the following is the strongest risk factor for developing this condition?

- A. Hypertension
- B. Poor diet
- C. Smoking
- D. Diabetes mellitus
- E. Alcohol excess

Question 9 of 45

A 67-year-old woman presents for review. She has recently been diagnosed with dry age-related macular degeneration. Which one of the following is the strongest risk factor for developing this condition?

- A. Hypertension
- B. Poor diet
- ✓ C. Smoking
- D. Diabetes mellitus
- E. Alcohol excess

Macular degeneration - smoking is risk factor

Having a balanced diet, with plenty of fresh fruits and vegetables may also slow the progression of macular degeneration. There is still ongoing research looking at the role of supplementary antioxidants

Macular degeneration

Macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral. Two forms of macular degeneration are seen:

- dry macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Risk factors

- age: most patients are over 60 years of age
- family history
- smoking
- more common in Caucasians
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
- high does of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Should be avoided in smokers due to an increased risk of lung cancer

Dry macular degeneration - no current medical treatments

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Question 10 of 45

Each one of the following is associated with retinitis pigmentosa, except:

- A. Usher syndrome
- B. Refsum disease
- C. Kearns-Sayre syndrome
- D. Tuberose sclerosis
- E. Abetalipoproteinaemia

Question 10 of 45

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- C. Kearns-Sayre syndrome
- ✓ D. Tuberose sclerosis
- E. Abetalipoproteinaemia

Ocular manifestations of tuberose sclerosis includes retinal hamartomas

Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in tunnel vision

Features
- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)

Associated diseases
- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

Question 11 of 45

A 71-year-old man presents with severe pain around his right eye and vomiting. On examination the right eye is red and decreased visual acuity is noted. Which one of the following options is the most appropriate initial treatment?

- A. Topical pilocarpine + oral prednisolone
- B. Topical pilocarpine + topical steroids
- C. Topical steroids
- D. Topical pilocarpine + intravenous acetazolamide
- E. Topical steroids + intravenous acetazolamide

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- C. Topical steroids
- ✓ D. Topical pilocarpine + intravenous acetazolamide
- E. Topical steroids + intravenous acetazolamide

Treatment of acute glaucoma - acetazolamide + pilocarpine

Acute angle closure glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

Features

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretion with acetazolamide and pupillary constriction with topical pilocarpine

Question 12 of 45

A 62-year-old man presents with sudden visual loss in his right eye. He is otherwise asymptomatic. Which one of the following conditions is least likely to be responsible?

- A. Ischaemic optic neuropathy
- B. Occlusion of the central retinal vein
- C. Occlusion of the central retinal artery
- D. Optic neuritis
- E. Vitreous haemorrhage

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Whilst optic neuritis can present with sudden loss, in this 62-year-old man it is the least likely option. Typically there is a unilateral decrease in visual acuity over hours or days. There may be poor discrimination of colours and eye pain on movement

Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
• Flashes of light (photopsia) - in the peripheral field of vision • Floaters, often on the temporal side of the central vision	• Dense shadow that starts peripherally progresses towards the central vision • A veil or curtain over the field of vision • Straight lines appear curved (positive Amsler grid test) • Central visual loss	• Large bleeds cause sudden visual loss • Moderate bleeds may be described as numerous dark spots • Small bleeds may cause floaters

Question 13 of 45

A 63-year-old man presents to his GP complaining of pain in his right eye. On examination the sclera is red and the pupil is dilated with a hazy cornea. What is the most likely diagnosis?

- A. Scleritis
- B. Conjunctivitis
- C. Acute angle closure glaucoma
- D. Anterior uveitis
- E. Subconjunctival haemorrhage

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Red eye - glaucoma or uveitis?
- glaucoma: severe pain, haloes, 'semi-dilated' pupil
- uveitis: small, fixed oval pupil, ciliary flush

Red eye

There are many possible causes of a red eye. It is important to be able to recognise the causes which require urgent referral to an ophthalmologist. Below is a brief summary of the key distinguishing features

Acute angle closure glaucoma
- severe pain (may be ocular or headache)
- decreased visual acuity, patient sees haloes
- semi-dilated pupil
- hazy cornea

Anterior uveitis
- acute onset
- pain
- blurred vision and photophobia
- small, fixed oval pupil, ciliary flush

Scleritis
- severe pain (may be worse on movement) and tenderness
- may be underlying autoimmune disease e.g. rheumatoid arthritis

Conjunctivitis
- purulent discharge if bacterial, clear discharge if viral

Subconjunctival haemorrhage
- history of trauma or coughing bouts

Question 14 of 45

A 74-year-old man presents to ophthalmology clinic after seeing his optician. They have noticed raised intra-ocular pressure and decreased peripheral vision. His past medical history includes asthma and type 2 diabetes mellitus. What is the most appropriate treatment given the likely diagnosis?

- A. Latanoprost
- B. Pilocarpine
- C. Timolol
- D. Dorzolamide
- E. Brimonidine

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A prostaglandin analogue should be used first-line in patients with a history of asthma.

Primary open-angle glaucoma: management

The majority of patients with primary open-angle glaucoma are managed with eye drops. These aim to lower intra-ocular pressure which in turn has been shown to prevent progressive loss of visual field.

Medication	Mode of action	Notes
Prostaglandin analogues (e.g. Latanoprost)	Increases uveoscleral outflow	Once daily administration Adverse effects include brown pigmentation of the iris
Beta-blockers (e.g. Timolol)	Reduces aqueous production	Should be avoided in asthmatics and patients with heart block
Sympathomimetics (e.g. Brimonidine, an alpha2-adrenoceptor agonist)	Reduces aqueous production and increases outflow	Avoid if taking MAOI or tricyclic antidepressants Adverse effects include hyperaemia
Carbonic anhydrase inhibitors (e.g. Dorzolamide)	Reduces aqueous production	Systemic absorption may cause sulphonamide-like reactions
Miotics (e.g. Pilocarpine)	Increases uveoscleral outflow	Adverse effects included a constricted pupil, headache and blurred vision

Surgery in the form of a trabeculectomy may be considered in refractory cases.

Question 15 of 45

A 35-year-old man presents with visual problems. He has had very poor vision in the dark for a long time but is now worried as he is developing 'tunnel vision'. He states his grandfather had a similar problem and was registered blind in his 50's. What is the most likely diagnosis?

- A. Leber's congenital amaurosis
- B. Vitelliform macular dystrophy
- C. Central serous retinopathy
- D. Primary open angle glaucoma
- E. Retinitis pigmentosa

Question 15 of 45

A 35-year-old man presents with visual problems. He has had very poor vision in the dark for a long time but is now worried as he is developing 'tunnel vision'. He states his grandfather had a similar problem and was registered blind in his 50's. What is the most likely diagnosis?

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- C. Central serous retinopathy
- D. Primary open angle glaucoma
- ✓ E. Retinitis pigmentosa

Retinitis pigmentosa - night blindness + funnel vision

Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in tunnel vision

Features
- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)

Associated diseases
- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

Question 16 of 45

Which one of the following statements regarding macular degeneration is true?

- A. Drusen are characteristic of wet macular degeneration
- B. Photodynamic therapy is useful in dry macular degeneration
- C. Asian ethnicity is a risk factor
- D. Male sex is a risk factor
- E. Wet macular degeneration carries the worst prognosis

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Macular degeneration

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- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Risk factors

- age: most patients are over 60 years of age
- family history
- smoking
- more common in Caucasians
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
- high does of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Should be avoided in smokers due to an increased risk of lung cancer

Dry macular degeneration - no current medical treatments

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Question 17 of 45

A 23-year-old female presents with recurrent headaches. Examination of her cranial nerves reveals the right pupil is 3 mm whilst the left pupil is 5 mm. The right pupil constricts to light but the left pupil is sluggish. What is the most likely diagnosis?

- A. Horner's syndrome
- B. Migraine
- C. Multiple sclerosis
- D. Holmes-Adie syndrome
- E. Argyll-Roberson syndrome

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Holmes-Adie pupil

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

Overview
- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

Holmes-Adie syndrome
- association of Holmes-Adie pupil with absent ankle/knee reflexes

Question 18 of 45

Which one of the following is least associated with the development of optic atrophy?

- A. Tobacco
- B. Methanol
- C. Vitamin B12 deficiency
- D. Lead
- E. Zinc deficiency

Question 18 of 45

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Optic atrophy

Optic atrophy is seen as pale, well demarcated disc on fundoscopy. It is usually bilateral and causes a gradual loss of vision. Causes may be acquired or congenital

Acquired causes

- multiple sclerosis
- papilloedema (longstanding)
- raised intraocular pressure (e.g. glaucoma, tumour)
- retinal damage (e.g. choroiditis, retinitis pigmentosa)
- ischaemia
- toxins: tobacco amblyopia, quinine, methanol, arsenic, lead
- nutritional: vitamin B1, B2, B6 and B12 deficiency

Congenital causes

- Friedreich's ataxia
- mitochondrial disorders e.g. Leber's optic atrophy
- DIDMOAD - the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Question 19 of 45

A 45-year-old woman with Graves' disease comes for review. She has recently been diagnosed with thyroid eye disease and is being considered for radiotherapy. Over the past three days her right eye has become red and painful. On examination there is proptosis and erythema of the right eye. Visual acuity is 6/9 in both eyes. What complication is she most likely to have developed?

- A. Exposure keratopathy
- B. Optic neuropathy
- C. Carbimazole-related neutropaenia
- D. Central retinal vein occlusion
- E. Sjogren's Syndrome

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- C. Carbimazole-related neutropaenia
- D. Central retinal vein occlusion
- E. Sjogren's Syndrome

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- papilloedema
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 20 of 45

A 68-year-old man with a type 2 diabetes mellitus present with worsening eye sight. Mydriatic drops are applied and fundoscopy reveals pre-proliferative diabetic retinopathy. A referral to ophthalmology is made. Later in the evening whilst driving home he develops pain in his left eye associated with decreased visual acuity. What is the most likely diagnosis?

- A. Keratitis secondary to mydriatic drops
- B. Proliferative diabetic retinopathy
- C. Acute angle closure glaucoma
- D. Central retinal artery occlusion
- E. Vitreous haemorrhage

Question 20 of 45

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- A. Keratitis secondary to mydriatic drops
- B. Proliferative diabetic retinopathy
- ✓ C. Acute angle closure glaucoma
- D. Central retinal artery occlusion
- E. Vitreous haemorrhage

Mydriatic drops are a known precipitant of acute angle closure glaucoma. This scenario is more common in exams than clinical practice.

Acute angle closure glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

Features

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretion with acetazolamide and pupillary constriction with topical pilocarpine

Question 21 of 45

A 71-year-old with a history of type 2 diabetes mellitus and hypertension presents due to the sensation of light flashes in his right eye. These symptoms have been present for the past 2 days and seem to occur more at the peripheral part of vision. There is no redness or pain in the affected eye. Corrected visual acuity is measured as 6/9 in both eyes. What is the most likely diagnosis?

- A. Change in shape of eye secondary to variations in blood sugar
- B. Primary open angle glaucoma
- C. Vitreous detachment
- D. Normal phenomenon in diabetic retinopathy
- E. Normal phenomenon in healthy eyes

Question 21 of 45

A 71-year-old with a history of type 2 diabetes mellitus and hypertension presents due to the sensation of light flashes in his right eye. These symptoms have been present for the past 2 days and seem to occur more at the peripheral part of vision. There is no redness or pain in the affected eye. Corrected visual acuity is measured as 6/9 in both eyes. What is the most likely diagnosis?

- A. Change in shape of eye secondary to variations in blood sugar
- B. Primary open angle glaucoma
- ✓ C. Vitreous detachment
- D. Normal phenomenon in diabetic retinopathy
- E. Normal phenomenon in healthy eyes

Flashes and floaters - vitreous/retinal detachment

Flashes and floaters are symptoms of vitreous detachment. The patient is at risk of retinal detachment and should be referred urgently to an ophthalmologist

Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
• Flashes of light (photopsia) - in the peripheral field of vision • Floaters, often on the temporal side of the central vision	• Dense shadow that starts peripherally progresses towards the central vision • A veil or curtain over the field of vision • Straight lines appear curved (positive Amsler grid test) • Central visual loss	• Large bleeds cause sudden visual loss • Moderate bleeds may be described as numerous dark spots • Small bleeds may cause floaters

Question 22 of 45

Which one of the following is not a risk factor for primary open-angle glaucoma?

- A. Diabetes mellitus
- B. Family history
- C. Hypertension
- D. Afro-Caribbean ethnicity
- E. Hypermetropia

Question 22 of 45

Which one of the following is not a risk factor for primary open-angle glaucoma?

- A. Diabetes mellitus
- B. Family history
- C. Hypertension
- D. Afro-Caribbean ethnicity
- ✓ E. Hypermetropia

Acute angle closure glaucoma is associated with hypermetropia, where as primary open-angle glaucoma is associated with myopia

Primary open-angle glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

Primary open-angle glaucoma (POAG, also referred to as chronic simple glaucoma) is present in around 2% of people older than 40 years. Other than age, risk factors include:

- family history
- black patients
- myopia
- hypertension
- diabetes mellitus

POAG may present insidiously and for this reason is often detected during routine optometry appointments. Features may include

- peripheral visual field loss - nasal scotomas progressing to 'tunnel vision'
- decreased visual acuity
- optic disc cupping

Question 23 of 45

Each one of the following are associated with angioid retinal streaks, except:

- A. Paget's disease
- B. Pseudoxanthoma elasticum
- C. Acromegaly
- D. Kearns-Sayre syndrome
- E. Ehler-Danlos syndrome

Question 23 of 45

Each one of the following are associated with angioid retinal streaks, except:

- A. Paget's disease
- B. Pseudoxanthoma elasticum
- C. Acromegaly
- ✓ D. Kearns-Sayre syndrome
- E. Ehler-Danlos syndrome

Kearns-Sayre syndrome is a mitochondrial disorder associated with retinitis pigmentosa

Angioid retinal streaks

Angioid retinal streaks are seen on fundoscopy as irregular dark red streaks radiating from the optic nerve head. The elastic layer of Bruch's membrane is characteristically thickened and calcified

Causes

- pseudoxanthoma elasticum
- Ehler-Danlos syndrome
- Paget's disease
- sickle-cell anaemia
- acromegaly

Question 24 of 45

Which one of the following causes of Horner's syndrome is due to a central lesion?

- A. Cavernous sinus thrombosis
- B. Internal carotid aneurysm
- C. Syringomyelia
- D. Pancoast's tumour
- E. Cervical rib

Question 24 of 45

Which one of the following causes of Horner's syndrome is due to a central lesion?

- A. Cavernous sinus thrombosis
- B. Internal carotid aneurysm
- ✓ C. Syringomyelia
- D. Pancoast's tumour
- E. Cervical rib

Horner's syndrome - anhydrosis determines site of lesion:
- head, arm, trunk = central lesion: stroke, syringomyelia
- just face = pre-ganglionic lesion: Pancoast's, cervical rib
- absent = post-ganglionic lesion: carotid artery

Horner's syndrome

Features
- miosis (small pupil)
- ptosis
- enophthalmos (sunken eye)
- anhydrosis (loss of sweating one side)

Distinguishing between causes
- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	**Pre-ganglionic lesions**	**Post-ganglionic lesions**
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke **S**yringomyelia Multiple **s**clerosis Tumour Encephalitis	Pancoast's **t**umour **T**hyroidectomy **T**rauma Cervical rib	**C**arotid artery dissection **C**arotid aneurysm **C**avernous sinus thrombosis **C**luster headache

Question 25 of 45

During routine follow-up at renal clinic a man is noted to have corpuscular pigmentation of the left retina. Which one of the following conditions is associated with retinitis pigmentosa?

- A. Autosomal dominant polycystic kidney disease
- B. Tuberous sclerosis
- C. Von Hippel-Lindau syndrome
- D. Alport's syndrome
- E. Medullary sponge kidney

Question 25 of 45

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- ✓ D. Alport's syndrome
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Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in tunnel vision

Features
- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)

Associated diseases
- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

Question 26 of 45

An 84-year-old man presents with loss of vision in his left eye since the morning. He is otherwise asymptomatic and of note has had no associated eye pain or headaches. His past medical history includes ischaemic heart disease but he is otherwise well. On examination he has no vision in his left eye. The left pupil responds poorly to light but the consensual light reaction is normal. Fundoscopy reveals a red spot over a pale and opaque retina. What is the most likely diagnosis?

- A. Vitreous haemorrhage
- B. Retinal detachment
- C. Ischaemic optic neuropathy
- D. Central retinal vein occlusion
- E. Central retinal artery occlusion

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- B. Retinal detachment
- C. Ischaemic optic neuropathy
- D. Central retinal vein occlusion
- ✓ E. Central retinal artery occlusion

Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
• Flashes of light (photopsia) - in the peripheral field of vision • Floaters, often on the temporal side of the central vision	• Dense shadow that starts peripherally progresses towards the central vision • A veil or curtain over the field of vision • Straight lines appear curved (positive Amsler grid test) • Central visual loss	• Large bleeds cause sudden visual loss • Moderate bleeds may be described as numerous dark spots • Small bleeds may cause floaters

Question 27 of 45

Each one of the following predisposes to cataract formation, except:

- A. Down's syndrome
- B. Hypercalcaemia
- C. Diabetes mellitus
- D. Long-term steroid use
- E. Uveitis

Question 27 of 45

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Cataracts

Majority
- age related
- UV light

Systemic
- DM
- steroids
- infection (congenital rubella)
- metabolic (hypocalcaemia, galactosaemia)
- myotonic dystrophy, Down's syndrome

Ocular
- trauma
- uveitis
- high myopia
- topical steroids

Classification
- Nuclear: change lens refractive index, common in old age
- Polar: localized, commonly inherited, lie in the visual axis
- Subcapsular: due to steroid use, just deep to the lens capsule, in the visual axis
- Dot opacities: common in normal lenses, also seen in diabetes and myotonic dystrophy

Question 28 of 45

Which one of the following is not a feature of background diabetic retinopathy?

- A. Microaneurysms
- B. Blot haemorrhages
- C. Cotton wool spots
- D. Seen in both type 1 and type 2 diabetes mellitus
- E. Hard exudates

Question 28 of 45

Which one of the following is not a feature of background diabetic retinopathy?

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- B. Blot haemorrhages
- ✓ C. Cotton wool spots
- D. Seen in both type 1 and type 2 diabetes mellitus
- E. Hard exudates

Cotton wool spots are seen in pre-proliferative retinopathy

Diabetic retinopathy

Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovasculization is thought to be caused by the production of growth factors in response to retinal ischaemia

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proprosed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	**New classification**
Background retinopathy • microaneurysms (dots) • blot haemorrhages (=3) • hard exudates Pre-proliferative retinopathy • cotton wool spots (soft exudates; ischaemic nerve fibres) • > 3 blot haemorrhages • venous beading/looping • deep/dark cluster haemorrhages • more common in Type I DM, treat with laser photocoagulation	Mild NPDR • 1 or more microaneurysm Moderate NPDR • microaneurysms • blot haemorrhages • hard exudates • cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR Severe NPDR • blot haemorrhages and microaneurysms in 4 quadrants • venous beading in at least 2 quadrants • IRMA in at least 1 quadrant

Proliferative retinopathy
- retinal neovascularisation - may lead to vitrous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

Maculopathy
- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

Question 29 of 45

Which one of the following is least recognised as a cause of tunnel vision?

- A. Papilloedema
- B. Choroidoretinitis
- C. Angioid retinal streaks
- D. Glaucoma
- E. Retinitis pigmentosa

Question 29 of 45

Which one of the following is least recognised as a cause of tunnel vision?

- A. Papilloedema
- B. Choroidoretinitis
- ✓ C. Angioid retinal streaks
- D. Glaucoma
- E. Retinitis pigmentosa

Tunnel vision

Tunnel vision is the concentric diminution of the visual fields

Causes

- papilloedema
- glaucoma
- retinitis pigmentosa
- choroidoretinitis
- optic atrophy secondary to tabes dorsalis
- hysteria

Question 30 of 45

A 65-year-old woman presents to the Emergency Department with visual problems. She has rheumatoid arthritis, depression and takes medication to control her blood pressure. Over the past few days she has been getting troublesome headaches and blurred vision but today has noted a marked reduction in vision in the right eye. On examination her right eye is red, has a sluggish pupil and a corrected visual acuity 6/30. Her medication has recently been changed. Which one of the following drugs is most to have precipitated this event?

- A. Methotrexate
- B. Doxazosin
- C. Amitriptyline
- D. Atenolol
- E. Bendroflumethiazide

Question 30 of 45

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- E. Bendroflumethiazide

Drugs which may precipitate acute glaucoma include anticholinergics and tricyclic antidepressants

Acute angle closure glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

Features

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretion with acetazolamide and pupillary constriction with topical pilocarpine

Question 31 of 45

A 70-year-old woman presents with loss of vision in her left eye. For the past two weeks she has painful frontal headaches and has been feeling generally lethargic. On examination visual acuity is 6/9 in the right eye but on the left side only hand movements can be made seen. Fundoscopy of the left side reveals a pale and oedematous optic disc. What is the most likely diagnosis?

- A. Acute angle closure glaucoma
- B. Central retinal artery occlusion
- C. Multiple sclerosis
- D. Methanol poisoning
- E. Temporal arteritis

Question 31 of 45

A 70-year-old woman presents with loss of vision in her left eye. For the past two weeks she has painful frontal headaches and has been feeling generally lethargic. On examination visual acuity is 6/9 in the right eye but on the left side only hand movements can be made seen. Fundoscopy of the left side reveals a pale and oedematous optic disc. What is the most likely diagnosis?

- A. Acute angle closure glaucoma
- B. Central retinal artery occlusion
- C. Multiple sclerosis
- D. Methanol poisoning
- ✓ E. Temporal arteritis

This patient has likely developed anterior ischemic optic neuropathy on the left side

Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others

Features
- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

Investigations
- ESR > 50 mm/hr (note ESR < 30 in 10% of patients)
- temporal artery biopsy: skip lesions may be present
- note CK and EMG normal
- reduced CD8+ T cells

Treatment
- high-dose prednisolone (there should be a dramatic response - if not the diagnosis should be reconsidered)

Question 32 of 45

Which one of the following is associated with heterochromia in congenital disease?

- A. Holmes-Adie pupil
- B. Third nerve palsy
- C. Sixth nerve palsy
- D. Argyll-Robertson pupil
- E. Horner's syndrome

Question 32 of 45

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- B. Third nerve palsy
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Horner's syndrome

Features
- miosis (small pupil)
- ptosis
- enophthalmos (sunken eye)
- anhydrosis (loss of sweating one side)

Distinguishing between causes
- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	**Pre-ganglionic lesions**	**Post-ganglionic lesions**
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke **S**yringomyelia Multiple **s**clerosis Tumour Encephalitis	Pancoast's **t**umour **T**hyroidectomy **T**rauma Cervical rib	**C**arotid artery dissection **C**arotid aneurysm **C**avernous sinus thrombosis **C**luster headache

Question 33 of 45

Which one of the following features is not characteristic of optic neuritis?

- A. Eye pain worse on movement
- B. Relative afferent pupillary defect
- C. Poor discrimination of colours, 'red desaturation'
- D. Sudden onset of visual loss
- E. Central scotoma

Question 33 of 45

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- A. Eye pain worse on movement
- B. Relative afferent pupillary defect
- C. Poor discrimination of colours, 'red desaturation'
- ✓ D. Sudden onset of visual loss
- E. Central scotoma

Optic neuritis

Causes
- multiple sclerosis
- diabetes
- syphilis

Features
- unilateral decrease in visual acuity over hours or days
- poor discrimination of colours, 'red desaturation'
- pain worse on eye movement
- relative afferent pupillary defect
- central scotoma

Prognosis
- MRI: if > 3 white-matter lesions, 5-year risk of developing multiple sclerosis is c. 50%

Question 34 of 45

A 25-year-old woman presents with a one-day history of a painful and red left eye. She describes how her eye is continually streaming tears. On examination she exhibits a degree of photophobia in the affected eye and application of fluorescein demonstrates a dendritic pattern of staining. Visual acuity is 6/6 in both eyes. What is the most appropriate management?

- A. Topical steroid
- B. Perform a lumbar puncture
- C. Treat with subcutaneous sumatriptan
- D. Topical aciclovir
- E. Topical chloramphenicol

Question 34 of 45

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- B. Perform a lumbar puncture
- C. Treat with subcutaneous sumatriptan
- ✓ D. Topical aciclovir
- E. Topical chloramphenicol

This patient has a dendritic corneal ulcer. Topical aciclovir and ophthalmology review is required. Giving a topical steroid in this situation could be disastrous as it may worsen the infection.

Herpes simplex keratitis

Herpes simplex keratitis most commonly presents with a dendritic corneal ulcer

Features
- red, painful eye
- photophobia
- epiphora
- visual acuity may be decreased
- fluorescein staining may show an epithelial ulcer

Management
- immediate referral to an ophthalmologist
- topical aciclovir

Question 35 of 45

A 64-year-old woman with type 2 diabetes mellitus presents as she has started to bump into things since the morning. Over the previous two days she had noticed some 'floating spots in her eyes'. Examination reveals she has no vision in her right eye. The red reflex on the right side is difficult to elicit and you are unable to visualise the retina on the right side during fundoscopy. Examination of the left fundus reveals changes consistent with pre-proliferative diabetic retinopathy. What is the most likely diagnosis?

- A. Occlusion of central retinal vein
- B. Vitreous haemorrhage
- C. Proliferative retinopathy
- D. Cataract
- E. Retinal detachment

Question 35 of 45

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- D. Cataract
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Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
• Flashes of light (photopsia) - in the peripheral field of vision • Floaters, often on the temporal side of the central vision	• Dense shadow that starts peripherally progresses towards the central vision • A veil or curtain over the field of vision • Straight lines appear curved (positive Amsler grid test) • Central visual loss	• Large bleeds cause sudden visual loss • Moderate bleeds may be described as numerous dark spots • Small bleeds may cause floaters

Question 36 of 45

A 69-year-old man presents to the Emergency Department with blurred vision. The examining doctor suspects a diagnosis of primary open-angle glaucoma (POAG). Which one of the following features would be most consistent with a diagnosis of POAG?

- A. Symptoms worse with mydriasis
- B. Eye pain
- C. Semi-dilated non-reacting pupil
- D. Peripheral visual field loss
- E. Red eye

Question 36 of 45

A 69-year-old man presents to the Emergency Department with blurred vision. The examining doctor suspects a diagnosis of primary open-angle glaucoma (POAG). Which one of the following features would be most consistent with a diagnosis of POAG?

- A. Symptoms worse with mydriasis
- B. Eye pain
- C. Semi-dilated non-reacting pupil
- ✓ D. Peripheral visual field loss
- E. Red eye

The other listed symptoms are seen with acute angle closure glaucoma

Primary open-angle glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

Primary open-angle glaucoma (POAG, also referred to as chronic simple glaucoma) is present in around 2% of people older than 40 years. Other than age, risk factors include:

- family history
- black patients
- myopia
- hypertension
- diabetes mellitus

POAG may present insidiously and for this reason is often detected during routine optometry appointments. Features may include

- peripheral visual field loss - nasal scotomas progressing to 'tunnel vision'
- decreased visual acuity
- optic disc cupping

Question 37 of 45

An 80-year-old woman presents with 'funny spots' affecting her vision. Over the past week she has noticed a number of flashes and floaters in the visual field of the right eye. What is the most likely diagnosis?

- A. Retinal detachment
- B. Posterior vitreous detachment
- C. Optic neuritis
- D. Depression
- E. Vitreous haemorrhage

Question 37 of 45

An 80-year-old woman presents with 'funny spots' affecting her vision. Over the past week she has noticed a number of flashes and floaters in the visual field of the right eye. What is the most likely diagnosis?

- A. Retinal detachment
- ✓ B. Posterior vitreous detachment
- C. Optic neuritis
- D. Depression
- E. Vitreous haemorrhage

Posterior vitreous detachment is thought to occur in up to 50-75% of the population over 65 years and is the most likely diagnosis here. Such patients are normally reviewed by an ophthalmologist to assess the risk of progressing to retinal detachment.

Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

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Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

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Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
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Question 38 of 45

A 74-year-old man presents with a severe throbbing headache on the right side of his head. He has now had this pain for around 6-7 days but reports no obvious trigger. There have been no visual disturbances or episodes of limb weakness. Neurological examination is unremarkable. The right side of his head is tender to touch but he cannot remember falling. Given the likely diagnosis what is the most important initial step?

- A. Give high-dose oral prednisolone
- B. Arrange an urgent orbital x-ray for suspected blow-out fracture
- C. Arrange an urgent temporal artery biopsy
- D. Arrange an urgent CT head
- E. Ocular pilocarpine + intravenous acetazolamide

Question 38 of 45

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B. Arrange an urgent orbital x-ray for suspected blow-out fracture

C. Arrange an urgent temporal artery biopsy

D. Arrange an urgent CT head

E. Ocular pilocarpine + intravenous acetazolamide

This patient has temporal arteritis and requires high-dose oral steroids to prevent ocular complications

Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- ESR > 50 mm/hr (note ESR < 30 in 10% of patients)
- temporal artery biopsy: skip lesions may be present
- note CK and EMG normal
- reduced CD8+ T cells

Treatment

- high-dose prednisolone (there should be a dramatic response - if not the diagnosis should be reconsidered)

Question 39 of 45

A 43-year-old who is noted to have a high-arched palate, arachnodactyly and a late-systolic murmur presents with visual problems. Which one of the following eye disorders is most associated with his underlying condition?

- A. Superotemporal ectopia lentis
- B. Inferonasal ectopia lentis
- C. Retinitis pigmentosa
- D. Acute glaucoma
- E. Retinal detachment

Question 39 of 45

A 43-year-old who is noted to have a high-arched palate, arachnodactyly and a late-systolic murmur presents with visual problems. Which one of the following eye disorders is most associated with his underlying condition?

- ✓ A. Superotemporal ectopia lentis
- B. Inferonasal ectopia lentis
- C. Retinitis pigmentosa
- D. Acute glaucoma
- E. Retinal detachment

This patient has features consistent with Marfan's syndrome. Whilst glaucoma and retinal detachment are seen they are not as common as superotemporal ectopia lentis (upwards lens dislocation), which is seen in around 50% of patients. Inferonasal ectopia lentis is characteristic of homocystinuria

Mitral valve prolapse may cause a late-systolic murmur. This feature helps distinguish the above description from that of a patient with homocystinuria

Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15

Features

- tall stature with arm span > height ratio > 1.05
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of > 20 degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic regurgitation, mitral valve prolapse (75%), aortic dissection
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera

Question 40 of 45

Which one of the following best describes the action of latanoprost in the management of primary open-angle glaucoma?

- A. Carbonic anhydrase inhibitor
- B. Reduces aqueous production + increases outflow
- C. Opens up drainage pores
- D. Increases uveoscleral outflow
- E. Reduces aqueous production

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Primary open-angle glaucoma: management

The majority of patients with primary open-angle glaucoma are managed with eye drops. These aim to lower intra-ocular pressure which in turn has been shown to prevent progressive loss of visual field.

Medication	Mode of action	Notes
Prostaglandin analogues (e.g. Latanoprost)	Increases uveoscleral outflow	Once daily administration Adverse effects include brown pigmentation of the iris
Beta-blockers (e.g. Timolol)	Reduces aqueous production	Should be avoided in asthmatics and patients with heart block
Sympathomimetics (e.g. Brimonidine, an alpha2-adrenoceptor agonist)	Reduces aqueous production and increases outflow	Avoid if taking MAOI or tricyclic antidepressants Adverse effects include hyperaemia
Carbonic anhydrase inhibitors (e.g. Dorzolamide)	Reduces aqueous production	Systemic absorption may cause sulphonamide-like reactions
Miotics (e.g. Pilocarpine)	Increases uveoscleral outflow	Adverse effects included a constricted pupil, headache and blurred vision

Surgery in the form of a trabeculectomy may be considered in refractory cases.

Question 41 of 45

A 71-year-old female with dry age-related macular degeneration is reviewed. Unfortunately her eyesight has deteriorated over the past six months. She has never smoked and is taking antioxidant supplements. What is the most appropriate next step?

- A. Retinal transplant
- B. Intravitreal ranibizumab
- C. Explain no other medical therapies currently available
- D. Photodynamic therapy
- E. Photocoagulation

Question 41 of 45

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Macular degeneration

Macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral. Two forms of macular degeneration are seen:

- dry macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Risk factors

- age: most patients are over 60 years of age
- family history
- smoking
- more common in Caucasians
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
- high does of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Should be avoided in smokers due to an increased risk of lung cancer

Dry macular degeneration - no current medical treatments

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Question 42 of 45

A 40-year-old man presents with bilateral dry, gritty eyes. A diagnosis of blepharitis is considered. Which one of the following is least likely to be associated with blepharitis?

- A. Meibomian gland dysfunction
- B. Seborrhoeic dermatitis
- C. Staphylococcal infection
- D. Acne rosacea
- E. Viral upper respiratory tract infection

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Blepharitis

Blepharitis is inflammation of the eyelid margins. It may due to either meibomian gland dysfunction (common, posterior blepharitis) or seborrhoeic dermatitis/staphylococcal infection (less common, anterior blepharitis). Blepharitis is also more common in patients with rosacea

The meibomian glands secrete oil on to the eye surface to prevent rapid evaporation of the tear film. Any problem affecting the meibomian glands (as in blepharitis) can hence cause drying of the eyes which in turns leads to irritation

Features

- symptoms are usually bilateral
- grittiness and discomfort, particularly around the eyelid margins
- eyes may be sticky in the morning
- eyelid margins may be red. Swollen eyelids may be seen in staphylococcal blepharitis
- styes and chalazions are more common in patients with blepharitis
- secondary conjunctivitis may occur

Management

- softening of the lid margin using hot compresses twice a day
- mechanical removal of the debris from lid margins - cotton wool buds dipped in a mixture of cooled boiled water and baby shampoo is often used*
- artificial tears may be given for symptom relief in people with dry eyes or an abnormal tear film

*an alternative is sodium bicarbonate, a teaspoonful in a cup of cooled water that has recently been boiled

Question 43 of 45

Which one of the following statements regarding the Holmes-Adie pupil is incorrect?

- A. May be associated with absent ankle/knee reflexes
- B. Bilateral in 80% of cases
- C. It is a benign condition
- D. Slowly reactive to accommodation but very poorly (if at all) to light
- E. Causes a dilated pupil

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- E. Causes a dilated pupil

The Holmes-Adie pupil is unilateral, rather than bilateral, in 80% of patients

Holmes-Adie pupil

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

Overview
- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

Holmes-Adie syndrome
- association of Holmes-Adie pupil with absent ankle/knee reflexes

Question 44 of 45

A 65-year-old man with a history of primary open-angle glaucoma presents with sudden painless loss of vision in his right eye. On examination of the right eye the optic disc is swollen with multiple flame-shaped and blot haemorrhages. What is the most likely diagnosis?

- A. Diabetic retinopathy
- B. Vitreous haemorrhage
- C. Ischaemic optic neuropathy
- D. Occlusion of central retinal vein
- E. Occlusion of central retinal artery

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Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
• Flashes of light (photopsia) - in the peripheral field of vision • Floaters, often on the temporal side of the central vision	• Dense shadow that starts peripherally progresses towards the central vision • A veil or curtain over the field of vision • Straight lines appear curved (positive Amsler grid test) • Central visual loss	• Large bleeds cause sudden visual loss • Moderate bleeds may be described as numerous dark spots • Small bleeds may cause floaters

Question 45 of 45

A 71-year-old man who has recently been diagnosed with macular degeneration asks for advice regarding antioxidant dietary supplements. Which one of the following may contraindicate the prescription of such supplements?

- A. Current smoker
- B. Pernicious anaemia
- C. Treated hypertension
- D. History of depression
- E. Previous episodes of tendonitis

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Beta-carotene has been found to increase the risk of lung cancer and hence antioxidant dietary supplements are not recommended for smokers.

Macular degeneration

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- smoking
- more common in Caucasians
- female sex

Features

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- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
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Dry macular degeneration - no current medical treatments

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Question 1 of 50

A 54-year-old man presents with a variety of physical symptoms that have been present for the past 9 years. Numerous investigations and review by a variety of specialties have indicated no organic basis for his symptoms. This is an example of:

- A. Munchausen's syndrome
- B. Hypochondrial disorder
- C. Dissociative disorder
- D. Somatisation disorder
- E. Conversion disorder

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- C. Dissociative disorder
- ✓ D. Somatisation disorder
- E. Conversion disorder

Unexplained symptoms
- **S**omatisation = **S**ymptoms
- hypo**C**hondria = **C**ancer

Somatisation disorder is the correct answer as the patient is concerned about persistent, unexplained symptoms rather than an underlying diagnosis such as cancer (hypochondrial disorder). Munchausen's syndrome describes the intentional production of symptoms, for example self poisoning

Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

Somatisation disorder
- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

Hypochondrial disorder
- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

Conversion disorder
- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

Dissociative disorder
- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

Munchausen's syndrome
- also known as factitious disorder
- the intentional production of physical or psychological symptoms

Malingering
- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

Question 2 of 50

A 45-year-old man who takes chlorpromazine for schizophrenia presents with severe restlessness. What side-effect of antipsychotic medication is this an example of?

- A. Akathisia
- B. Neuroleptic malignant syndrome
- C. Acute dystonia
- D. Tardive dyskinesia
- E. Parkinsonism

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Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

Extrapyramidal side-effects
- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:
- increased risk of stroke
- increased risk of venous thromboembolism

Other side-effects
- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

Question 3 of 50

A 34-year-old man confides in you that he experienced childhood sexual abuse. Which one of the following features is not a characteristic feature of post-traumatic stress disorder?

- A. Hyperarousal
- B. Emotional numbing
- C. Nightmares
- D. Loss of inhibitions
- E. Avoidance

Question 3 of 50

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Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached from other people
- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended

Question 4 of 50

Each one of the following is a recognised feature of anorexia nervosa, except:

- A. Hypokalaemia
- B. Low LH
- C. Impaired glucose tolerance
- D. Low FSH
- E. Reduced growth hormone levels

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Anorexia features
- most things low
- **G**'s and **C**'s raised: **g**rowth hormone, **g**lucose, salivary **g**lands, **c**ortisol, **c**holesterol, **c**arotinaemia

Anorexia nervosa: features

Anorexia nervosa is associated with a number of characteristic clinical signs and physiological abnormalities which are summarised below

Features
- reduced body mass index
- bradycardia
- hypotension
- enlarged salivary glands

Physiological abnormalities
- hypokalaemia
- low FSH, LH, oestrogens and testosterone
- raised cortisol and growth hormone
- impaired glucose tolerance
- hypercholesterolaemia
- hypercarotinaemia
- low T3

Question 5 of 50

A 25-year-old man demands a CT scan of his abdomen in clinic. He states it is 'obvious' he has cancer despite previous negative investigations. This is an example of a:

- A. Hypochondrial disorder
- B. Conversion disorder
- C. Munchausen's syndrome
- D. Dissociative disorder
- E. Somatisation disorder

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- typically involves loss of motor or sensory function
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Question 6 of 50

Which one of the following symptoms may indicate mania rather than hypomania?

- A. Predominately elevated mood
- B. Delusions of grandeur
- C. Increased appetite
- D. Flight of ideas
- E. Irritability

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Hypomania vs. mania

The presence of psychotic symptoms differentiates mania from hypomania

Psychotic symptoms
- delusions of grandeur
- auditory hallucinations

The following symptoms are common to both hypomania and mania

Mood
- predominately elevated
- irritable

Speech and thought
- pressured
- flight of ideas
- poor attention

Behaviour
- insomnia
- loss of inhibitions: sexual promiscuity, overspending, risk-taking
- increased appetite

Question 7 of 50

You are considering prescribing a tricyclic antidepressant for a patient who has not responded to two different types of selective serotonin reuptake inhibitors. Which one of the following tricyclic antidepressants is most dangerous in overdose?

- A. Dosulepin
- B. Imipramine
- C. Clomipramine
- D. Nortriptyline
- E. Lofepramine

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Dosulepin - avoid as dangerous in overdose

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose.They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

Common side-effects

- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

Choice of tricyclic

- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) and considered the most dangerous in overdose

More sedative	Less sedative
Amitriptline Clomipramine Dosulepine Trazadone	Imipramine Lofepramine Nortriptyline

Question 8 of 50

A 18-year-old sprinter who is currently preparing for a national athletics meeting asks to see the team doctor due to an unusual sensation in his legs. He describes a numb sensation below his knee. On examination the patient there is apparent sensory loss below the right knee in a non-dermatomal distribution. The team doctor suspects a non-organic cause of his symptoms. This is an example of a:

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Question 9 of 50

A 23-year-old man presents as he concerned about a number of recent episodes related to sleep. He finds when he wakes up and less often when he is falling asleep he is 'paralysed' and unable to move. This sometimes associated with what the patient describes as 'hallucinations' such as seeing another person in the room. He is becoming increasingly anxious about these recent episodes. What is the most likely diagnosis?

- A. Frontal lobe epilepsy
- B. Generalised anxiety disorder
- C. Sleep paralysis
- D. Night terrors
- E. Acute schizophrenia

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Sleep paralysis

Sleep paralysis is a common condition characterized by transient paralysis of skeletal muscles which occurs when awakening from sleep or less often while falling asleep. It is thought to be related to the paralysis that occurs as a natural part of REM (rapid eye movement) sleep. Sleep paralysis is recognised in a wide variety of cultures

Features
- paralysis - this occurs after waking up or shortly before falling asleep
- hallucinations - images or speaking that appear during the paralysis

Management
- if troublesome clonazepam may be used

Question 10 of 50

A woman who gave birth 5 days ago presents for review as she is concerned about her mood. She is having difficulty sleeping and feels generally anxious and tearful. Since giving birth she has also found herself snapping at her husband. This is her first pregnancy, she is not breast feeding and there is no history of mental health disorders in the past. What is the most appropriate management?

- A. Explanation and reassurance
- B. Cognitive behavioural therapy
- C. Trial of fluoxetine
- D. Trial of citalopram
- E. Discuss with psychiatric team to consider admission to mother and baby unit

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This woman has the baby-blues which is seen in around two-thirds of women. Whilst poor sleeping can be a sign of depression it is to be expected with a new baby!

Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	Postnatal depression	Puerperal psychosis
Seen in around 60-70% of women Typically seen 3-7 days following birth and is more common in primips Mothers are characteristically anxious, tearful and irritable	Affects around 10% of women Most cases start within a month and typically peaks at 3 months Features are similar to depression seen in other circumstances	Affects approximately 0.2% of women Onset usually within the first 2-3 weeks following birth Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline may be used if symptoms are severe* - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required There is around a 20% risk of recurrence following future pregnancies

*fluoxetine is best avoided due to a long half-life

Question 11 of 50

An elderly patient in a nursing home is started on quetiapine due to persistent aggressive behaviour that has not responded to non-pharmacological approaches. Which of the following adverse effects do antipsychotics increase the risk of in elderly patients?

- A. Atrial fibrillation
- B. Myocardial infarction
- C. Aspiration pneumonia
- D. Stroke
- E. Breast cancer

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Antipsychotics in the elderly - increased risk of stroke and VTE

Antipsychotics

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- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
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- increased risk of venous thromboembolism

Other side-effects
- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

Question 12 of 50

A 23-year-old man asks to be referred to a plastic surgeon. From his records you can see he has been treated for anxiety and depression with fluoxetine previously and has been off work with back pain for the past three months. He is concerned that his ears are too big in proportion to his face. He reports that he now seldom leaves the house because of this. On examination his ears appear to be within normal limits. What is the most appropriate description of this behaviour?

- A. Hypochondriasis
- B. Generalised anxiety disorder
- C. Somatisation
- D. Malingering
- E. Dysmorphophobia

Question 12 of 50

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- B. Generalised anxiety disorder
- C. Somatisation
- D. Malingering
- ✓ E. Dysmorphophobia

Body dysmorphic disorder

Body dysmorphic disorder (sometimes referred to as dysmorphophobia) is a mental disorder where patients have a significantly distorted body image

Diagnostic and Statistical Manual (DSM) IV criteria:

- Preoccupation with an imagine defect in appearance. If a slight physical anomaly is present, the person's concern is markedly excessive
- The preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The preoccupation is not better accounted for by another mental disorder (e.g., dissatisfaction with body shape and size in Anorexia Nervosa)

Question 13 of 50

A 68-year-old female is noted to be depressed following a recent admission for an exacerbation of chronic obstructive pulmonary disease. What would be the most appropriate antidepressant to start?

- A. Fluoxetine
- B. Citalopram
- C. Venlafaxine
- D. Paroxetine
- E. Imipramine

Question 13 of 50

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- A. Fluoxetine
- ✓ B. Citalopram
- C. Venlafaxine
- D. Paroxetine
- E. Imipramine

Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is more appropriate in this scenario as it has a lower propensity for drug interactions.

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 14 of 50

A 23-year-old male presents two weeks after a road traffic accident concerned about increased anxiety levels, lethargy and headache. At the time he had a CT brain which revealed no abnormality. Six months following this episode his symptoms have resolved. What did his original symptoms likely represent?

- A. Conversion disorder
- B. Post-traumatic stress disorder
- C. Somatisation disorder
- D. Generalised anxiety disorder
- E. Post-concussion syndrome

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- A. Conversion disorder
- B. Post-traumatic stress disorder
- C. Somatisation disorder
- D. Generalised anxiety disorder
- ✓ E. Post-concussion syndrome

In post-traumatic stress disorder the onset of symptoms is usually delayed and it tends to run a prolonged course

Post-concussion syndrome

Post-concussion syndrome is seen after even minor head trauma

Typical features include

- headache
- fatigue
- anxiety/depression
- dizziness

Question 15 of 50

A 24-year-old male is admitted to the Emergency Department complaining of severe abdominal pain. On examination he is shivering and rolling around the trolley. He has previously been investigated for abdominal pain and no cause has been found. He states that unless he is given morphine for the pain he will kill himself. This is an example of:

- A. Hypochondrial disorder
- B. Conversion disorder
- C. Malingering
- D. Munchausen's syndrome
- E. Somatisation disorder

Question 15 of 50

A 24-year-old male is admitted to the Emergency Department complaining of severe abdominal pain. On examination he is shivering and rolling around the trolley. He has previously been investigated for abdominal pain and no cause has been found. He states that unless he is given morphine for the pain he will kill himself. This is an example of:

- A. Hypochondrial disorder
- B. Conversion disorder
- ✓ C. Malingering
- D. Munchausen's syndrome
- E. Somatisation disorder

This is difficult as the patient may well be an opiate abuser who is withdrawing. However, given the above options the most appropriate term to use is malingering as the patient is reporting symptoms with the deliberate intention of getting morphine

Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

Somatisation disorder
- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

Hypochondrial disorder
- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

Conversion disorder
- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

Dissociative disorder
- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

Munchausen's syndrome
- also known as factitious disorder
- the intentional production of physical or psychological symptoms

Malingering
- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

Question 16 of 50

A patient you are looking after is started on imipramine for depression. Which combination of side-effects is most likely to be seen in a patient taking this class of antidepressants?

- A. Dry mouth + urinary frequency
- B. Hypertension + sweating
- C. Gastrointestinal bleeding + dyspepsia
- D. Headache + myoclonus
- E. Blurred vision + dry mouth

Question 16 of 50

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- ✓ E. Blurred vision + dry mouth

These antimuscarinic side-effects are more common with imipramine than other types of tricyclic antidepressants.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose.They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

Common side-effects
- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

Choice of tricyclic
- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) and considered the most dangerous in overdose

More sedative	Less sedative
Amitriptline Clomipramine Dosulepine Trazadone	Imipramine Lofepramine Nortriptyline

Question 17 of 50

A 29-year-old fireman presents following a recent traumatic incident where a child died in a house fire. He describes recurrent nightmares and flashbacks which have been present for the past 3 months. A diagnosis of post-traumatic stress disorder is suspected. What is the most appropriate first-line treatment?

- A. Arrange a CT head to exclude an organic cause
- B. Cognitive behavioural therapy or eye movement desensitisation and reprocessing therapy
- C. Cognitive behavioural therapy or graded exposure therapy
- D. Cognitive behavioural therapy or psychodynamic therapy
- E. Watchful waiting

Question 17 of 50

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- C. Cognitive behavioural therapy or graded exposure therapy
- D. Cognitive behavioural therapy or psychodynamic therapy
- E. Watchful waiting

Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached from other people
- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended

Question 18 of 50

A 54-year-old man with a history of depression presents for review. He was started on fluoxetine eight weeks ago and is now requesting to stop his medication as he feels so well. What should be recommended regarding his treatment?

- A. It should be stopped straight away
- B. It should be continued for at least 6 weeks
- C. It should be continued for at least 3 months
- D. It should be continued for at least 6 months
- E. It should be continued for at least 12 months

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- B. It should be continued for at least 6 weeks
- C. It should be continued for at least 3 months
- ✓ D. It should be continued for at least 6 months
- E. It should be continued for at least 12 months

This greatly reduces the risk of relapse. Patients should be reassured that antidepressants are not addictive.

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 19 of 50

You review a patient who has been taking citalopram for the past two years to treat depression. He has felt well now for the past year and you agree a plan to stop the antidepressant. How should the citalopram be stopped?

- A. Can be stopped immediately
- B. Withdraw gradually over the next 3 days
- C. Withdraw gradually over the next week
- D. Withdraw gradually over the next 2 weeks
- E. Withdraw gradually over the next 4 weeks

Question 19 of 50

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- B. Withdraw gradually over the next 3 days
- C. Withdraw gradually over the next week
- D. Withdraw gradually over the next 2 weeks
- ✓ E. Withdraw gradually over the next 4 weeks

This not necessary with fluoxetine due to its longer half-life.

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

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- restlessness
- difficulty sleeping
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- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 20 of 50

A 34-year-old man originally from West Africa is seen in January with depression. There is no past medical history of note but he is known to smoke cannabis. He has had similar episodes for the past two winters. What is the most likely diagnosis?

- A. Cyclothymic disorder
- B. Atypical depression
- C. Seasonal affective disorder
- D. Schizophrenia
- E. Drug-induced depression

Question 20 of 50

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- B. Atypical depression
- ✓ C. Seasonal affective disorder
- D. Schizophrenia
- E. Drug-induced depression

Seasonal affective disorder

Seasonal affective disorder (SAD) describes depression which occurs predominately around the winter months. Bright light therapy has been shown to be more effective than placebo for patients with SAD

Question 21 of 50

Which one of the following side-effects is more common with atypical than conventional anti-psychotics?

- A. Akathisia
- B. Weight gain
- C. Galactorrhoea
- D. Parkinsonism
- E. Tardive dyskinesia

Question 21 of 50

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- A. Akathisia
- ✓ B. Weight gain
- C. Galactorrhoea
- D. Parkinsonism
- E. Tardive dyskinesia

Atypical antipsychotics commonly cause weight gain

Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics
- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:
- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics
- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine
- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Question 22 of 50

Which of the following conditions is least associated with obsessive compulsive disorder?

- A. Tourette's syndrome
- B. Anorexia nervosa
- C. Schizophrenia
- D. Depression
- E. Wilson's disease

Question 22 of 50

Which of the following conditions is least associated with obsessive compulsive disorder?

- A. Tourette's syndrome
- B. Anorexia nervosa
- C. Schizophrenia
- D. Depression
- ✓ E. Wilson's disease

OCD

Pathophysiology
- some research suggest childhood group A beta-haemolytic streptococcal infection may have a role

Associations
- depression (30%)
- schizophrenia (3%)
- Sydenham's chorea
- Tourette's syndrome
- anorexia nervosa

Question 23 of 50

A 24-year-old female is reviewed following a course of cognitive behaviour therapy for bulimia. She feels there has been no improvement in her condition and is interested in trying pharmacological treatments. Which one of the following is most suitable?

- A. Low-dose citalopram
- B. Low-dose fluoxetine
- C. Low-dose amitriptyline
- D. High-dose amitriptyline
- E. High-dose fluoxetine

Question 23 of 50

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- B. Low-dose fluoxetine
- C. Low-dose amitriptyline
- D. High-dose amitriptyline
- ✓ E. High-dose fluoxetine

Bulimia nervosa

Bulimia nervosa is a type of eating disorder characterised by episodes of binge eating followed by intentional vomiting

Management

- referral for specialist care is appropriate in all cases
- cognitive behaviour therapy (CBT) is currently consider first-line treatment
- interpersonal psychotherapy is also used but takes much longer than CBT
- pharmacological treatments have a limited role - a trial of high-dose fluoxetine is currently licensed for bulimia but long-term data is lacking

Question 24 of 50

Which one of the following statements regarding post-partum mental health problems is incorrect?

- A. Post-natal depression is seen in around 2-3% of women
- B. Puerperal psychosis has a recurrence rate of around 20%
- C. Baby-blues are seen in the majority of women
- D. Post-natal depression usually develops within the first month
- E. Sertraline can be used whilst mothers are breast feeding

Question 24 of 50

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- C. Baby-blues are seen in the majority of women
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- E. Sertraline can be used whilst mothers are breast feeding

Post-natal depression is seen in around 10% of women

Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	Postnatal depression	Puerperal psychosis
Seen in around 60-70% of women Typically seen 3-7 days following birth and is more common in primips Mothers are characteristically anxious, tearful and irritable	Affects around 10% of women Most cases start within a month and typically peaks at 3 months Features are similar to depression seen in other circumstances	Affects approximately 0.2% of women Onset usually within the first 2-3 weeks following birth Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline may be used if symptoms are severe* - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required There is around a 20% risk of recurrence following future pregnancies

*fluoxetine is best avoided due to a long half-life

Question 25 of 50

A 27-year-old woman is brought in by her husband. She has been refusing to go outside for the past 3 months, telling her husband she is afraid of catching avian flu. On exploring this further she is concerned due to the high number of migrating birds she can see in her garden. She reports that the presence of her husbands socks on the washing line in the garden alerted her to this. What is the most likely diagnosis?

- A. Depression
- B. Hypochondrial disorder
- C. Formal thought disorder
- D. Borderline personality disorder
- E. Acute paranoid schizophrenia

Question 25 of 50

A 27-year-old woman is brought in by her husband. She has been refusing to go outside for the past 3 months, telling her husband she is afraid of catching avian flu. On exploring this further she is concerned due to the high number of migrating birds she can see in her garden. She reports that the presence of her husbands socks on the washing line in the garden alerted her to this. What is the most likely diagnosis?

- A. Depression
- B. Hypochondrial disorder
- C. Formal thought disorder
- D. Borderline personality disorder
- ✓ E. Acute paranoid schizophrenia

The washing line comment is an example of a delusional perception - see below

Schizophrenia: features

Schneider's first rank symptoms may be divided into auditory hallucinations, thought disorders, passivity phenomena and delusional perceptions:

Auditory hallucinations of a specific type:
- two or more voices discussing the patient in the third person
- thought echo
- voices commenting on the patient's behaviour

Thought disorder*:
- thought insertion
- thought withdrawal
- thought broadcasting

Passivity phenomena:
- bodily sensations being controlled by external influence
- actions/impulses/feelings - experiences which are imposed on the individual or influenced by others

Delusional perceptions
- a two stage process) where first a normal object is perceived then secondly there is a sudden intense delusional insight into the objects meaning for the patient e.g. 'The traffic light is green therefore I am the King'.

Other features of schizophrenia include
- impaired insight
- incongruity/blunting of affect (inappropriate emotion for circumstances)
- decreased speech
- neologisms: made-up words
- catatonia
- negative symptoms: incongruity/blunting of affect, anhedonia (inability to derive pleasure), alogia (poverty of speech), avolition (poor motivation)

*occasionally referred to as thought alienation

Question 26 of 50

A 45-year-old man is admitted due to haematemesis. He drinks 120 units of alcohol a week. What is the peak incidence of seizures following alcohol withdrawal?

- A. 2 hours
- B. 6 hours
- C. 12 hours
- D. 24 hours
- E. 36 hours

Question 26 of 50

A 45-year-old man is admitted due to haematemesis. He drinks 120 units of alcohol a week. What is the peak incidence of seizures following alcohol withdrawal?

- A. 2 hours
- B. 6 hours
- C. 12 hours
- D. 24 hours
- ✓ E. 36 hours

Alcohol withdrawal
- symptoms: 6-12 hours
- seizures: 36 hours
- delirium tremens: 72 hours

Alcohol withdrawal

Mechanism
- chronic alcohol consumption enhances GABA mediated inhibition in the CNS (similar to benzodiazepines) and inhibits NMDA-type glutamate receptors
- alcohol withdrawal is thought to be lead to the opposite (decreased inhibitory GABA and increased NMDA glutamate transmission)

Features
- symptoms start at 6-12 hours
- peak incidence of seizures at 36 hours
- peak incidence of delirium tremens is at 72 hours

Management
- benzodiazepines
- carbamazepine also effective in treatment of alcohol withdrawal
- phenytoin is said not to be as effective in the treatment of alcohol withdrawal seizures

Question 27 of 50

Which one of the following statements regarding anorexia nervosa is correct?

- A. The BMI should be < 16.5 kg/m^2 before making the diagnosis
- B. If amenorrhoea is present a hormonal disorder needs to be excluded
- C. It is the most common cause of admissions to child and adolescent psychiatric wards
- D. Around 75-80% of the patients are female
- E. Has a good prognosis if treated

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Anorexia nervosa

Anorexia nervosa is the most common cause of admissions to child and adolescent psychiatric wards.

Epidemiology
- 90% of patients are female
- predominately affects teenage and young-adult females
- prevalence of between 1:100 and 1:200

Diagnosis (based on the DSM-IV criteria)
- person chooses not to eat - BMI < 17.5 kg/m^2, or < 85% of that expected
- intense fear of being obese
- disturbance of weight perception
- amenorrhoea = 3 consecutive cycles

The prognosis of patients with anorexia nervosa remains poor. Up to 10% of patients will eventually die because of the disorder.

Question 28 of 50

Which one of the following is not associated with a poor prognosis in schizophrenia?

- A. Acute onset
- B. Strong family history
- C. Low IQ
- D. Premorbid history of social withdrawal
- E. Lack of obvious precipitant

Question 28 of 50

Which one of the following is not associated with a poor prognosis in schizophrenia?

- ✓ A. Acute onset
- B. Strong family history
- C. Low IQ
- D. Premorbid history of social withdrawal
- E. Lack of obvious precipitant

A gradual, rather than acute, onset is associated with a poor prognosis

Schizophrenia: prognostic indicators

Factors associated with poor prognosis
- strong family history
- gradual onset
- low IQ
- premorbid history of social withdrawal
- lack of obvious precipitant

Question 29 of 50

A 65-year-old female with a history of ischaemic heart disease is noted to be depressed following a recent myocardial infarction. What would be the most appropriate antidepressant to start?

- A. Paroxetine
- B. Imipramine
- C. Flupentixol
- D. Venlafaxine
- E. Sertraline

Question 29 of 50

A 65-year-old female with a history of ischaemic heart disease is noted to be depressed following a recent myocardial infarction. What would be the most appropriate antidepressant to start?

- A. Paroxetine
- B. Imipramine
- C. Flupentixol
- D. Venlafaxine
- ✓ E. Sertraline

Sertraline is the preferred antidepressant following a myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 30 of 50

A 31-year-old woman who gave birth two weeks ago presents for review with her husband. He is worried by her mood as she now seems depressed and is interacting poorly with the baby. He describes her mood three days ago being much different, when she was talking in a rapid and incoherent fashion about the future. The mother denies any hallucinations but states that her child has been brought into a 'very bad world'. What is the most appropriate management?

- A. Start fluoxetine
- B. Reassurance + review by health visitor
- C. Cognitive behavioural therapy
- D. Start lithium
- E. Arrange urgent admission

Question 30 of 50

A 31-year-old woman who gave birth two weeks ago presents for review with her husband. He is worried by her mood as she now seems depressed and is interacting poorly with the baby. He describes her mood three days ago being much different, when she was talking in a rapid and incoherent fashion about the future. The mother denies any hallucinations but states that her child has been brought into a 'very bad world'. What is the most appropriate management?

- A. Start fluoxetine
- B. Reassurance + review by health visitor
- C. Cognitive behavioural therapy
- D. Start lithium
- ✓ E. Arrange urgent admission

The mother may be suffering from puerperal psychosis and needs urgent admission to allow psychiatric evaluation

Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	**Postnatal depression**	**Puerperal psychosis**
Seen in around 60-70% of women Typically seen 3-7 days following birth and is more common in primips Mothers are characteristically anxious, tearful and irritable	Affects around 10% of women Most cases start within a month and typically peaks at 3 months Features are similar to depression seen in other circumstances	Affects approximately 0.2% of women Onset usually within the first 2-3 weeks following birth Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline may be used if symptoms are severe* - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required There is around a 20% risk of recurrence following future pregnancies

*fluoxetine is best avoided due to a long half-life

Question 31 of 50

A 42-year-old woman presents for review. Her husband reports that she has had an argument with their son which resulted in him leaving home. Since this happened she has not been able to speak. Clinical examination of her throat and chest is unremarkable. Which one of the following terms best describes this presentation?

- A. Aprosodia
- B. Schizophasia
- C. Expressive aphasia
- D. Akinetic mutism
- E. Psychogenic aphonia

Question 31 of 50

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- A. Aprosodia
- B. Schizophasia
- C. Expressive aphasia
- D. Akinetic mutism
- ✓ E. Psychogenic aphonia

Psychogenic aphonia is considered to be a form of conversion disorder. Please see the link for more details.

Aphonia

Aphonia describes the inability to speak. Causes include:

- recurrent laryngeal nerve palsy (e.g. Post-thyroidectomy)
- psychogenic

Question 32 of 50

A 36-year-old patient presents with nausea, headaches and palpitations. He has had multiple previous admissions with such symptoms over the past 2 years, each time no organic cause was found. What kind of disorder is this likely to represent?

- A. Munchausen's syndrome
- B. Hypochondrial disorder
- C. Somatisation disorder
- D. Conversion disorder
- E. Dissociative disorder

Question 32 of 50

A 36-year-old patient presents with nausea, headaches and palpitations. He has had multiple previous admissions with such symptoms over the past 2 years, each time no organic cause was found. What kind of disorder is this likely to represent?

- A. Munchausen's syndrome
- B. Hypochondrial disorder
- ✓ C. Somatisation disorder
- D. Conversion disorder
- E. Dissociative disorder

Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

Somatisation disorder
- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

Hypochondrial disorder
- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

Conversion disorder
- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

Dissociative disorder
- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

Munchausen's syndrome
- also known as factitious disorder
- the intentional production of physical or psychological symptoms

Malingering
- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

Question 33 of 50

A 35-year-old man with a history of schizophrenia is brought to the Emergency Department by worried friends due to drowsiness. On examination he is generally rigid. A diagnosis of neuroleptic malignant syndrome is suspected. Each one of the following is a feature of neuroleptic malignant syndrome, except:

- A. Renal failure
- B. Pyrexia
- C. Elevated creatine kinase
- D. Usually occurs after prolonged treatment
- E. Tachycardia

Question 33 of 50

A 35-year-old man with a history of schizophrenia is brought to the Emergency Department by worried friends due to drowsiness. On examination he is generally rigid. A diagnosis of neuroleptic malignant syndrome is suspected. Each one of the following is a feature of neuroleptic malignant syndrome, except:

- A. Renal failure
- B. Pyrexia
- C. Elevated creatine kinase
- ✓ D. Usually occurs after prolonged treatment
- E. Tachycardia

Neuroleptic malignant syndrome is typically seen in patients who have just commenced treatment. Renal failure may occur secondary to rhabdomyolysis

Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics

Features
- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

Management
- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene may be useful in selected cases

Question 34 of 50

The risk of developing schizophrenia if one monozygotic twin is affected is approximately:

- A. 10%
- B. 20%
- C. 50%
- D. 75%
- E. >95%

Question 34 of 50

The risk of developing schizophrenia if one monozygotic twin is affected is approximately:

- A. 10%
- B. 20%
- ✓ C. 50%
- D. 75%
- E. >95%

Schizophrenia: epidemiology

Risk of developing schizophrenia
- monozygotic twin has schizophrenia = 50%
- parent has schizophrenia = 10-15%
- sibling has schizophrenia = 10%
- no relatives with schizophrenia = 1%

Question 35 of 50

A patient with a history of depression presents for review. Which one of the following suggests an increased risk of suicide?

- A. Young age
- B. History of arm cutting
- C. Being married
- D. Female sex
- E. Having a busy job

Question 35 of 50

A patient with a history of depression presents for review. Which one of the following suggests an increased risk of suicide?

- A. Young age
- ✓ B. History of arm cutting
- C. Being married
- D. Female sex
- E. Having a busy job

Whilst arm cutting may sometimes be characterised as attention-seeking or 'releasing the pain' studies show that any history of deliberate self harm significantly increases the risk of suicide. Employment is a protective factor

Suicide

Factors associated with risk of suicide following an episode of deliberate self harm:

- efforts to avoid discovery
- planning
- leaving a written note
- final acts such as sorting out finances
- violent method

These are in addition to standard risk factors for suicide

- male sex
- advancing age
- unemployment or social isolation
- divorced or widowed
- history of mental illness (depression, schizophrenia)
- history of deliberate self harm
- alcohol or drug misuse

Question 36 of 50

A 64-year-old woman presents as she is feeling down and sleeping poorly. After speaking to the patient and using a validated symptom measure you decide she has moderate depression. She has a past history of cerebrovascular disease and currently takes aspirin, ramipril and simvastatin. What is the most appropriate couse of action?

- A. Stop aspirin, start citalopram
- B. Start venlafaxine
- C. Start citalopram + lansoprazole
- D. Stop aspirin, start clopidogrel + citalopram
- E. Start citalopram

Question 36 of 50

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- D. Stop aspirin, start clopidogrel + citalopram
- E. Start citalopram

SSRI + NSAID = GI bleeding risk - give a PPI

There is an increased incidence of gastrointestinal bleeding when aspirin / NSAIDs are combined with selective serotonin reuptake inhibitors. This patient should therefore also be offered a proton pump inhibitor such as lansoprazole. It would be inappropriate to stop aspirin in a patient with a history of cerebrovascular disease.

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 37 of 50

Which one of the following statements regarding cognitive behavioural therapy is incorrect?

- A. May be useful in the management of generalised anxiety disorder
- B. Can be used for patients already taking antidepressants
- C. Usually consists of one to two hour sessions once per week
- D. Should be completed within 6 months
- E. Patients usually get around 35-40 hours in total

Question 37 of 50

Which one of the following statements regarding cognitive behavioural therapy is incorrect?

- A. May be useful in the management of generalised anxiety disorder
- B. Can be used for patients already taking antidepressants
- C. Usually consists of one to two hour sessions once per week
- D. Should be completed within 6 months
- ✓ E. Patients usually get around 35-40 hours in total

Cognitive behavioural therapy

Main points

- useful in the management of depression and anxiety disorders
- usually consists of one to two hour sessions once per week
- should be completed within 6 months
- patients usually get around 16-20 hours in total

Question 38 of 50

Which one of the following intervention is most likely to be beneficial in a patient recently diagnosed with schizophrenia?

- A. Counselling
- B. Supportive psychotherapy
- C. Social skills training
- D. Adherence therapy
- E. Cognitive behavioural therapy

Question 38 of 50

Which one of the following intervention is most likely to be beneficial in a patient recently diagnosed with schizophrenia?

- A. Counselling
- B. Supportive psychotherapy
- C. Social skills training
- D. Adherence therapy
- ✓ E. Cognitive behavioural therapy

Schizophrenia: management

NICE published guidelines on the management of schizophrenia in 2009.

Key points:

- oral atypical antipsychotics are first-line
- cognitive behavioural therapy should be offered to all patients
- close attention should be paid to cardiovascular risk-factor modification due to the high rates of cardiovascular disease in schizophrenic patients (linked to antipsychotic medication and high smoking rates)

Question 39 of 50

A 43-year-old man with a history of schizophrenia is taken off chlorpromazine due to troublesome parkinsonian symptoms. Which one of the following atypical antipsychotic is it least suitable to commence as a first-line treatment?

- A. Quetiapine
- B. Amisulpride
- C. Olanzapine
- D. Risperidone
- E. Clozapine

Question 39 of 50

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- A. Quetiapine
- B. Amisulpride
- C. Olanzapine
- D. Risperidone
- ✓ E. Clozapine

Clozapine is no longer used first-line due to the risk of agranulocytosis

Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics
- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:
- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics
- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine
- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Question 40 of 50

A patient reports feeling unwell after suddenly stopping paroxetine. Which one of the following symptoms is most consistent with selective serotonin reuptake inhibitor discontinuation syndrome?

- A. Postural hypotension
- B. Diarrhoea
- C. Myoclonic jerks
- D. Hallucinations
- E. Seizures

Question 40 of 50

A patient reports feeling unwell after suddenly stopping paroxetine. Which one of the following symptoms is most consistent with selective serotonin reuptake inhibitor discontinuation syndrome?

- A. Postural hypotension
- ✓ B. Diarrhoea
- C. Myoclonic jerks
- D. Hallucinations
- E. Seizures

Selective serotonin reuptake inhibitor discontinuation syndrome can present with a wide variety of symptoms including diarrhoea, vomiting and abdominal pain.

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 41 of 50

A 69-year-old man is diagnosed as having Parkinson's disease. Which one of the following psychiatric problems is most likely to occur in this patient?

- A. Tics
- B. Psychosis
- C. Mania
- D. Dementia
- E. Depression

Question 41 of 50

A 69-year-old man is diagnosed as having Parkinson's disease. Which one of the following psychiatric problems is most likely to occur in this patient?

- A. Tics
- B. Psychosis
- C. Mania
- D. Dementia
- ✓ E. Depression

Parkinson's disease - most common psychiatric problem is depression

Whilst dementia is common in patients with Parkinson's disease depression is known to exist in around 40%

Parkinson's disease: features

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

Bradykinesia
- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

Tremor
- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

Rigidity
- lead pipe
- cogwheel: due to superimposed tremor

Other characteristic features
- flexed posture
- short, shuffling steps
- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur

Drug-induced parkinsonism has slightly different features to Parkinson's disease:
- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

Question 42 of 50

A 34-year-old ex-soldier with a history of post-traumatic stress disorder returns for review. He has had a course of eye movement desensitisation and reprocessing therapy which was not helpful and is reluctant to try cognitive behavioural therapy. Of the options listed, which medication may be useful in such patients?

- A. Fluoxetine
- B. Citalopram
- C. Mirtazapine
- D. Topiramate
- E. Bupropion

Question 42 of 50

A 34-year-old ex-soldier with a history of post-traumatic stress disorder returns for review. He has had a course of eye movement desensitisation and reprocessing therapy which was not helpful and is reluctant to try cognitive behavioural therapy. Of the options listed, which medication may be useful in such patients?

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Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached from other people
- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended

Question 43 of 50

Which one of the following selective serotonin reuptake inhibitors has the highest incidence of discontinuation symptoms?

- A. Paroxetine
- B. Citalopram
- C. Escitalopram
- D. Fluoxetine
- E. Sertraline

Question 43 of 50

Which one of the following selective serotonin reuptake inhibitors has the highest incidence of discontinuation symptoms?

- ✓ A. Paroxetine
- B. Citalopram
- C. Escitalopram
- D. Fluoxetine
- E. Sertraline

Paroxetine - higher incidence of discontinuation symptoms

Depression: selective serotonin reuptake inhibitors

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Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 44 of 50

Which one of the following is least recognised as a potential adverse effect of electroconvulsive therapy?

- A. Shoulder dislocations
- B. Epilepsy
- C. Cardiac arrhythmias
- D. Short term memory impairment
- E. Headache

Question 44 of 50

Which one of the following is least recognised as a potential adverse effect of electroconvulsive therapy?

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- ✓ B. Epilepsy
- C. Cardiac arrhythmias
- D. Short term memory impairment
- E. Headache

Although electroconvulsive therapy, by definition, causes a controlled seizure there is no increased risk of epilepsy in the long-term.

Electroconvulsive therapy

Electroconvulsive therapy is a useful treatment option for patients with severe depression refractory to medication or those with psychotic symptoms. The only absolute contraindications is raised intracranial pressure.

Short-term side-effects
- headache
- short term memory impairment
- memory loss of events prior to ECT
- cardiac arrhythmia
- physical complications: fractures, dislocations etc

Long-term side-effects
- some patients report impaired memory

Question 45 of 50

A 24-year-old man is brought to the Emergency Department by his brother who is concerned about his odd behaviour. Over the past two weeks he has started to tell his brother that he can hear people talking about him on the radio. He denies any auditory hallucinations. During the consultation he scores 10/10 on the mini-mental state examination. When asked to explain the meaning of the statement 'people in glass houses shouldn't throw stones' he replies 'you make break the glass'. What is this an example of?

- A. Depression
- B. Autistic thinking
- C. Concrete thinking
- D. Delusional disorder
- E. Acute mania

Question 45 of 50

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- A. Depression
- B. Autistic thinking
- ✓ C. Concrete thinking
- D. Delusional disorder
- E. Acute mania

This is an example of concrete thinking where a patient cannot use abstraction to understand the meaning of a sentence. It is more common in schizophrenia. Literal thinking is of course a feature of autism but this would not explain his delusional perception and is unlikely to present in a sub-acute fashion at this age

Schizophrenia: features

Schneider's first rank symptoms may be divided into auditory hallucinations, thought disorders, passivity phenomena and delusional perceptions:

Auditory hallucinations of a specific type:
- two or more voices discussing the patient in the third person
- thought echo
- voices commenting on the patient's behaviour

Thought disorder*:
- thought insertion
- thought withdrawal
- thought broadcasting

Passivity phenomena:
- bodily sensations being controlled by external influence
- actions/impulses/feelings - experiences which are imposed on the individual or influenced by others

Delusional perceptions
- a two stage process) where first a normal object is perceived then secondly there is a sudden intense delusional insight into the objects meaning for the patient e.g. 'The traffic light is green therefore I am the King'.

Other features of schizophrenia include
- impaired insight
- incongruity/blunting of affect (inappropriate emotion for circumstances)
- decreased speech
- neologisms: made-up words
- catatonia
- negative symptoms: incongruity/blunting of affect, anhedonia (inability to derive pleasure), alogia (poverty of speech), avolition (poor motivation)

*occasionally referred to as thought alienation

Question 46 of 50

A 16-year-old girl is brought for review by her father. She is talented violinist and is due to start music college in a few weeks time. Her parents are concerned she has had a stroke as she is reporting weakness on her right side. Neurological examination is inconsistent and you suspect a non-organic cause for her symptoms. Despite reassurance about the normal examination findings the girl remains unable to move her right arm. What is the most appropriate term for this behaviour?

- A. Hypochondrial disorder
- B. Munchausen's syndrome
- C. Somatisation disorder
- D. Conversion disorder
- E. Munchausen's-by-proxy syndrome

Question 46 of 50

A 16-year-old girl is brought for review by her father. She is talented violinist and is due to start music college in a few weeks time. Her parents are concerned she has had a stroke as she is reporting weakness on her right side. Neurological examination is inconsistent and you suspect a non-organic cause for her symptoms. Despite reassurance about the normal examination findings the girl remains unable to move her right arm. What is the most appropriate term for this behaviour?

- A. Hypochondrial disorder
- B. Munchausen's syndrome
- C. Somatisation disorder
- ✓ D. Conversion disorder
- E. Munchausen's-by-proxy syndrome

This is a typical conversion disorder. There may be underlying tension regarding her musical career which be manifesting itself as apparent limb weakness.

Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

Somatisation disorder
- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

Hypochondrial disorder
- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

Conversion disorder
- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

Dissociative disorder
- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

Munchausen's syndrome
- also known as factitious disorder
- the intentional production of physical or psychological symptoms

Malingering
- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

Question 47 of 50

Which of the following types of tricyclic antidepressant is considered the safest in overdosage?

- A. Nortriptyline
- B. Imipramine
- C. Dosulepin
- D. Lofepramine
- E. Clomipramine

Question 47 of 50

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- C. Dosulepin
- ✓ D. Lofepramine
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Lofepramine - the safest TCA in overdosage

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose.They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

Common side-effects

- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

Choice of tricyclic

- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) and considered the most dangerous in overdose

More sedative	Less sedative
Amitriptline Clomipramine Dosulepine Trazadone	Imipramine Lofepramine Nortriptyline

Question 48 of 50

You are considering prescribing a selective serotonin reuptake inhibitor for a patient with depression. Which class of drug is most likely to interact with a selective serotonin reuptake inhibitor?

- A. Beta-blocker
- B. Thiazolidinediones
- C. Tetracycline
- D. Statin
- E. Triptan

Question 48 of 50

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Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first-line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressant

Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline and more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', buf if given coprescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paresthesia

Question 49 of 50

Which class of drug have the Medicines and Healthcare products Regulatory Agency warned may be associated with an increased risk of venous thromboembolism in elderly patients?

- A. Tricyclic antidepressants
- B. 5HT3 antagonists
- C. Third generation cephalosporins
- D. Benzodiazepines
- E. Atypical antipsychotics

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Antipsychotics in the elderly - increased risk of stroke and VTE

Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

Extrapyramidal side-effects
- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:
- increased risk of stroke
- increased risk of venous thromboembolism

Other side-effects
- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

Question 50 of 50

A 46-year-old man is seen by an occupation health doctor due to long-term sickness leave. He states chronic lower back pain prevents him from working but examination findings are inconsistent and the doctor suspects a non-organic cause of his symptoms. This is an example of a:

- A. Conversion disorder
- B. Munchausen's syndrome
- C. Malingering
- D. Hypochondrial disorder
- E. Somatisation disorder

Question 50 of 50

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- D. Hypochondrial disorder
- E. Somatisation disorder

Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

Somatisation disorder
- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

Hypochondrial disorder
- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

Conversion disorder
- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

Dissociative disorder
- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

Munchausen's syndrome
- also known as factitious disorder
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Malingering
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Question 1 of 220

A 62-year-old is started on allopurinol prophylaxis following his second episode of gout in the past 12 months. What is the mechanism of action of allopurinol?

- A. Promotes excretion of uric acid
- B. Causes the depolymerisation of intracellular microtubules
- C. Uric acid chelator
- D. Inhibits xanthine oxidase
- E. Xanthine oxidase activator

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Allopurinol inhibits xanthine oxidase

Xanthine oxidase is responsible for the oxidation of 6-mercaptopurine to 6-thiouric acid

Allopurinol

Allopurinol is used in the prevention of gout. It works by inhibiting xanthine oxidase

Initiating allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Interactions

Azathioprine
- metabolised to active compound 6-mercaptopurine
- xanthine oxidase is responsible for the oxidation of 6-mercaptopurine to 6-thiouric acid
- allopurinol can therefore lead to high levels of 6-mercaptopurine
- a much reduced dose (e.g. 25%) must therefore be used if the combination cannot be avoided

Cyclophosphamide
- allopurinol reduces renal clearance, therefore may cause marrow toxicity

Question 2 of 220

A 45-year-old man with a history of epilepsy and psychiatric problems is admitted to the Emergency Department with confusion following a seizure earlier in the day. On examination he is noted to have a coarse tremor, blood pressure is 134/86 mmHg, pulse is 84/min and the temperature is 36.7ºC. What is the most likely diagnosis?

- A. Carbamazepine overdose
- B. Lithium toxicity
- C. Benzodiazepine toxicity
- D. Tricyclic overdose
- E. Neuroleptic malignant syndrome

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Lithium: fine tremor in chronic treatment, coarse tremor in acute toxicity

A tricyclic overdose may present with seizures but it does not typical cause a tremor

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:
- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects
- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 3 of 220

A 44-year-old Bangladeshi man with a history of mitral stenosis and atrial fibrillation is diagnosed with tuberculosis. He is commenced on anti-tuberculosis therapy. Three weeks after starting treatment his INR has increased to 5.6. Which one of the following medications is most likely to be responsible for this increase?

- A. Pyrazinamide
- B. Isoniazid
- C. Rifampicin
- D. Ethambutol
- E. Streptomycin

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- D. Ethambutol
- E. Streptomycin

Isoniazid **inhibits** the P450 system

It is important when answering questions relating to liver enzymes to be sure whether the question is asking about induction or inhibition. Drugs causing induction are often well known and *Candida*tes may rush to give these as the answer. A raised INR is a result of **inhibited** liver enzymes

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 4 of 220

A patient develops a broad complex tachycardia two days following a myocardial infarction. Intravenous amiodarone is given. Which one of the following best describes the mechanism of action of amiodarone?

- A. Blocks potassium channels
- B. Shortens QT interval
- C. Blocks sodium channels
- D. Opens sodium channels
- E. Blocks calcium channels

Question 4 of 220

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Amiodarone - MOA: blocks potassium channels

Amiodarone

Amiodarone is a class III antiarrhythmic agent used in the treatment of both atrial and ventricular tachycardias. The main mechanism of action is by blocking potassium channels which inhibits repolarisation and hence prolongs the action potential. Amiodarone also has other actions such as blocking sodium channels (a class I effect)

The use of amiodarone is limited by a number of factors

- long half-life (20-100 days)
- should ideally be given into central veins (causes thrombophlebitis)
- has proarrhythmic effects due to lengthening of the QT interval
- interacts with drugs commonly used concurrently e.g. decreases metabolism of warfarin
- numerous long-term adverse effects (see below)

Adverse effects of amiodarone use

- thyroid dysfunction
- corneal deposits
- pulmonary fibrosis/pneumonitis
- liver fibrosis/hepatitis
- peripheral neuropathy, myopathy
- photosensitivity
- 'slate-grey' appearance

Question 5 of 220

Which one of the following immunosuppressant drugs inhibits calcineurin in T cells?

- A. Mycophenolate mofetil
- B. Basiliximab
- C. Azathioprine
- D. Ciclosporin
- E. Methotrexate

Question 5 of 220

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- ✓ D. Ciclosporin
- E. Methotrexate

Ciclosporin + tacrolimus - MOA: inhibit calcineurin thus decreasing IL-2

Mycophenolate mofetil inhibits inosine monophosphate dehydrogenase. Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits DNA synthesis. Methotrexate is an antimetabolite which inhibits dihydrofolate reductase

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin
- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications
- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 6 of 220

Which one of the following statements regarding metformin is true?

- A. Should be stopped in a patient admitted with a myocardial infarction
- B. Hypoglycaemia is a recognised adverse effect
- C. May cause a metabolic alkalosis
- D. May aggravate necrobiosis lipoidica diabeticorum
- E. Increases vitamin B12 absorption

Question 6 of 220

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- D. May aggravate necrobiosis lipoidica diabeticorum
- E. Increases vitamin B12 absorption

Metformin should be stopped following a myocardial infarction due to the risk of lactic acidosis. It may be introduced at a later date. Diabetic control may be achieved through the use of a insulin/dextrose infusion (e.g. the DIGAMI regime)

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action
- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects
- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis* with severe liver disease or renal failure

Contraindications**
- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 7 of 220

A 67-year-old man with lung cancer is currently taking MST 30mg bd for pain relief. What dose of oral morphine solution should he be prescribed for breakthrough pain?

- A. 5 mg
- B. 10 mg
- C. 15 mg
- D. 20 mg
- E. 30 mg

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- D. 20 mg
- E. 30 mg

Breakthrough dose = 1/6th of daily morphine dose

The total daily morphine dose is 30 * 2 = 60 mg, therefore the breakthrough dose should be one-sixth of this, 10 mg

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 8 of 220

What is the main mechanism of action of simvastatin?

- A. Bile acid sequestrant
- B. Decreases hepatic HDL synthesis
- C. Inhibits lipoprotein lipase
- D. Decreases intrinsic cholesterol synthesis
- E. Agonists of PPAR-alpha

Question 8 of 220

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Statins inhibit HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 9 of 220

A 56-year-old man with a history of epilepsy, atrial fibrillation and ischaemic heart disease is noted to have a rash on his forearms and face in the cardiology clinic. Which one of the following drugs is most likely to be responsible?

- A. Verapamil
- B. Carbamazepine
- C. Amiodarone
- D. Digoxin
- E. Clopidogrel

Question 9 of 220

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- ✓ C. Amiodarone
- D. Digoxin
- E. Clopidogrel

A rash on the forearms and face is typical of a photosensitivity rash

Drugs causing photosensitivity

Causes of drug-induced photosensitivity

- thiazides
- tetracyclines, sulphonamides, ciprofloxacin
- amiodarone
- NSAIDs e.g. piroxicam
- psoralens
- sulphonylureas

Question 10 of 220

A 65-year-old female is admitted to the Emergency Department following an overdose of a long-acting propranolol preparation. On admission she is bradycardic with a pulse of 36/min and BP 90/50. The bradycardia fails to respond to atropine. What is the most appropriate management?

- A. Temporary cardiac pacing
- B. Haemodialysis
- C. Glucagon
- D. Noradrenaline infusion
- E. Salbutamol infusion

Question 10 of 220

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Beta-blocker overdose management: atropine + glucagon

Glucagon has a positive inotropic action on the heart and decreases renal vascular resistance. It is therefore useful in patients with beta-blocker cardiotoxicity
Cardiac pacing should be reserved for patients unresponsive to pharmacological therapy

Beta-blocker overdose

Features
- bradycardia
- hypotension
- heart failure
- syncope

Management
- if bradycardic then atropine
- in resistant cases glucagon may be used

Haemodialysis is not effective in beta-blocker overdose

Question 11 of 220

A 69-year-old man is started on tamsulosin for benign prostatic hyperplasia. Which one of the following best describes the side-effects he may experience?

- A. Urgency + insomnia
- B. Dizziness + postural hypotension
- C. Urinary retention + nausea
- D. Urgency + erectile dysfunction
- E. Erectile dysfunction + reduced libido

Question 11 of 220

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Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

Risk factors
- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:
- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

Management options
- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin
- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride
- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

Question 12 of 220

Which one of the following drugs may be cleared by haemodialysis?

- A. Beta-blockers
- B. Tricyclics
- C. Aspirin
- D. Benzodiazepines
- E. Digoxin

Question 12 of 220

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- E. Digoxin

Haemodialysis in overdose

Drugs that can be cleared with haemodialysis - mnemonic: BLAST
- Barbiturate
- Lithium
- Alcohol (inc methanol, ethylene glycol)
- Salicylates
- Theophyllines (charcoal haemoperfusion is preferable)

Drugs which cannot be cleared with haemodialysis include
- tricyclics
- benzodiazepines
- dextropropoxyphene (Co-proxamol)
- digoxin
- beta-blockers

Question 13 of 220

A 78-year-old women is discharged following a fractured neck of femur. On review she is making good progress but consideration is given to secondary prevention of further fractures. What is the most suitable management?

- A. Arrange DEXA scan + start strontium ranelate if T-score < -2.5 SD
- B. Start oral bisphosphonate
- C. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.0 SD
- D. Arrange DEXA scan + start hormone replacement therapy if T-score < -2.5 SD
- E. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.5 SD

Question 13 of 220

A 78-year-old women is discharged following a fractured neck of femur. On review she is making good progress but consideration is given to secondary prevention of further fractures. What is the most suitable management?

- A. Arrange DEXA scan + start strontium ranelate if T-score < -2.5 SD
- ✓ B. Start oral bisphosphonate
- C. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.0 SD
- D. Arrange DEXA scan + start hormone replacement therapy if T-score < -2.5 SD
- E. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.5 SD

NICE guidelines support starting bisphosphonates without waiting for a DEXA scan in such scenarios

Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of – 2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risedronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

Risk factors (for use in the tables below)

- parental history of hip fracture
- alcohol intake of 4 or more units
- rheumatoid arthritis

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50–54	Not indicated	– 3.0	– 2.5
55–59	– 3.0	– 3.0	– 2.5
60–64	– 3.0	– 3.0	– 2.5
65–69	– 3.0	– 2.5	– 2.5
70 or older	– 2.5	– 2.5	– 2.5

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50–54	Not indicated	– 3.5	– 3.5
55–59	– 4.0	– 3.5	– 3.5
60–64	– 4.0	– 3.5	– 3.5
65–69	– 4.0	– 3.5	– 3.0
70–74	– 3.0	– 3.0	– 2.5
75 or older	– 3.0	– 2.5	– 2.5

Supplementary notes on treatment

Bisphosphonates

- alendronate, risedronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risedronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts and reduces the resorption of bone by osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients

Question 14 of 220

A 62-year-old man is commenced on finasteride for symptoms of bladder outflow obstruction. Which one of the following adverse effects is most associated with this treatment?

- A. Alopecia
- B. Gynaecomastia
- C. Prostate cancer
- D. Increased levels of serum prostate specific antigen
- E. Postural hypotension

Question 14 of 220

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Finasteride

Finasteride is an inhibitor of 5 alpha-reductase, an enzyme which metabolises testosterone into dihydrotestosterone

Indications
- benign prostatic hyperplasia
- male-pattern baldness

Adverse effects
- impotence
- decrease libido
- ejaculation disorders
- gynaecomastia and breast tenderness

Finasteride causes decreased levels of serum prostate specific antigen

Question 15 of 220

Which one of the following statements regarding statin-induced myopathy is incorrect?

- A. Rhabdomyolysis may cause renal failure
- B. Patients with an elevated creatine kinase often have no symptoms
- C. Female sex is a risk factor
- D. Creatine kinase does not need to be routinely checked prior to commencing a statin
- E. Pravastatin is more likely to cause myopathy than simvastatin

Question 15 of 220

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- D. Creatine kinase does not need to be routinely checked prior to commencing a statin
- ✓ E. Pravastatin is more likely to cause myopathy than simvastatin

Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 16 of 220

A 54-year-old patient takes hydrocortisone 20mg in the mornings and 5mg at night for Addison's disease. The endocrinology consultant would like her to take prednisolone instead. What dose of prednisolone should be started?

- A. 5 mg
- B. 6 mg
- C. 7 mg
- D. 10 mg
- E. 25 mg

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1mg prednisolone = 4mg hydrocortisone

As 1mg prednisolone equals 4mg hydrocortisone then the actual equivalent daily dose is 6.25mg. This was not given as an option in the exam. It would therefore be better to err on the side of caution and over replace steroid initially to avoid the potential risk of hypoadrenalism

Steroid doses

Equivalence

- 1mg prednisolone = 4mg hydrocortisone
- 1mg dexamethasone = 7mg prednisolone

Question 17 of 220

A 41-year-old woman is admitted following a deliberate overdose of ethylene glycol. She is confused and unable to give any further history. On examination the pulse is 96 / min, blood pressure is 142/84 mmHg and temperature 37.1ºC. Blood tests show:

Na^+	139 mmol/l
K^+	4.0 mmol/l
Chloride	104 mmol/l
Bicarbonate	26 mmol/l
Urea	4.0 mmol/l
Creatinine	88 µmol/l

What is the most appropriate management of this patient?

- A. Ethanol
- B. Fomepizole
- C. Haemodialysis
- D. Haemofiltration
- E. Dantrolene

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Ethylene glycol toxicity management - fomepizole. Also ethanol / haemodialysis

Fomepizole is now used first-line rather than ethanol in ethylene glycol toxicity. There is no indication for haemodialysis at this stage, as a metabolic acidosis has not yet developed

Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

Question 18 of 220

A 19-year-old student is admitted after being found friends confused and sweating in her room. She is unable to give a history. On examination temperature is 38.1ºC, pulse 108/min, BP 130/70 mmHg and respiratory rate 30/min. Heart sounds are normal but she has bibasal fine inspiratory crackles on her chest.

ABGs on air:
pH 7.28
pCO2 2.8 kPa
pO2 14.2 kPa

What is the most likely diagnosis?

- A. Paracetamol overdose
- B. Acute pancreatitis
- C. Mycoplasma septicaemia
- D. Legionella pneumonia
- E. Aspirin overdose

Question 18 of 220

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- C. Mycoplasma septicaemia
- D. Legionella pneumonia
- ✓ E. Aspirin overdose

The mixed respiratory alkalosis and metabolic acidosis in a sweaty, confused patient point towards salicylate overdose. The development of pulmonary oedema suggests severe poisoning and is an indication for haemodialysis

Salicylate overdose

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

Features
- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

Treatment
- general (ABC, charcoal)
- urinary alkalinization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

Indications for haemodialysis in salicylate overdose
- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure
- pulmonary oedema
- seizures
- coma

*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production

Question 19 of 220

A patient is started on cyclophosphamide for vasculitis associated with Wegener's granulomatosis. Which of the following is most characteristically associated with cyclophosphamide?

- A. Haemorrhagic cystitis
- B. Cardiomyopathy
- C. Ototoxicity
- D. Alopecia
- E. Weight gain

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 20 of 220

A 61-year-old man develops aortic regurgitation after taking medication for Parkinson's disease. Which one of the following medications is he most likely to have taken?

- A. Pergolide
- B. Cabergoline
- C. Selegiline
- D. Ropinirole
- E. Amantadine

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Pergolide is particularly associated with valvular dysfunction.

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 21 of 220

A 41-year-old woman is investigated for hot flushes and night sweats. Bloods show a significantly raised FSH level and her symptoms are attributed to the menopause. Following discussions with the patient she elects to have hormone replacement treatment. What is the most significant risk of failing to prescribe a combined oestrogen-progestogen preparation rather than an oestrogen-only preparation?

- A. Increased risk of venous thromboembolism
- B. Increased risk of ovarian cancer
- C. Increased risk of endometrial canceri
- D. Increased risk of breast cancer
- E. Increased risk of colorectal cancer

Question 21 of 220

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- ✓ C. Increased risk of endometrial cancer
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- E. Increased risk of colorectal cancer

HRT: unopposed oestrogen increases risk of endometrial cancer

Hormone replacement therapy: adverse effects

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen (combined with a progestogen in women with a uterus) to help alleviate menopausal symptoms.

Side-effects
- nausea
- breast tenderness
- fluid retention and weight gain

Potential complications
- increased risk of breast cancer: increased by the addition of a progestogen
- increased risk of endometrial cancer: reduced by the addition of a progestogen but not eliminated completely. The BNF states that the additional risk is eliminated if a progestogen is given continuously
- increased risk of venous thromboembolism: increased by the addition of a progestogen

Breast cancer
- in the Women's Health Initiative (WHI) study there was a relative risk of 1.26 at 5 years of developing breast cancer
- the increased risk relates to duration of use
- breast cancer incidence is higher in women using combined preparations compared to oestrogen-only preparations
- the risk of breast cancer begins to decline when HRT is stopped and by 5 years it reaches the same level as in women who have never taken HRT

Question 22 of 220

A 72-year-old female known to have osteoporosis is started on alendronate. Which one of the following side-effects is it most important to warn her about?

- A. Sore throat
- B. Heartburni
- C. Headache
- D. Diarrhoea
- E. Palpitations

Question 22 of 220

A 72-year-old female known to have osteoporosis is started on alendronate. Which one of the following side-effects is it most important to warn her about?

- A. Sore throat
- ✓ B. Heartburn
- C. Headache
- D. Diarrhoea
- E. Palpitations

Bisphosphonates can cause a variety of oesophageal problems

Whilst the development of any new problem following the introduction of a new drug warrants medical review it is particularly important to warn patients starting bisphosphonates about symptoms which could suggest an oesophageal reaction, especially with alendronate

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses
- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metatases

Adverse effects
- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw

The BNF suggests the following counselling for patients taking oral bisphosphonates
- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

Question 23 of 220

A 70-year-old man who takes warfarin for atrial fibrillation is found to have an INR of 6.2. Which of the following drugs is he most likely to have recently taken?

- A. Ciprofloxacin
- B. Flucloxacillin
- C. St John's Wort
- D. Carbamazepine
- E. Aspirin

Question 23 of 220

A 70-year-old man who takes warfarin for atrial fibrillation is found to have an INR of 6.2. Which of the following drugs is he most likely to have recently taken?

- ✓ A. Ciprofloxacin
- B. Flucloxacillin
- C. St John's Wort
- D. Carbamazepine
- E. Aspirin

Ciprofloxacin is a known inhibitor of the P450 system and hence may cause an increase in INR.

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 24 of 220

Where is the site of action of furosemide?

- A. Proximal collecting duct
- B. Ascending loop of Henle
- C. Descending loop of Henle
- D. Distal collecting duct
- E. Macula densa

Question 24 of 220

Where is the site of action of furosemide?

- A. Proximal collecting duct
- ✓ B. Ascending loop of Henle
- C. Descending loop of Henle
- D. Distal collecting duct
- E. Macula densa

Furosemide

Furosemide (previously called frusemide) is a loop diuretic that acts by inhibiting chloride absorption in the ascending limb of the loop of Henle

Adverse effects

- hyponatraemia
- hypokalaemia
- hypochloraemic alkalosis
- ototoxicity
- renal impairment (from dehydration + direct toxic effect)

Question 25 of 220

A 25-year-old female who works in a photograph development laboratory is taken to the Emergency Department due to confusion. On admission she is hypoxic and hypotensive. Cyanide poisoning is suspected following discussion with the local poisons unit. What is the definitive treatment?

- A. Haemodialysis
- B. Dicobalt edetate
- C. Penicillamine
- D. Ferrous sulphate
- E. Desferioxamine

Question 25 of 220

A 25-year-old female who works in a photograph development laboratory is taken to the Emergency Department due to confusion. On admission she is hypoxic and hypotensive. Cyanide poisoning is suspected following discussion with the local poisons unit. What is the definitive treatment?

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- C. Penicillamine
- D. Ferrous sulphate
- E. Desferioxamine

Cyanide poisoning

Cyanide may be used in insecticides, photograph development and the production of certain metals. Toxicity results from reversible inhibition of cellular oxidising enzymes

Presentation
- 'classical' features: brick-red skin, smell of bitter almonds
- acute: hypoxia, hypotension, headache, confusion
- chronic: ataxia, peripheral neuropathy, dermatitis

Management
- supportive measures: 100% oxygen
- definitive: IV dicobalt edetate

Question 26 of 220

A 62-year-old man with a history of hypertension and epilepsy is noted to have gingival hyperplasia on examination in the cardiology clinic. Which one of the following drugs is most likely to be responsible?

- A. Sodium valproate
- B. Lisinopril
- C. Atorvastatin
- D. Nifedipine
- E. Carbamazepine

Question 26 of 220

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- B. Lisinopril
- C. Atorvastatin
- ✓ D. Nifedipine
- E. Carbamazepine

Gingival hyperplasia: phenytoin, ciclosporin, calcium channel blockers and AML

Gingival hyperplasia

Drug causes of gingival hyperplasia
- phenytoin
- ciclosporin
- calcium channel blockers (especially nifedipine)

Other causes of gingival hyperplasia include
- acute myeloid leukaemia (myelomonocytic and monocytic types)

Question 27 of 220

A 45-year-old man with a history of depression and gastro-oesophageal reflux disease presents due to a milky discharge from his nipples. The following blood results are obtained:

Prolactin 700 mu/l

Which one of his medications is most likely to be responsible?

- A. Omeprazole
- B. Fluoxetine
- C. Metoclopramide
- D. Cimetidine
- E. Amitriptyline

Question 27 of 220

A 45-year-old man with a history of depression and gastro-oesophageal reflux disease presents due to a milky discharge from his nipples. The following blood results are obtained:
Prolactin 700 mu/l

Which one of his medications is most likely to be responsible?

- A. Omeprazole
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- ✓ C. Metoclopramide
- D. Cimetidine
- E. Amitriptyline

Causes of raised **p**rolactin - the **p**'s
- **p**regnancy
- **p**rolactinoma
- **p**hysiological
- **p**olycystic ovarian syndrome
- **p**rimary hypothyroidism
- **p**henothiazines, metoclo**p**ramide, dom**p**eridone

Selective serotonin reuptake inhibitors such as fluoxetine have rarely been associated with hyperprolactinaemia but the most likely cause in this patient is metoclopramide. Cimetidine is associated with gynaecomastia, rather than galactorrhoea

Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin
- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin
- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin
- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

Question 28 of 220

Which one of the following side-effects is least recognised in patients taking ciclosporin?

- A. Hypokalaemia
- B. Hyperplasia of the gum
- C. Hypertension
- D. Tremor
- E. Excessive hair growth

Question 28 of 220

Which one of the following side-effects is least recognised in patients taking ciclosporin?

- ✓ A. Hypokalaemia
- B. Hyperplasia of the gum
- C. Hypertension
- D. Tremor
- E. Excessive hair growth

Hyperkalaemia rather than hypokalaemia is seen with ciclosporin use

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications

- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 29 of 220

Which one of the following types of reaction takes place in phase II metabolism of a drug?

- A. Conjugation
- B. Hydrolysis
- C. Reduction
- D. Deamination
- E. Dealkylation

Question 29 of 220

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Drug metabolism
- phase I: oxidation, reduction, hydrolysis
- phase II: conjugation

Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are need orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil

Questions concerning zero-order kinetics and acetylator status are also common in the MRCP

Zero-order kinetics

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

Acetylator status

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Question 30 of 220

A 54-year-old man with a history of hypertension comes for review. He currently takes lisinopril 10mg od, simvastatin 40mg on and aspirin 75mg od. His blood pressure is well controlled at 124/76 mmHg but he also mentions that he is due to have a tooth extraction next week. What advice should be given with regards to his aspirin use?

- A. Take aspirin as normal but take tranexamic 1g tds acid 24 hours before and after procedure
- B. Stop 72 hours before, restart 24 hours after procedure
- C. Stop 24 hours before, restart 12 hours after procedure
- D. Take aspirin as normal
- E. Stop 48 hours before, restart 24 hours after procedure

Question 30 of 220

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- C. Stop 24 hours before, restart 12 hours after procedure
- ✓ D. Take aspirin as normal
- E. Stop 48 hours before, restart 24 hours after procedure

In the BNF section 'Prescribing in dental practice' it advises that patients in this situation should continue taking anti-platelets as normal

Aspirin

Aspirin works by blocking the action of both cyclooxygenase-1 and 2.

Who should receive aspirin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- all people aged 50 years and over with a 10-year cardiovascular risk = 20%
- all people with diabetes mellitus (type 1 or 2) who are = 50 years old or who have: diabetes > 10 years, taking treatment for hypertension or evidence of target organ damage
- all people with target organ damage from hypertension

Potentiates

- oral hypoglycaemics
- warfarin
- steroids

Question 31 of 220

A 47-year-old man is reviewed in the smoking cessation clinic. Which one of the following conditions would contraindicate the prescription of bupropion?

- A. History of supraventricular tachycardia
- B. Previous episodes of acute pancreatitis
- C. Epilepsy
- D. Depression
- E. Hypertension

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- D. Depression
- E. Hypertension

Bupropion: contraindicated in epilepsy

Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Question 32 of 220

A patient known to have bipolar disorder presents to the Emergency Department with confusion. Which one of the following drugs is most likely to precipitate lithium toxicity?

- A. Frusemide
- B. Sodium valproate
- C. Digoxin
- D. Sodium bicarbonate
- E. Bendroflumethiazide

Question 32 of 220

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The BNF states that 'loop diuretics are safer than thiazides' in the interactions section.

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:
- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects
- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 33 of 220

A 35-year-old man with a known history of peanut allergy is admitted to the Emergency Department with a swollen face. On examination blood pressure is 85/60 mmHg, pulse 120 bpm and there is a bilateral expiratory wheeze. What is the most appropriate form of adrenaline to give?

- A. 10ml 1:10,000 IV
- B. 0.5ml 1:1,000 IMi
- C. 0.5ml 1:10,000 IM
- D. 5ml 1:1,000 IM
- E. Nebulised adrenaline

Question 33 of 220

A 35-year-old man with a known history of peanut allergy is admitted to the Emergency Department with a swollen face. On examination blood pressure is 85/60 mmHg, pulse 120 bpm and there is a bilateral expiratory wheeze. What is the most appropriate form of adrenaline to give?

- A. 10ml 1:10,000 IV
- ✓ B. 0.5ml 1:1,000 IM
- C. 0.5ml 1:10,000 IM
- D. 5ml 1:1,000 IM
- E. Nebulised adrenaline

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications
- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection
- local infiltration of phentolamine

Question 34 of 220

What is the mechanism of action of flecainide?

- A. Calcium channel blockers
- B. Potassium channel blocker
- C. Sodium channel blockeria
- D. Potassium channel activator
- E. ADP receptor antagonist

Question 34 of 220

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Flecainide

Flecainide is a Vaughan Williams class 1c antiarrhythmic. It slows conduction of the action potential by acting as a potent sodium channel blocker. This may be reflected by widening of the QRS complex and prolongation of the PR interval

The Cardiac Arrhythmia Suppression Trial (CAST, 1989) investigated the use of agents to treat asymptomatic or mildly symptomatic premature ventricular complexes (PVCs) post myocardial infarction. The hypothesis was that this would reduce deaths from ventricular arrhythmias. Flecainide was actually shown to increase mortality post myocardial infarction and is therefore contraindicated in this situation

Indications
- atrial fibrillation
- SVT associated with accessory pathway e.g. Wolf-Parkinson-White syndrome

Adverse effects
- negatively inotropic
- bradycardia
- proarrhythmic
- oral paraesthesia
- visual disturbances

Question 35 of 220

Which one of the following is not an indication for haemodialysis in salicylate overdose?

- A. Acute renal failure
- B. Seizures
- C. Serum concentration = 400 mg/l
- D. Pulmonary oedema
- E. Metabolic acidosis resistant to treatment

Question 35 of 220

Which one of the following is not an indication for haemodialysis in salicylate overdose?

- A. Acute renal failure
- B. Seizures
- ✓ C. Serum concentration = 400 mg/l
- D. Pulmonary oedema
- E. Metabolic acidosis resistant to treatment

A serum concentration of greater than 700mg/l is an indication for haemodialysis

Salicylate overdose

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

Features
- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

Treatment
- general (ABC, charcoal)
- urinary alkalinization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

Indications for haemodialysis in salicylate overdose
- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure
- pulmonary oedema
- seizures
- coma

*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production

Question 36 of 220

A 78-year-old woman with a history of recurrent ventricular tachycardia has routine blood tests 3 months after starting amiodarone therapy:

TSH 14.5 mu/l

Free T4 8.2 pmol/l

How should her thyroid dysfunction be managed?

- A. Continue amiodarone and add folic acid
- B. Stop amiodarone and start thyroxine
- C. Stop amiodarone and add carbimazole and thyroxine
- D. Stop amiodarone and repeat bloods in 4 weeks
- E. Continue amiodarone and add thyroxine

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Patients who develop hypothyroidism whilst taking amiodarone can continue to take the drug if this is desirable. Given that this patient has a history of ventricular tachycardia it would be unwise to withdraw amiodarone abruptly

Amiodarone and the thyroid gland

Around 1 in 6 patients taking amiodarone develop thyroid dysfunction

Amiodarone-induced hypothyroidism

The pathophysiology of amiodarone-induced hypothyroidism (AIH) is thought to be due to the high iodine content of amiodarone causing a Wolff-Chaikoff effect*

Amiodarone may be continued if this is desirable

Amiodarone-induced thyrotoxicosis

Amiodarone-induced thyrotoxicosis (AIT) may be divided into two types:

	AIT type 1	AIT type 2
Pathophysiology	Excess iodine-induced thyroid hormone synthesis	Amiodarone-related destructive thyroiditis
Goitre	Present	Absent
Management	Carbimazole or potassium perchlorate	Corticosteroids

Unlike in AIH, amiodarone should be stopped if possible in patients who develop AIT

*an autoregulatory phenomenon where thyroxine formation is inhibited due to high levels of circulating iodide

Question 37 of 220

Which one of the following is least likely to precipitate haemolysis in a patient with G6PD deficiency?

- A. Broad beans
- B. Sepsis
- C. Ciprofloxacin
- D. Primaquine
- E. Penicillin

Question 37 of 220

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G6PD deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in a X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Features
- neonatal jaundice is often seen
- intravascular haemolysis
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

Some drugs causing haemolysis
- anti-malarials: primaquine
- ciprofloxacin
- sulphonamides

Some drugs thought to be safe
- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Question 38 of 220

A 21-year-old student is brought to the Emergency Department by his friends due to him being confused. They report he has been complaining of headaches for the past few weeks. He is pyrexial and on examination is noted to have abnormally pink mucosa. What is the most likely diagnosis?

- A. Carbon monoxide poisoning
- B. Meningitis
- C. Paracetamol overdose
- D. Subarachnoid haemorrhage
- E. Methaemoglobinaemia

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- E. Methaemoglobinaemia

Confusion, pyrexia and pink mucosae are typical features of carbon monoxide poisoning

Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity
- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels
- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management
- 100% oxygen
- hyperbaric oxygen

Indications for hyperbaric oxygen*
- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

Question 39 of 220

A 45-year-old female with a history of epilepsy is reviewed in the neurology clinic. Which one of the following features may be attributable to therapy with sodium valproate?

- A. Clubbing
- B. Weight loss
- C. Hirsuitism
- D. Renal impairment
- E. Tremor

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Sodium valproate

Sodium valproate is used in the management epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity

Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- teratogenic

Question 40 of 220

A 63-year-old female on long-term warfarin for atrial fibrillation attends the anticoagulation clinic. Despite having a stable INR for the past 4 years on the same dose of warfarin her INR is measured at 5.4. Which one of the following is most likely to be responsible?

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- B. Smoking
- C. Carrot juice
- D. Cranberry juice
- E. Camomile tea

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St John's Wort is an inducer of the P450 enzyme system so would cause the INR to decrease, rather than increase.

Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C

Factors that may potentiate warfarin
- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

Side-effects
- haemorrhage
- teratogenic
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

Question 41 of 220

Which of the following drugs demonstrate zero-order kinetics?

- A. Enalapril
- B. Bendrofluazide
- C. Atenolol
- D. Phenytoin
- E. Paracetamol

Question 41 of 220

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Pharmacokinetics: metabolism

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- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

First-pass metabolism

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- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil

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Zero-order kinetics

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

Acetylator status

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Question 42 of 220

A 49-year-old female asks about hormone replacement therapy (HRT). What is the most compelling indication for starting HRT?

- A. Prevention of ischaemic heart disease
- B. Prevention of osteoporosis
- C. Reversal of vaginal atrophy
- D. Control of vasomotor symptoms such as flushing
- E. Prevention of Alzheimer's disease

Question 42 of 220

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- B. Prevention of osteoporosis
- C. Reversal of vaginal atrophy
- ✓ D. Control of vasomotor symptoms such as flushing
- E. Prevention of Alzheimer's disease

Main indication for HRT: control of vasomotor symptoms

Hormone replacement therapy: indications

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen, combined with a progestogen (in women with a uterus), to help alleviate menopausal symptoms.

The indications for HRT have changed significantly over the past ten years as the long-term risks became apparent, primarily as a result of the Women's Health Initiative (WHI) study.

Indications

- vasomotor symptoms such as flushing, insomnia and headaches
- premature menopause: should be continued until the age of 50 years
- osteoporosis: but should only be used as second-line treatment

The main indication is the control of vasomotor symptoms. The other indications such as reversal of vaginal atrophy and prevention of osteoporosis should be treated with other agents as first-line therapies

Other benefits include a reduced incidence of colorectal cancer

Question 43 of 220

A 69-year-old man with terminal lung cancer is reviewed. He currently takes MST 60mg bd for pain. He has become unable to take oral medications and a decision is made to set-up a syringe driver. What dose of diamorphine should be prescribed for the syringe driver?

- A. 60 mg
- B. 40 mg
- C. 120 mg
- D. 30 mg
- E. 20 mg

Question 43 of 220

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- A. 60 mg
- ✓ B. 40 mg
- C. 120 mg
- D. 30 mg
- E. 20 mg

To convert from oral morphine to diamorphine the total daily morphine dose (60 * 2 = 120mg) should be divided by 3 (120 / 3 = 40mg)

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 44 of 220

Which of the following relating to St John's Wort is false?

- A. Adverse effects in trials is similar to placebo
- B. May cause serotonin syndrome
- C. Mechanism of action is similar to selective serotonin reuptake inhibitors
- D. Causes inhibition of the P450 system
- E. Has been shown to be effective in treating mild-moderate depression

Question 44 of 220

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- E. Has been shown to be effective in treating mild-moderate depression

St John's Wort is a known inducer of the P450 system

St John's Wort

Overview

- shown to be as effective as tricyclic antidepressants in the treatment of mild-moderate depression
- mechanism: thought to be similar to SSRIs (although noradrenaline uptake inhibition has also been demonstrated)
- NICE advise 'may be of benefit in mild or moderate depression, but its use should not be prescribed or advised because of uncertainty about appropriate doses, variation in the nature of preparations, and potential serious interactions with other drugs'

Adverse effects

- profile in trials similar to placebo
- can cause serotonin syndrome
- inducer of P450 system, therefore decreased levels of drugs such as warfarin, ciclosporin. The effectiveness of the combined oral contraceptive pill may also be reduced

Question 45 of 220

Which of the following may reduce the action of aminophylline in patients?

- A. Ciprofloxacin
- B. Acute ethanol consumption
- C. Omeprazole
- D. Smoking
- E. Erythromycin

Question 45 of 220

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- A. Ciprofloxacin
- B. Acute ethanol consumption
- C. Omeprazole
- ✓ D. Smoking
- E. Erythromycin

Smoking is known to induce CYP1A2 isoenzyme, reducing the effectiveness of aminophylline

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 46 of 220

What is the mechanism of action of heparin?

- A. Activates antithrombin III
- B. Vitamin K antagonist
- C. Activates tissue plasminogen activator
- D. Inhibits antithrombin III
- E. Inhibits protein C

Question 46 of 220

What is the mechanism of action of heparin?

- ✓ A. Activates antithrombin III
- B. Vitamin K antagonist
- C. Activates tissue plasminogen activator
- D. Inhibits antithrombin III
- E. Inhibits protein C

Heparin

Heparin can be given as either unfractionated, intravenous heparin, or low molecular weight heparin (LMWH), given subcutaneously. Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

Heparin overdose may be reversed by protamine sulphate

Question 47 of 220

A 62-year-old man presents with nocturia, hesitancy and terminal dribbling. Prostate examination reveals a moderately enlarged prostate with no irregular features and a well defined median sulcus. Blood tests show:

PSA 2.1 ng/ml

What is the most appropriate management?

- A. Alpha-1 antagonist
- B. 5 alpha-reductase inhibitor
- C. Non-urgent referral for transurethral resection of prostate
- D. Empirical treatment with ciprofloxacin for 2 weeks
- E. Urgent referral to urology

Question 47 of 220

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- D. Empirical treatment with ciprofloxacin for 2 weeks
- E. Urgent referral to urology

Alpha-1 antagonists are first-line in patients with benign prostatic hyperplasia

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin

- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

Question 48 of 220

Where is the site of action of spironolactone?

- A. Proximal convoluted tubule
- B. Ascending loop of Henle
- C. Descending loop of Henle
- D. Distal convoluted tubule
- E. Macula densa

Question 48 of 220

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Spironolactone

Spironolactone is an aldosterone antagonist which acts act in the distal convoluted tubule

Indications
- ascites: patients with cirrhosis develop a secondary hyperaldosteronism. Relatively large doses such as 100 or 200mg are often used
- heart failure (see RALES study below)
- nephrotic syndrome
- Conn's syndrome

Adverse effects
- hyperkalaemia
- gynaecomastia

RALES
- NYHA III + IV, patients already taking ACE inhibitor
- low dose spironolactone reduces all cause mortality

Question 49 of 220

A patient is started on the monoclonal antibody trastuzumab. What is the most likely indication?

- A. Crohn's disease
- B. Chronic lymphocytic leukaemia
- C. Renal cancer
- D. Colorectal cancer
- E. Breast cancer

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- ✓ E. Breast cancer

Trastuzumab (Herceptin) - monoclonal antibody that acts on the HER2/neu receptor

Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Question 50 of 220

A woman who is 24-weeks pregnant presents with a productive cough. On examination crackles can be heard in the left base and a decision is made to give an antibiotic. Which one of the following is least suitable to prescribe?

- A. Ciprofloxacin
- B. Erythromycin
- C. Co-amoxiclav
- D. Cefalexin
- E. Cefaclor

Question 50 of 220

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- D. Cefalexin
- E. Cefaclor

The BNF advises avoiding quinolones in pregnancy due to arthropathy in animal studies

Pregnancy: prescribing

Very few drugs are known to be completely safe in pregnancy. The list below largely comprises of those known to be harmful. Some countries have developed a grading system - see the link.

Antibiotics
- tetracyclines
- aminoglycosides
- sulphonamides and trimethoprim
- quinolones: the BNF advises to avoid due to arthropathy in some animal studies

Other drugs
- ACE inhibitors, angiotensin II receptor antagonists
- statins
- warfarin
- sulfonylureas
- retinoids (including topical)
- cytotoxic agents

The majority of antiepileptics including valproate, carbamazepine and phenytoin are known to be potentially harmful. The decision to stop such treatments however is difficult as uncontrolled epilepsy is also a risk

Question 51 of 220

A 56-year-old female with a history of depression is brought in to the Emergency Department by a concerned neighbour. Beside the patient are empty blister packets of co-codamol 30/500, indicating that she may have taken up to 50 tablets. She is confused with a GCS of 14/15 and is unable to say when she took the tablets. What is the most appropriate initial management?

- A. Start N-acetyl cysteine immediately
- B. Immediate referral for haemodialysis
- C. Give naloxone
- D. Start N-acetyl cysteine 4 hours after presentation if levels are elevated
- E. Observe

Question 51 of 220

A 56-year-old female with a history of depression is brought in to the Emergency Department by a concerned neighbour. Beside the patient are empty blister packets of co-codamol 30/500, indicating that she may have taken up to 50 tablets. She is confused with a GCS of 14/15 and is unable to say when she took the tablets. What is the most appropriate initial management?

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- C. Give naloxone
- D. Start N-acetyl cysteine 4 hours after presentation if levels are elevated
- E. Observe

She may have consumed 25g of paracetamol which is a life-threatening overdose. N-acetyl cysteine needs to be commenced immediately.

There is no mention in the question of respiratory depression or hypoxia to justify the use of naloxone

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)
Arterial pH < 7.3, 24 hours after ingestion or all of the following: • prothrombin time > 100 seconds • creatinine > 300 µmol/l • grade III or IV encephalopathy

Question 52 of 220

Which one of the following pairs of features would be expected to occur following administration of an anticholinesterase (acetylcholinesterase inhibitor)?

- A. Bradycardia and miosis
- B. Bradycardia and urinary retention
- C. Tachycardia and diarrhoea
- D. Bradycardia and mydriasis
- E. Tachycardia and lacrimation

Question 52 of 220

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- C. Tachycardia and diarrhoea
- D. Bradycardia and mydriasis
- E. Tachycardia and lacrimation

A clinical example of an anticholinesterase is organophosphate compounds

Organophosphate insecticide poisoning

One of the effects of organophosphate poisoning is inhibition of acetylcholinesterase

Features can be predicted by the accumulation of acetylcholine (mnemonic = SLUD)

- Salivation
- Lacrimation
- Urination
- Defecation
- cardiovascular: hypotension, bradycardia
- also: small pupils, muscle fasciculation

Management

- atropine
- the role of pralidoxime is still unclear - meta-analyses to date have failed to show any clear benefit

Question 53 of 220

Which one of the following is least associated with lead poisoning?

- A. Peripheral neuropathy
- B. Acute glomerulonephritis
- C. Blue lines on gum margin
- D. Abdominal pain
- E. Microcytic anaemia

Question 53 of 220

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Lead poisoning

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs

Features
- abdominal pain
- peripheral neuropathy (mainly motor)
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

Investigations
- microcytic anaemia
- blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)

Management - various chelating agents are currently used:
- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol

Question 54 of 220

Olanzapine is known to block D2 dopamine receptors. What other type of receptor does it mainly act on?

- A. Alpha-adrenoceptors
- B. Acetylcholine receptors
- C. Serotonin receptors
- D. D1 dopamine receptors
- E. H1 histamine receptors

Question 54 of 220

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- D. D1 dopamine receptors
- E. H1 histamine receptors

Olanzapine, like other atypical antipsychotics, is known to block serotonin receptors (especially the 5-HT2 subtype) as well as D2 dopamine receptors

Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics
- weight gain
- olanzapine and risperidone are associated with an increased risk of stroke in elderly patients
- clozapine is associated with agranulocytosis (see below)

Examples of atypical antipsychotics
- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine
- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Question 55 of 220

A 35-year-old female diabetic is started on erythromycin for gastroparesis. What is the mechanism of action?

- A. Promotes gastric emptying
- B. Inhibits bacterial overgrowth
- C. Acts on central chemoreceptor trigger zone
- D. Relaxation of pyloric sphincter
- E. Stimulates cholecystokinin release

Question 55 of 220

A 35-year-old female diabetic is started on erythromycin for gastroparesis. What is the mechanism of action?

- ✓ A. Promotes gastric emptying
- B. Inhibits bacterial overgrowth
- C. Acts on central chemoreceptor trigger zone
- D. Relaxation of pyloric sphincter
- E. Stimulates cholecystokinin release

Erythromycin is used in gastroparesis as it has prokinetic properties

Macrolides

Erythromycin was the first macrolide used clinically. Newer examples include clarithromycin and azithromycin

Macrolides act by inhibiting bacterial protein synthesis. If pushed to give an answer they are bacteriostatic in nature, but in reality this depends on the dose and type of organism being treated

Adverse effects of erythromycin

- GI side-effects are common
- cholestatic jaundice: risk may be reduced if erythromycin stearate is used
- P450 inhibitor

Question 56 of 220

Which one of the following statements regarding metformin is false?

- A. Does not cause hypoglycaemia
- B. Increases insulin sensitivity
- C. Decreases hepatic gluconeogenesis
- D. Increases endogenous insulin secretion
- E. Reduces GI absorption of carbohydrates

Question 56 of 220

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- B. Increases insulin sensitivity
- C. Decreases hepatic gluconeogenesis
- ✓ D. Increases endogenous insulin secretion
- E. Reduces GI absorption of carbohydrates

Sulphonylureas have the property of increasing endogenous insulin secretion

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action
- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects
- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis* with severe liver disease or renal failure

Contraindications**
- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 57 of 220

Which one of the following drugs is not known to induce the cytochrome p450 enzyme system?

- A. Rifampicin
- B. Isoniazid
- C. Phenobarbitone
- D. Griseofulvin
- E. Carbamazepine

Question 57 of 220

Which one of the following drugs is not known to induce the cytochrome p450 enzyme system?

- A. Rifampicin
- ✓ B. Isoniazid
- C. Phenobarbitone
- D. Griseofulvin
- E. Carbamazepine

Isoniazid is an inhibitor of the P450 system

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 58 of 220

A 39-year-old patient is taking phenelzine, a monoamine oxidase inhibitor, for the treatment of depression. Which one of the following foods can the patient safely eat?

- A. Bovril
- B. Cheese
- C. Oxo
- D. Eggs
- E. Broad beans

Question 58 of 220

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Monoamine oxidase inhibitors

Overview
- serotonin and noradrenaline are metabolised by monoamine oxidase in the presynaptic cell

Non-selective monoamine oxidase inhibitors
- e.g. tranylcypromine, phenelzine
- used in the treatment of depression and other psychiatric disorder
- not used frequently due to side-effects

Adverse effects of non-selective monoamine oxidase inhibitors
- hypertensive reacting with tyramine containing foods e.g. cheese, pickled herring, Bovril, Oxo, Marmite, broad beans
- anticholinergic effects

Question 59 of 220

A 25-year-old woman is diagnosed with a urinary tract infection. She has a past history of epilepsy and is currently taking sodium valproate. Which one of the following antibiotics should be avoided if possible

- A. Co-amoxiclav
- B. Nitrofurantoin
- C. Cefixime
- D. Trimethoprim
- E. Ciprofloxacin

Question 59 of 220

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- C. Cefixime
- D. Trimethoprim
- ✓ E. Ciprofloxacin

Whilst many antibiotics can lower the seizure threshold, this affect is seen particularly with quinolones. The BNF advises that quinolones 'should be used with caution in patients with a history of epilepsy, or conditions that predispose to seizures'

Quinolones

Quinolones are a group of antibiotics which work by inhibiting DNA synthesis and are bactericidal in nature. Examples include:

- ciprofloxacin
- levofloxacin

Adverse effects

- lower seizure threshold in patients with epilepsy
- tendon damage (including rupture) - the risk is increased in patients also taking steroids

Question 60 of 220

A patient develops methaemoglobinaemia after being prescribed isosorbide mononitrate. Which substance is most likely to be depleted?

- A. Pyruvate kinase
- B. Hyponitrite reductase
- C. Pyridoxine 5-dehydrogenase
- D. Glucose-6-phosphate dehydrogenase
- E. NADH

Question 60 of 220

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Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes
- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes
- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features
- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO2 but decreased oxygen saturation

Management
- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

Question 61 of 220

Which one of the following may enhance the effects of adenosine?

- A. Diltiazem
- B. Aspirin
- C. Clopidogrel
- D. Dipyridamole
- E. Aminophylline

Question 61 of 220

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- B. Aspirin
- C. Clopidogrel
- ✓ D. Dipyridamole
- E. Aminophylline

Adenosine
• dipyridamole enhances effect • aminophylline reduces effect

Adenosine

The effects of adenosine are enhanced by dipyridamole (anti-platelet agent) and blocked by theophyllines. It should be avoided in asthmatics due to possible bronchospasm

Adverse effects

- chest pain
- bronchospasm
- can enhance conduction down accessory pathways, resulting in increased ventricular rate (e.g. WPW syndrome)

Question 62 of 220

A 54-year-old man with a history of epilepsy and ischaemic heart disease is seen in clinic with a 3 month history of lethargy. Blood tests are as follows:

Hb 7.6 g/dl

MCV 123 fl

Plt 134 * 10^9/l

WCC 2.6 *10^9/l

Which one of his medications is most likely to be responsible?

- A. Clopidogrel
- B. Atorvastatin
- C. Carbamazepine
- D. Atenolol
- E. Phenytoin

Question 62 of 220

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- B. Atorvastatin
- C. Carbamazepine
- D. Atenolol
- ✓ E. Phenytoin

Phenytoin may cause a megaloblastic anaemia by altering folate metabolism

Phenytoin: side-effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute
- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic
- common: gingival hyperplasia, hirsuitism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic
- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic
- associated with cleft palate and congenital heart disease

*although not listed in the BNF

Question 63 of 220

What is the most appropriate time to take blood samples for therapeutic monitoring of lithium levels?

- A. At any time
- B. Immediately before next dose
- C. 4 hours after last dose
- D. 6 hours after last dose
- E. 12 hours after last dose

Question 63 of 220

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- ✓ E. 12 hours after last dose

Therapeutic drug monitoring

Lithium
- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

Ciclosporin
- trough levels immediately before dose

Digoxin
- at least 6 hrs post-dose

Phenytoin
- trough levels immediately before dose

Question 64 of 220

Which one of the following drugs is most likely to cause a prolonged QT interval?

- A. Metoclopramide
- B. Verapamil
- C. Ceftriaxone
- D. Sotalol
- E. Digoxin

Question 64 of 220

Which one of the following drugs is most likely to cause a prolonged QT interval?

- A. Metoclopramide
- B. Verapamil
- C. Ceftriaxone
- ✓ D. Sotalol
- E. Digoxin

Long QT syndrome

Long QT syndrome (LQTS) is associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT is less than 440 ms in males and 450 ms in females.

Congenital
- Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)
- Romano-Ward syndrome (no deafness)

Drugs
- amiodarone
- sotalol
- class 1a antiarrhythmic drugs
- tricyclic antidepressants
- chloroquine
- terfenadine**
- erythromycin

Other causes
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- acute MI
- myocarditis
- hypothermia
- subarachnoid haemorrhage

Management
- beta-blockers***
- implantable cardioverter defibrillators in high risk cases

*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

**note sotalol may exacerbate long QT syndrome

Question 65 of 220

A 49-year-old man with a history of bipolar disorder, COPD and hypertension is started on a new anti-hypertensive medication. Two weeks later he is admitted to hospital with lithium toxicity. Which medication is most likely to have precipitated this?

- A. Ramipril
- B. Aminophylline
- C. Atenolol
- D. Amlodipine
- E. Doxazosin

Question 65 of 220

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- B. Aminophylline
- C. Atenolol
- D. Amlodipine
- E. Doxazosin

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:
- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects
- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 66 of 220

A 34-year-old man with a history of depression is admitted to the Emergency Department. He states he has taken an overdose of both diazepam and dosulepin. On examination blood pressure is 116/78 and the pulse is 140 bpm. His respiratory rate is 8 per minute and the oxygen saturations are 97% on room air. What is the most appropriate next course of action?

- A. Give flumazenil
- B. Insert a haemodialysis line
- C. Obtain an ECG
- D. Give naloxone
- E. Start N-acetylcysteine infusion

Question 66 of 220

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- B. Insert a haemodialysis line
- ✓ C. Obtain an ECG
- D. Give naloxone
- E. Start N-acetylcysteine infusion

As this patient has a marked tachycardia the first step would be to obtain an ECG. If changes such as QRS widening are seen then intravenous bicarbonate should be given

Some users have argued that an 'ABC' approach should be taken, with flumazenil given to reverse the respiratory depression. The potential risk of doing this would be inducing a seizure given the coexistent tricyclic overdose

Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to A&E departments

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:
- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:
- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated with ventricular arrhythmias

Management
- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. quinidine) and class Ic antiarrhythmics (e.g. flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

Question 67 of 220

A 52-year-old man with a history of hypertension is found to have a 10-year cardiovascular disease risk of 28%. A decision is made to start simvastatin 40mg on. Liver function tests are performed prior to initialising treatment:

Bilirubin	10 µmol/l (3 - 17 µmol/l)
ALP	96 u/l (30 - 150 u/l)
ALT	30 u/l (10 - 45 u/l)
Gamma-GT	28 u/l (10 - 40 u/l)

Three months later the LFTs are repeated:

Bilirubin	12 µmol/l (3 - 17 µmol/l)
ALP	107 u/l (30 - 150 u/l)
ALT	104 u/l (10 - 45 u/l)
Gamma-GT	76 u/l (10 - 40 u/l)

What is the most appropriate course of action?

- A. Continue treatment and repeat LFTs in 1 month
- B. Check creatine kinase
- C. Reduce dose to simvastatin 10mg on and repeat LFTs in 1 month
- D. Stop treatment and consider alternative lipid lowering drug
- E. Stop treatment and refer to gastroenterology

Question 67 of 220

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Treatment with statins should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range.

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 68 of 220

What is the mechanism of action of goserelin in prostate cancer?

- A. Androgen receptor antagonist
- B. Oestrogen agonist
- C. GnRH agonist
- D. Luteinising hormone receptor antagonist
- E. GnRH antagonist

Question 68 of 220

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- ✓ C. GnRH agonist
- D. Luteinising hormone receptor antagonist
- E. GnRH antagonist

Goserelin (Zoladex) is a synthetic GnRH agonist which provides negative feedback to the anterior pituitary

Prostate cancer: management

Localised disease = T1/2

T1 - clinically unapparent disease
- if life expectancy < 10 years then watchful waiting
- if life expectancy > 10 years then offer
- radical prostatectomy
- radical radiotherapy

T2 - palpable disease confined to prostate
- radical prostatectomy
- radical radiotherapy (often if older patient)

Locally advanced disease (T3/4)
- T3 = beyond prostatic capsule
- T4 = involves bladder neck or rectum
- most men will have occult mets
- radiotherapy

Disseminated disease - hormonal therapy

Synthetic GnRH agonist
- e.g. goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen
- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Orchidectomy

Question 69 of 220

A 63-year-old female is brought to the Emergency Department due to a decreased level of consciousness. An urgent CT head is performed as she takes warfarin for atrial fibrillation and shows an intracranial haemorrhage. What is the most appropriate management?

- A. Protamine sulphate
- B. IV vitamin K alone
- C. IV vitamin K + prothrombin complex concentrate
- D. Fresh frozen plasma alone
- E. IV vitamin K + fresh frozen plasma

Question 69 of 220

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- ✓ C. IV vitamin K + prothrombin complex concentrate
- D. Fresh frozen plasma alone
- E. IV vitamin K + fresh frozen plasma

As fresh frozen plasma takes time to defrost prothrombin complex concentrate (PCC) should be used in such an urgent situation. The use of PCC is currently limited by availability

Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding

Major bleeding	Stop warfarin Vitamin K 5mg IV Prothrombin complex concentrate - if not available then FFP*
INR > 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0 If risk factors for bleeding then give vitamin K 0.5mg IV or 5mg po. Risk factors include: • age > 70 years • first year of warfarin therapy • history of gastrointestinal bleeding • hypertension • alcohol excess Dose can be repeated after 24 hours if INR still high
INR 6.0 - 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0

*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

Question 70 of 220

A 45-year-old man is started on ciclosporin following a renal transplant. Which one of the following adverse effects is most likely to occur?

- A. Depression
- B. Increased risk of ischaemic heart disease
- C. Pulmonary fibrosis
- D. Optic neuritis
- E. Nephrotoxicity

Question 70 of 220

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Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin
- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications
- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 71 of 220

A 59-year-old man with a known history of type 2 diabetes mellitus, atrial fibrillation and epilepsy presents as he is feeling generally unwell. His main complaint is a blue tinge to his vision. Which one of his medications is most likely to be responsible?

- A. Phenytoin
- B. Metformin
- C. Sildenafil
- D. Pioglitazone
- E. Digoxin

Question 71 of 220

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- B. Metformin
- ✓ C. Sildenafil
- D. Pioglitazone
- E. Digoxin

Digoxin can cause a yellow-green tinge to vision.

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications
- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Adverse effects
- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects

Question 72 of 220

A 69-year-old man with a history of ischaemic heart disease and type 2 diabetes mellitus is seen in the diabetes clinic. Which one of the following medications is it most important to avoid?

- A. Nateglinide
- B. Metformin
- C. Pioglitazone
- D. Glimepiride
- E. Rosiglitazone

Question 72 of 220

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- B. Metformin
- C. Pioglitazone
- D. Glimepiride
- ✓ E. Rosiglitazone

The Medicines and Healthcare products Regulatory Agency issued guidance in 2008 that patients rosiglitazone should be avoided in patients with a history of ischaemic heart disease.

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 73 of 220

In line with NICE guidelines on the secondary prevention of osteoporotic fractures in postmenopausal women, which one of the following patients should not automatically be started on treatment?

- A. A 81-year-old woman who has had a fractured neck of femur
- B. A 64-year-old women with a wedge fractures of her thoracic spine. DEXA scan shows a T-score of -3.1 SD
- C. A 55-year-old women who had a Colles fracture of the wrist. DEXA scan shows a T-score of -3.3 SD
- D. A 64-year-old women with a BMI of 18 kg/m2. She has a wedge fractures of her thoracic spine. DEXA scan shows a T-score of -2.7 SD
- E. A 71-year-old women who had a Colles fracture of the wrist. DEXA scan shows a T-score of -2.1 SD

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- ✓ E. A 71-year-old women who had a Colles fracture of the wrist. DEXA scan shows a T-score of -2.1 SD

Question 74 of 220

Which one of the following may be associated with an increased risk of venous thromboembolism?

- A. Fluoxetine
- B. Selegiline
- C. Diazepam
- D. Amitriptyline
- E. Olanzapine

Question 74 of 220

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- D. Amitriptyline
- ✓ E. Olanzapine

DVT: risk factors

Haematological
- thrombophilia: e.g. activated protein C resistance, protein C and S deficiency
- polycythaemia
- paroxysmal nocturnal haemoglobinuria
- hyperviscosity syndrome

Autoimmune
- antiphospholipid syndrome
- Behcet's

Drugs
- combined oral contraceptive pill: 3rd generation more than 2nd generation
- antipsychotics (especially olanzapine) have recently been shown to be a risk factor

Other conditions
- homocystinuria

Question 75 of 220

Which one of the following adverse effects is most likely to be seen in patients taking ciclosporin?

- A. Hypertension
- B. Hypokalaemia
- C. Alopecia
- D. Dehydration
- E. Atrophy of the gums

Question 75 of 220

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- E. Atrophy of the gums

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications

- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 76 of 220

Which one of the following statements regarding quinupristin is incorrect?

- A. Thrombophlebitis is a recognised side-effect
- B. Has broad Gram positive cover
- C. Inhibits bacterial protein synthesis
- D. Acts as a P450 inhibitor
- E. Particularly useful against *Enterococcus faecalis*

Question 76 of 220

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Quinupristin & dalfopristin antibiotics

Overview
- injectable streptogrammin antibiotic
- combination of group A and group B streptogrammin
- inhibits bacterial protein synthesis by blocking tRNA complexes binding to the ribosome

Spectrum
- most Gram positive bacteria
- exception: *Enterococcus faecalis*

Adverse effects
- thrombophlebitis (give via a central line)
- arthralgia
- P450 inhibitor

Question 77 of 220

A 57-year-old man with a history of ischaemic heart disease is keen to try sildenafil for erectile dysfunction. Which one of the following medications may contraindicate its use?

- A. Nebivolol
- B. Losartan
- C. Nicorandil
- D. Nifedipine
- E. Ramipril

Question 77 of 220

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- B. Losartan
- ✓ C. Nicorandil
- D. Nifedipine
- E. Ramipril

Viagra? - contraindicated by nitrates and nicorandil

Nicorandil has a nitrate component as well as being a potassium channel activator

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications
- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Adverse effects
- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects

Question 78 of 220

A 43-year-old man with a history of bipolar disorder is admitted with acute confusion. Whilst being transferred to hospital he had generalised seizure which terminated spontaneously after around 30 seconds. On arrival in the Emergency Department his GCS is 14/15 and he is noted to have a coarse tremor. A diagnosis of lithium toxicity is suspected. Intravenous access is obtained, bloods are taken and a saline infusion is started. Blood results reveal the following:

Lithium level	4.2 mmol/l
Na^+	136 mmol/l
K^+	4.6 mmol/l
Urea	8.1 mmol/l
Creatinine	99 µmol/l
Bicarbonate	18 mmol/l

What is the most appropriate management?

- A. Arrange haemodialysis
- B. Intravenous magnesium
- C. Intravenous bicarbonate
- D. Intravenous hypertonic saline
- E. Arrange plasma exchange

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- C. Intravenous bicarbonate
- D. Intravenous hypertonic saline
- E. Arrange plasma exchange

The high lithium level and reduced GCS are an indication for haemodialysis in this patient

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:

- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects

- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 79 of 220

What is the minimum steroid intake a patient should be taking before an assessment of osteoporosis prophylaxis should be undertaken?

- A. Equivalent of prednisolone 10 mg or more each day for 6 months
- B. Equivalent of prednisolone 7.5 mg or more each day for 6 weeks
- C. Equivalent of prednisolone 5 mg or more each day for 6 weeks
- D. Equivalent of prednisolone 7.5 mg or more each day for 3 months
- E. Equivalent of prednisolone 10 mg or more each day for 6 weeks

Question 79 of 220

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- C. Equivalent of prednisolone 5 mg or more each day for 6 weeks
- ✓ D. Equivalent of prednisolone 7.5 mg or more each day for 3 months
- E. Equivalent of prednisolone 10 mg or more each day for 6 weeks

Osteoporosis: glucocorticoid-induced

Patients who take the equivalent of prednisolone 7.5 mg or more each day for 3 months or longer should be assessed and where necessary given prophylactic treatment

Assessment for treatment - patients taking the equivalent of prednisolone 7.5 mg or more each day for 3 months, and one of the following

- are over the age of 65 years
- have a history of a fragility fracture
- have a T-score less than - 1.5 SD

Treatment

- first-line: oral bisphosphonate
- second-line: alfacalcidol or calcitriol

Question 80 of 220

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

- A. Hypokalaemia
- B. Pseudogout
- C. Hypercalcaemia
- D. Impotence
- E. Impaired glucose tolerance

Question 80 of 220

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

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- ✓ B. Pseudogout
- C. Hypercalcaemia
- D. Impotence
- E. Impaired glucose tolerance

Bendroflumethiazide predisposes to gout, rather than pseudogout

Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide currently is in hypertension (part of the effect is due to vasodilation)

Common adverse effects
- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects
- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

Question 81 of 220

A 46-year-old man with a history of hyperlipidaemia is reviewed in clinic. He is currently taking simvastatin 10mg on but his cholesterol level remains high. Previous attempts to increase the dose of simvastatin have resulted in myalgia. Given the history of myalgia, which lipid-regulating drug should be avoided?

- A. Nicotinic acid
- B. Bezafibrate
- C. Colestyramine
- D. Omega-3 fatty acid
- E. Ezetimibe

Question 81 of 220

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- C. Colestyramine
- D. Omega-3 fatty acid
- E. Ezetimibe

Tough question as both fibrates and nicotinic acid have been associated with myositis, especially when combined with a statin. However, the Committee on Safety of Medicines has produced guidance which specifically warns about the concomitant prescription of fibrates with statins in relation to muscle toxicity

Hyperlipidaemia: drug adverse effects

The following table compares the side-effects of drugs used in hyperlipidaemia:

Drugs	**Adverse effects**
Statins (HMG CoA reductase inhibitors)	Myositis, deranged LFTs
Ezetimibe	Headache
Nicotinic acid	Flushing, myositis
Fibrates	Myositis, pruritus, cholestasis
Anion-exchange resins	GI side-effects

Question 82 of 220

A 14-year-old boy is brought to the Emergency Department. Whilst in school he injected his friends EpiPen into the palm of his left hand. Shortly afterwards the left middle finger became cold and pale. The capillary refill time was around 5-6 seconds. What is the most appropriate management?

- A. Inhalation of Nitrox (mixture of nitrogen + oxygen)
- B. Intravenous nitrate infusion
- C. Local infiltration of histamine
- D. Intravenous prostacyclin infusion
- E. Local infiltration of phentolamine

Question 82 of 220

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- ✓ E. Local infiltration of phentolamine

Adrenaline induced ischaemia - phentolamine

Phentolamine, a short acting alpha blocker, may be used in this situation. It is normally used mainly to control blood pressure during surgical resection of phaeochromocytoma

Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications
- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection
- local infiltration of phentolamine

Question 83 of 220

A 72-year-old man is reviewed in the diabetes clinic. He has a history of heart failure and type 2 diabetes mellitus. His current medications include furosemide 40mg od, ramipril 10mg od and bisoprolol 5mg od. Clinical examination is unremarkable with no evidence of peripheral oedema, a clear chest and blood pressure of 130/76 mmHg. Recent renal and liver function tests are normal. Which one of the following medications is contraindicated?

- A. Sitagliptin
- B. Pioglitazone
- C. Gliclazide
- D. Exenatide
- E. Metformin

Question 83 of 220

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- E. Metformin

Thiazolidinediones are absolutely contraindicated in heart failure

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 84 of 220

What is the most appropriate time to take blood samples for therapeutic monitoring of ciclosporin levels?

- A. 6 hours after last dose
- B. Immediately before next dose
- C. At any time
- D. 12 hours after last dose
- E. 4 hours after last dose

Question 84 of 220

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- ✓ B. Immediately before next dose
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- D. 12 hours after last dose
- E. 4 hours after last dose

Therapeutic drug monitoring

Lithium
- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

Ciclosporin
- trough levels immediately before dose

Digoxin
- at least 6 hrs post-dose

Phenytoin
- trough levels immediately before dose

Question 85 of 220

A 34-year-old female with a history of anti-phospholipid syndrome is reviewed in clinic. She is on long-term warfarin and her INR has been stable at 3.0 for over 2 years. Measurement from one week ago and today shows values of 1.5 and 1.3 respectively. Which one of the following medications is most likely to be responsible?

- A. Ciprofloxacin
- B. Fluconazole
- C. Sodium valproate
- D. Carbamazepine
- E. Cimetidine

Question 85 of 220

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- ✓ D. Carbamazepine
- E. Cimetidine

Carbamazepine is an enzyme inducer, the other listed medications are inhibitors

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 86 of 220

A 79-year-old female with a history of COPD and metastatic lung cancer is admitted with increasing shortness of breath. Following discussion with family it is decided to withdraw active treatment, including fluids and antibiotics, as the admission likely represents a terminal event. Two days after admission she becomes agitated and restless. What is the most appropriate management?

- A. Subcutaneous midazolam
- B. Intramuscular haloperidol
- C. Oral lormetazepam
- D. Oral haloperidol
- E. Recommence fluids and antibiotics

Question 86 of 220

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Palliative care prescribing: agitation and confusion

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness (for example a patient on the Care of the Dying pathway) then agitation or restlessness is best treated with midazolam

Question 87 of 220

Which one of the following drugs used in the management of diabetes mellitus is most likely to cause cholestasis?

- A. Metformin
- B. Gliclazide
- C. Acarbose
- D. Rosiglitazone
- E. Insulin

Question 87 of 220

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- E. Insulin

Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 88 of 220

A 62-year-old woman who is known to have metastatic breast cancer presents with increasing shortness of breath. She is currently receiving a chemotherapy regime. On examination she has a third heart sound and the apex beat is displaced to the 6th intercostal space, anterior axillary line. Which one of the following chemotherapeutic agents is most likely to be responsible?

- A. Paclitaxel
- B. Docetaxel
- C. Bleomycin
- D. Dactinomycin
- E. Doxorubicin

Question 88 of 220

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- D. Dactinomycin
- ✓ E. Doxorubicin

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 89 of 220

What is the main mechanism of action of ondansetron?

- A. Dopamine receptor agonist
- B. 5-HT2 receptor antagonist
- C. Dopamine receptor antagonist
- D. 5-HT2 receptor agonist
- E. 5-HT3 receptor antagonist

Question 89 of 220

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Drugs which act on serotonin receptors

Below is a summary of drugs which are known to act via modulation of the serotonin (5-HT) system. It should be noted that 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis

Agonists

- sumatriptan is a 5-HT1D receptor agonist which is used in the acute treatment of migraine
- ergotamine is a partial agonist of 5-HT1 receptors

Antagonists

- pizotifen is a 5-HT2 receptor antagonist used in the prophylaxis of migraine attacks. Methysergide is another antagonist of the 5-HT2 receptor but is rarely used due to the risk of retroperitoneal fibrosis
- cyproheptadine is a 5-HT2 receptor antagonist which is used to control diarrhoea in patients with carcinoid syndrome
- ondansetron is a 5-HT3 receptor antagonist and is used as an antiemetic

Question 90 of 220

A 72-year-old man with metastatic colon cancer is reviewed. He currently takes co-codamol 30/500 2 tablets qds for pain relief. Unfortunately this is not controlling his pain. What is the most appropriate change to his medication?

- A. Switch to MST 15mg bd + paracetamol 1g qds
- B. Switch to MST 35mg bd + paracetamol 1g qds
- C. Add tramadol 50-100mg 1-2 qds
- D. Switch to MST 25mg bd
- E. Switch to MST 15mg bd

Question 90 of 220

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- D. Switch to MST 25mg bd
- E. Switch to MST 15mg bd

His total codeine dose is 30 * 2 * 4 = 240 mg/day. Converting this to oral morphine = 24 mg/day. It is therefore reasonable to start MST 15mg bd as his pain is not currently controlled. Paracetamol should be continued as it has been shown to give benefits even to patients on large doses of morphine

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 91 of 220

In the Vaughan Williams classification of antiarrhythmics lidocaine is an example of a:

- A. Class Ia agent
- B. Class Ib agent
- C. Class Ic agent
- D. Class II agent
- E. Class IV agent

Question 91 of 220

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- E. Class IV agent

Antiarrhythmics: Vaughan Williams classification

The Vaughan Williams classification of antiarrhythmics is still widely used although it should be noted that a number of common drugs are not included in the classification e.g. adenosine, atropine, digoxin and magnesium

Class	Example	Mechanism of action
Ia	Disopyramide	Block sodium channels
Ib	Lidocaine	Block sodium channels
Ic	Flecainide	Block sodium channels
II	Propranolol	Beta-adrenoceptor antagonists
III	Amiodarone	Block potassium channels
IV	Verapamil	Calcium channel blockers

Question 92 of 220

A 37-year-old who is 38 weeks pregnancy is an inpatient on the obstetric ward for the management of pre-eclampsia. Blood pressure is 172/114 mmHg and urine dipstick shows proteinuria +++. A decision has been made to start magnesium sulphate therapy as she is deemed at risk of eclampsia. Of the following options, which are the most important parameters to monitor whilst the patient is receiving magnesium?

- A. Blood sugar + pulse rate
- B. Reflexes + respiratory rate
- C. Blood sugar + respiratory rate
- D. Reflexes + pulse rate
- E. Glasgow coma scale + pulse rate

Question 92 of 220

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- ✓ B. Reflexes + respiratory rate
- C. Blood sugar + respiratory rate
- D. Reflexes + pulse rate
- E. Glasgow coma scale + pulse rate

Magnesium sulphate - monitor reflexes + respiratory rate

Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

Question 93 of 220

A 67-year-old man with a history of atrial fibrillation and ischaemic heart disease presents with symptoms consistent with a chest infection. His current medication includes amiodarone, warfarin and simvastatin. Which one of the following antibiotics is it most important to avoid if possible?

- A. Trimethoprim
- B. Co-amoxiclav
- C. Cefaclor
- D. Levofloxacin
- E. Erythromycin

Question 93 of 220

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- C. Cefaclor
- D. Levofloxacin
- ✓ E. Erythromycin

Erythromycin may potentially interact with amiodarone, warfarin and simvastatin. Levofloxacin reacts to a lesser extent with both amiodarone and warfarin.

Macrolides

Erythromycin was the first macrolide used clinically. Newer examples include clarithromycin and azithromycin

Macrolides act by inhibiting bacterial protein synthesis. If pushed to give an answer they are bacteriostatic in nature, but in reality this depends on the dose and type of organism being treated

Adverse effects of erythromycin

- GI side-effects are common
- cholestatic jaundice: risk may be reduced if erythromycin stearate is used
- P450 inhibitor

Question 94 of 220

Which one of the following ECG changes is most consistent with a tricyclic overdose?

- A. QRS widening
- B. Bradycardia
- C. Shortening of QT interval
- D. First degree heart block
- E. ST elevation

Question 94 of 220

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- B. Bradycardia
- C. Shortening of QT interval
- D. First degree heart block
- E. ST elevation

Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to A&E departments

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:
- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:
- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated with ventricular arrhythmias

Management
- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. quinidine) and class Ic antiarrhythmics (e.g. flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

Question 95 of 220

Which one of the following is not a recognised indication for the use of octreotide?

- A. Acute variceal haemorrhage
- B. Acromegaly
- C. VIPoma
- D. Carcinoid syndrome
- E. Hepatic encephalopathy

Question 95 of 220

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Octreotide

Overview
- long-acting analogue of somatostatin
- somatostatin is release from D cells of pancreas and inhibits the release of growth hormone

Uses
- acute treatment of variceal haemorrhage
- acromegaly
- carcinoid syndrome
- prevent complications following pancreatic surgery
- VIPomas

Adverse effects
- gallstones (secondary to biliary stasis)

Question 96 of 220

You receive the blood results of a 76-year-old man who takes warfarin following a pulmonary embolism two months ago. He recently completed a course of antibiotics.

INR 8.4

On reviewing the patient he is well with no bleeding or bruising. What is the most appropriate action?

- A. Stop warfarin + restart when INR < 5.0 + give low-molecular weight heparin until warfarin restarted
- B. Intravenous vitamin K 0.5mg + stop warfarin + restart when INR < 5.0
- C. Stop warfarin + restart when INR < 3.0
- D. Stop warfarin + restart when INR < 5.0
- E. Fresh frozen plasma + restart warfarin when INR < 5.0

Question 96 of 220

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- D. Stop warfarin + restart when INR < 5.0
- E. Fresh frozen plasma + restart warfarin when INR < 5.0

Being elderly is a risk factor for bleeding. The BNF advises reversal of anticoagulation in this scenario.

Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding

Major bleeding	Stop warfarin Vitamin K 5mg IV Prothrombin complex concentrate - if not available then FFP*
INR > 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0 If risk factors for bleeding then give vitamin K 0.5mg IV or 5mg po. Risk factors include: • age > 70 years • first year of warfarin therapy • history of gastrointestinal bleeding • hypertension • alcohol excess Dose can be repeated after 24 hours if INR still high
INR 6.0 - 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0

*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

Question 97 of 220

A 52-year-old man with a history of epilepsy is reviewed. Since having his medication change he has experienced a 'numbness' of his hands and feet. On examination he has reduced sensation in a glove-and-stocking distribution associated with a reduced ankle reflex. He is also noted to have lymphadenopathy in the cervical and inguinal region and some bleeding around the gums. Which one of the following medications is he most likely to have been taking?

- A. Carbamazepine
- B. Phenytoin
- C. Topiramate
- D. Sodium valproate
- E. Lamotrigine

Question 97 of 220

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Phenytoin: side-effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute
- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic
- common: gingival hyperplasia, hirsuitism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic
- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic
- associated with cleft palate and congenital heart disease

*although not listed in the BNF

Question 98 of 220

An 80-year-old woman is started on oral alendronate following a fractured neck of femur. How would you explain how to take the tablet?

- A. Take it on a full stomach to minimise gastric irritation and avoid lying down for 30 minutes afterwards
- B. Dissolve tablet in water and take just before breakfast + sit-upright for 30 minutes following
- C. Take during main evening meal + sit-upright for 2 hours following
- D. Take at least 30 minutes before breakfast with plenty of water + sit-upright for 30 minutes following
- E. Take at least 30 minutes after a main meal + sit-upright for 30 minutes following

Question 98 of 220

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Bisphosphonates can cause a variety of oesophageal problems

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses
- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metatases

Adverse effects
- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw

The BNF suggests the following counselling for patients taking oral bisphosphonates
- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

Question 99 of 220

A 54-year-old female is being investigated for a macrocytic anaemia. Bloods test reveal a low vitamin B12 level. Which one of the following medications may be contributing to this?

- A. Bendroflumethiazide
- B. Digoxin
- C. Amiodarone
- D. Sodium valproate
- E. Metformin

Question 99 of 220

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- D. Sodium valproate
- ✓ E. Metformin

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action
- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects
- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis* with severe liver disease or renal failure

Contraindications**
- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 100 of 220

What is the mechanism of action of exenatide?

- A. Glucagon inhibitor
- B. Dipeptidyl peptidase-4 (DPP-4) inhibitor
- C. Glucagon-like peptide-1 (GLP-1) mimetic
- D. Incretin inhibitor
- E. Alpha-glucosidase inhibitor

Question 100 of 220

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Exenatide = Glucagon-like peptide-1 (GLP-1) mimetic

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)
- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide
- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)
- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors
- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 101 of 220

A 24-year-old with a history of Crohn's disease is started on azathioprine. What is the mechanism of action of azathioprine?

- A. Inhibits purine synthesis
- B. Inhibits inosine monophosphate dehydrogenase
- C. Mercaptopurine antagonist
- D. Thiopurine methyltransferase inhibitor
- E. Causes cross-linking in DNA

Question 101 of 220

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Azathioprine

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and lower doses of azathioprine should be used

Question 102 of 220

A 45-year-old man is prescribed bupropion to help him quit smoking. What is the mechanism of action of bupropion?

- A. Nicotinic receptor partial agonist
- B. Selective serotonin reuptake inhibitor
- C. Norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- D. Dopamine agonist
- E. Dopamine antagonist

Question 102 of 220

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- ✓ C. Norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- D. Dopamine agonist
- E. Dopamine antagonist

Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Question 103 of 220

A 45-year-old man presents to the Emergency Department stating he has drunk a bottle of antifreeze. Which one of the following features are least associated with this kind of poisoning?

- A. Metabolic acidosis with high anion gap
- B. Acute renal failure
- C. Hypertension
- D. Confusion
- E. Loss of vision

Question 103 of 220

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- B. Acute renal failure
- C. Hypertension
- D. Confusion
- ✓ E. Loss of vision

Loss of vision is seen in methanol rather than ethylene glycol poisoning

Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

Question 104 of 220

What is the mechanism of action of aminophylline?

- A. Leukotriene receptor antagonists
- B. Beta 2-adrenoceptor agonist
- C. Muscarinic receptor antagonist
- D. Phosphodiesterase inhibitor
- E. Beta 2-adrenoceptor antagonist

Question 104 of 220

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- B. Beta 2-adrenoceptor agonist
- C. Muscarinic receptor antagonist
- ✓ D. Phosphodiesterase inhibitor
- E. Beta 2-adrenoceptor antagonist

This is a rather unfair question as the mechanism of action of theophyllines has yet to be fully unravelled

Theophylline

Theophylline, like caffeine, is one of the naturally occurring methylxanthines. The main use of theophyllines in clinical medicine is as a bronchodilator in the management of asthma and COPD

The exact mechanism of action has yet to be discovered. One theory suggests theophyllines may be a non-specific inhibitor of phosphodiesterase resulting in an increase in cAMP. Other proposed mechanisms include antagonism of adenosine and prostaglandin inhibition

Theophylline poisoning

Features
- acidosis, hypokalaemia
- vomiting
- tachycardia, arrhythmias
- seizures

Management
- activated charcoal
- charcoal haemoperfusion is preferable to haemodialysis

Question 105 of 220

Which one of the following drugs is most likely to cause impaired glucose tolerance?

- A. Sulfasalazine
- B. Azathioprine
- C. Leflunomide
- D. Methotrexate
- E. Tacrolimus

Question 105 of 220

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Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

Question 106 of 220

Which one of the following drugs cannot be cleared by haemodialysis?

- A. Aspirin
- B. Tricyclics
- C. Lithium
- D. Barbiturates
- E. Aminophylline

Question 106 of 220

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Haemodialysis in overdose

Drugs that can be cleared with haemodialysis - mnemonic: BLAST
- Barbiturate
- Lithium
- Alcohol (inc methanol, ethylene glycol)
- Salicylates
- Theophyllines (charcoal haemoperfusion is preferable)

Drugs which cannot be cleared with haemodialysis include
- tricyclics
- benzodiazepines
- dextropropoxyphene (Co-proxamol)
- digoxin
- beta-blockers

Question 107 of 220

Which one of the following enzymes is involved in phase I drug metabolism?

- A. UDP-glucuronosyl transferases
- B. Pyruvate carboxylase
- C. Succinic dehydrogenase
- D. N-acetyl transferases
- E. Alcohol dehydrogenase

Question 107 of 220

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Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

First-pass metabolism
This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are need orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil

Questions concerning zero-order kinetics and acetylator status are also common in the MRCP

Zero-order kinetics
Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

Acetylator status
50% of the UK population are deficient in hepatic N-acetyltransferase
Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Question 108 of 220

A 67-year-old female is found to have decreased visual acuity during follow-up in the medical outpatient clinic. Which one of the following drugs is most likely to be the cause?

- A. Amiodarone
- B. Sodium valproate
- C. Methotrexate
- D. Frusemide
- E. Amoxicillin

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- C. Methotrexate
- D. Frusemide
- E. Amoxicillin

Amiodarone therapy can result in both corneal opacities and optic neuritis

Drugs causing visual disturbance

Cataracts
- steroids

Corneal opacities
- amiodarone
- indomethacin

Optic neuritis
- ethambutol
- amiodarone
- metronidazole

Retinopathy
- chloroquine, quinine

Sildenafil can cause both blue discolouration and non-arteritic anterior ischaemic neuropathy

Question 109 of 220

Which one of the following patients should not automatically be prescribed a statin in the absence of any contraindication?

- A. A 51-year-old man who had a myocardial infarction 4 years ago and is now asymptomatic
- B. A 57-year-old female smoker with a 10-year cardiovascular risk of 23%
- C. A 53-year-old man with intermittent claudication
- D. A 62-year-old man who had a transient ischaemic attack 10 months ago
- E. A 37-year-old man with well controlled diabetes mellitus type 1

Question 109 of 220

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Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 110 of 220

A 65-year-old man with a history of type 2 diabetes mellitus and ischaemic heart disease presents with erectile dysfunction. It is decided to try sildenafil therapy. Which one of the following existing medications may be continued without qualification?

- A. GTN spray
- B. Nicorandil
- C. Nateglinide
- D. Doxazosin
- E. Isosorbide mononitrate

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The BNF recommends avoiding alpha-blockers for 4 hours after sildenafil

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications
- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Adverse effects
- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects

Question 111 of 220

A 55-year-old man who has a history of ischaemic heart disease presents with myalgia. His long-term medications include aspirin, simvastatin and atenolol. Given his statin use a creatine kinase is measured and reported as follows:

Creatine kinase 1,420 u/l (< 190 u/l)

His problems seem to have followed the prescription of a new medication. Which one of the following is most likely to have caused the elevation in creatine kinase?

- A. Rifampicin
- B. Felodipine
- C. Clarithromycin
- D. Isosorbide mononitrate
- E. Amitriptyline

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- E. Amitriptyline

This patient has developed statin-induced myopathy secondary to clarithromycin, which is a known inhibitor of the CYP3A4 enzyme system.

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
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Question 112 of 220

A 19-year-old female is brought to the Emergency Department by her friends following a night out. Her friends state she has taken an unknown drug whilst out clubbing. Which one of the following features would most point towards the use of ecstasy?

- A. Temperature of 39.5ºC
- B. Respiratory depression
- C. Hypernatraemia
- D. Miosis
- E. Urinary incontinence

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- D. Miosis
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Ecstasy poisoning

Ecstasy (MDMA, 3,4-Methylenedioxymethamphetamine) use became popular in the 1990's during the emergence of dance music culture

Clinical features
- neurological: agitation, anxiety, confusion, ataxia
- cardiovascular: tachycardia, hypertension
- water intoxication
- hyperthermia
- rhabdomyolysis

Management
- supportive
- dantrolene may be used for hyperthermia if simple measures fail

Question 113 of 220

Which one of the following statements regarding drug metabolism is incorrect?

- A. Reduction is an example of a phase I reaction
- B. The majority of both phase I and phase II reactions take place in the liver
- C. Aspirin undergoes extensive first-pass metabolism
- D. Products of phase I reactions are typically more lipid soluble
- E. Products of phase II reactions are typically inactive and excreted in urine or bile

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- E. Products of phase II reactions are typically inactive and excreted in urine or bile

Usually both phase I and II reactions decrease lipid solubility

Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are need orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil

Questions concerning zero-order kinetics and acetylator status are also common in the MRCP

Zero-order kinetics

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

Acetylator status

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Question 114 of 220

Low molecular weight heparin has the greatest inhibitory effect on which one of the following proteins involved in the coagulation cascade?

- A. Factor IXa
- B. Factor XIa
- C. Factor Xa
- D. Thrombin
- E. Factor XIIa

Question 114 of 220

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- ✓ C. Factor Xa
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- E. Factor XIIa

Heparin

Heparin can be given as either unfractionated, intravenous heparin, or low molecular weight heparin (LMWH), given subcutaneously. Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

Heparin overdose may be reversed by protamine sulphate

Question 115 of 220

A 26-year-old female is commenced on carbamazepine for complex partial seizures. She has no previous medical history of note and consumes a moderate amount of alcohol. Three months later she is admitted due to series of seizures and carbamazepine levels are noted to be subtherapeutic. A pill-count reveals the patient is fully compliant. What is the most likely explanation?

- A. Auto-inhibition of liver enzymes
- B. Prescription of omeprazole
- C. Prescription of fluoxetine
- D. Auto-induction of liver enzymes
- E. Alcohol binge

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Carbamazepine is an inducer of the P450 system. This in turn increases the metabolism of carbamazepine itself - auto-induction

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 116 of 220

A 47-year-old female is reviewed in the neurology clinic. She was diagnosed with epilepsy whilst a teenager and her seizures are well controlled. She is however concerned about increasing numbness of her fingers and soles of her feet. Which one of the following medications is most likely to be responsible?

- A. Phenytoin
- B. Lamotrigine
- C. Sodium valproate
- D. Ethosuximide
- E. Levetiracetam

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- E. Levetiracetam

Peripheral neuropathy is a known adverse effect of phenytoin

Phenytoin: side-effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute
- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic
- common: gingival hyperplasia, hirsuitism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic
- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic
- associated with cleft palate and congenital heart disease

*although not listed in the BNF

Question 117 of 220

Which one of the following is an absolute contraindication to combined oral contraceptive pill use?

- A. Controlled hypertension
- B. History of cholestasis
- C. Women more than 35 years old and smoking more than 15 cigarettes/day
- D. BMI of 38 kg/m^2
- E. Migraine without aura

Question 117 of 220

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Combined oral contraceptive pill: contraindications

The decision of whether to start a women on the combined oral contraceptive pill is now guided by the UK Medical Eligibility Criteria (UKMEC). This scale categorises the potential cautions and contraindications according to a four point scale, as detailed below:

- UKMEC 1: a condition for which there is no restriction for the use of the contraceptive method
- UKMEC 2: advantages generally outweigh the disadvantages
- UKMEC 3: disadvantages generally outweigh the advantages
- UKMEC 4: represents an unacceptable health risk

Examples of UKMEC 3 conditions include

- more than 35 years old and smoking less than 15 cigarettes/day
- BMI 35-39 kg/m^2
- migraine without aura and more than 35 years old
- family history of thromboembolic disease in first degree relatives < 45 years
- controlled hypertension
- immobility e.g. wheel chair use
- breast feeding 6 weeks - 6 months postpartum

Examples of UKMEC 4 conditions include

- more than 35 years old and smoking more than 15 cigarettes/day
- BMI > 40 kg/m^2
- migraine with aura
- history of thromboembolic disease or thombogenic mutation
- history of stroke or ischaemic heart disease
- uncontrolled hypertension
- breast cancer
- major surgery with prolonged immobilisation

Diabetes mellitus diagnosed > 20 years ago is classified as UKMEC 3 or 4 depending on severity

Question 118 of 220

Which of the following drugs is least likely to be affected by a patients acetylator status?

- A. Hydralazine
- B. Isoniazid
- C. Rifampicin
- D. Procainamide
- E. Sulphonamides

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Question 119 of 220

Which one of the following side-effects is least recognised in patients taking isotretinoin?

- A. Hypertension
- B. Teratogenicity
- C. Nose bleeds
- D. Depression
- E. Raised triglycerides

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- E. Raised triglycerides

Isotretinoin adverse effects
- teratogenicity - females MUST be taking contraception
- low mood
- dry eyes and lips
- raised triglycerides
- hair thinning
- nose bleeds

Hypertension is not listed in the British National Formulary as a side-effect

Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

Adverse effects
- teratogenicity: females MUST be using two forms of contraception (e.g. combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Question 120 of 220

A 22-year-old man consults you as he and his housemate have been feeling generally unwell for the past few weeks. Which one of the following is the most common symptom seen in carbon monoxide poisoning?

- A. Hyperpyrexia
- B. Nausea
- C. Cherry red skin
- D. Confusion
- E. Headache

Question 120 of 220

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- C. Cherry red skin
- D. Confusion
- ✓ E. Headache

Carbon monoxide poisoning - most common feature = headache

Cherry red skin is a sign of severe toxicity and is usually seen post-mortem

Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity
- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels
- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management
- 100% oxygen
- hyperbaric oxygen

Indications for hyperbaric oxygen*
- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

Question 121 of 220

Which one of the following drugs is most likely to cause impaired glucose tolerance?

- A. Bezafibrate
- B. Simvastatin
- C. Nicotinic acid
- D. Cholestyramine
- E. Gemfibrozil

Question 121 of 220

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Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

Question 122 of 220

Which of the following drugs is considered least likely to precipitate an attack of acute intermittent porphyria?

- A. Diazepam
- B. Penicillin
- C. Thiopentone
- D. Sulphonamides
- E. Alcohol

Question 122 of 220

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Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack
- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use
- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin

Question 123 of 220

A 76-year-old woman is diagnosed with Alzheimer's disease. Which one of the following could be a contraindication to the prescription of donepezil?

- A. History of depression
- B. Sick sinus syndrome
- C. Concurrent simvastatin therapy
- D. Concurrent citalopram therapy
- E. Ischaemic heart disease

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- E. Ischaemic heart disease

Donepezil may cause bradycardia and atrioventricular node block.

Alzheimer's disease

Alzheimer's disease is a progressive degenerative disease of the brain accounting for the majority of dementia seen in the UK

Genetics

- most cases are sporadic
- 5% are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form
- apoprotein E allele E4 - encodes a cholesterol transport protein

Pathological changes

- macroscopic = widespread cerebral atrophy, particularly involving the cortex and hippocampus
- microscopic = intraneuronal neurofibrillary tangles, neuronal plaques, deficiency of neurons
- biochemical = deposition of type A-Beta-amyloid protein in cortex, deficit of Ach from damage to an ascending forebrain projection

Neurofibrillary tangles

- paired helical filaments are partly made from a protein called tau
- in AD are tau proteins are excessively phosphorylated

Management

- cholinesterase inhibitor (e.g. donepezil) - currently licensed for patients with Alzheimer’s disease of moderate severity only, classified as a Mini-Mental State Examination (MMSE) score of 10-20 out of 30

Question 124 of 220

A 61-year-old female is reviewed in the rheumatology clinic with increasing shortness of breath. She has been on long-term drug therapy to control her rheumatoid arthritis and has a 40 pack-year history os smoking . Her oxygen saturations on room air are on 89%. Investigations reveal the following:

FEV1%	80%
Transfer factor coefficient (TLCO)	41%

What is the most likely cause for her symptoms?

- A. Pulmonary nodules
- B. Methotrexate pneumonitis
- C. Pulmonary haemorrhage
- D. Bronchiolitis obliterans
- E. Chronic obstructive pulmonary disease

Question 124 of 220

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- E. Chronic obstructive pulmonary disease

A FEV1% of 80% would not support a diagnosis of COPD or bronchiolitis obliterans. Methotrexate pneumonitis is potentially life-threatening and occurs in 1-5% of patients who are treated with methotrexate. Pulmonary fibrosis should be part of the differential diagnosis

Rheumatoid arthritis: pulmonary manifestations

A variety of respiratory problems may be seen in patients with rheumatoid arthritis:

- pulmonary fibrosis
- pleural effusion
- pulmonary nodules
- bronchiolitis obliterans
- complications of drug therapy e.g. methotrexate pneumonitis
- pleurisy
- Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure
- infection (possibly atypical) secondary to immunosuppression

Question 125 of 220

A 65-year-old man with a history of ischaemic heart disease is admitted with chest pain. The 12-hour troponin T is negative. During admission his medications were altered to reduce the risk of cardiovascular disease and to treat previously undiagnosed type 2 diabetes mellitus. Shortly after discharge he presents to his GP complaining of diarrhoea. Which one of the following medications is most likely to be responsible?

- A. Gliclazide
- B. Clopidogrel
- C. Rosiglitazone
- D. Metformin
- E. Atorvastatin

Question 125 of 220

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- C. Rosiglitazone
- ✓ D. Metformin
- E. Atorvastatin

Gastrointestinal problems are a common side-effect of many medications but are frequently seen in patients taking metformin

If this patient had a raised troponin T then metformin may not be suitable as it is contraindicated following recent episodes of tissue hypoxia.

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action
- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects
- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis* with severe liver disease or renal failure

Contraindications**
- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 126 of 220

Which one of the following is a mixed alpha and beta adrenoceptor antagonist?

- A. Doxazosin
- B. Phenoxybenzamine
- C. Yohimbine
- D. Propranolol
- E. Carvedilol

Question 126 of 220

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Adrenoceptor antagonists

Alpha antagonists
- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists
- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

Question 127 of 220

Which one of the following is an established indication for the use of Botulinum toxin?

- A. Strabismus
- B. Hirschsprung's disease
- C. Blepharospasm
- D. Bell's palsy
- E. Upper limb rigidity in Parkinson's disease

Question 127 of 220

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Botulinum toxin

As well as the well publicised cosmetic uses of Botulinum toxin ('Botox') there are also a number of licensed indications:

- blepharospasm
- hemifacial spasm
- focal spasticity including cerebral palsy patients, hand and wrist disability associated with stroke
- spasmodic torticollis
- severe hyperhidrosis of the axillae
- achalasia

Question 128 of 220

A 52-year-old homeless man is admitted with suspected ethylene glycol toxicity. Following admission to the High Dependency Unit it is decided to give fomepizole. What is the mechanism of action of fomepizole?

- A. Competitive inhibitor of aldehyde dehydrogenase
- B. Binds to glycoaldehyde
- C. Binds to glycolic acid
- D. Promotes renal excretion of ethylene glycol
- E. Competitive inhibitor of alcohol dehydrogenase

Question 128 of 220

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- D. Promotes renal excretion of ethylene glycol
- ✓ E. Competitive inhibitor of alcohol dehydrogenase

Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

Question 129 of 220

Which of the following conditions may not be treated by dopamine receptor agonists?

- A. Parkinson's disease
- B. Prolactinoma
- C. Nausea
- D. Cyclical breast disease
- E. Acromegaly

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Dopamine receptor agonists

Indications
- Parkinson's disease
- prolactinoma/galactorrhoea
- cyclical breast disease
- acromegaly

Currently accepted practice in the management of patients with Parkinson's disease is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, L-dopa is sometimes used as an initial treatment

Overview
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Adverse effects
- nausea/vomiting
- postural hypotension
- hallucinations
- daytime somnolence

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 130 of 220

Which one of the following drugs is contra-indicated whilst breast feeding?

- A. Aminophylline
- B. Carbamazepine
- C. Sodium valproate
- D. Methyldopa
- E. Amiodarone

Question 130 of 220

Which one of the following drugs is contra-indicated whilst breast feeding?

- A. Aminophylline
- B. Carbamazepine
- C. Sodium valproate
- D. Methyldopa
- ✓ E. Amiodarone

Breast feeding: contraindications

The major breastfeeding contraindications tested in exams relate to drugs (see below). Other contraindications of note include:

- galactosaemia
- viral infections - this is controversial with respect to HIV in the developing world. This is because there is such an increased infant mortality and morbidity associated with bottle feeding that some doctors think the benefits outweigh the risk of HIV transmission

Drug contraindications - always check the BNF

The following drugs can be given to mothers who are breast feeding:

- antibiotics: penicillins, cephalosporins, trimethoprim
- endocrine: glucocorticoids (avoid high doses), levothyroxine*
- epilepsy: sodium valproate, carbamazepine
- asthma: salbutamol, theophyllines
- psychiatric drugs: tricyclic antidepressants, antipsychotics**
- hypertension: beta-blockers, hydralazine, methyldopa
- anticoagulants: warfarin, heparin
- digoxin

The following drugs should be avoided:

- antibiotics: ciprofloxacin, tetracycline, chloramphenicol, sulphonamides
- psychiatric drugs: lithium, benzodiazepines
- aspirin
- carbimazole
- sulphonylureas
- cytotoxic drugs
- amiodarone

*the BNF advises that the amount is too small to affect neonatal hypothyroidism screening

**clozapine should be avoided

Question 131 of 220

A 61-year-old man with peripheral arterial disease is prescribed simvastatin. What is the most appropriate blood test monitoring?

- A. LFTs + creatinine kinase at baseline, 1-3 months and at intervals of 6 months for 1 year
- B. LFTs at baseline and every 3 months for first year
- C. Routine blood tests not recommended
- D. LFTs at baseline and annually
- E. LFTs at baseline, 1-3 months and at intervals of 6 months for 1 year

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- D. LFTs at baseline and annually
- ✓ E. LFTs at baseline, 1-3 months and at intervals of 6 months for 1 year

A fasting lipid profile may also be checked during monitoring to assess response to treatment. Recent NICE guidelines for monitoring patients on statins vary slightly to the BNF - see below

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 132 of 220

Which of the following drugs is least likely to cause cholestasis?

- A. Gliclazide
- B. Amiodarone
- C. Chlorpromazine
- D. Oral contraceptive pill
- E. Co-amoxiclav

Question 132 of 220

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Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 133 of 220

A 46-year-old man is admitted to hospital with chest pain. An ECG shows an anterior ST elevation myocardial infarction and he receives thrombolysis. His past medical history includes hypertension and he drinks around 70 units of alcohol per week. Three days following admission he becomes confused. What treatment is most likely to help?

- A. Benzodiazepines
- B. Thiamine
- C. Frusemide
- D. Renal angioplasty
- E. Neurosurgical referral

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The most likely cause for confusion in this man is alcohol withdrawal which should be treated with benzodiazepines in the acute phase. Wernicke's encephalopathy can cause confusion, but questions would normally hint at more classical features such as ataxia, ophthalmoplegia or nystagmus. Also, if there were focal signs or failure to improve with benzodiazepines then a CT scan should be performed to exclude a subdural, given that he has a history of alcohol excess and has been thrombolysed

Alcohol withdrawal

Mechanism
- chronic alcohol consumption enhances GABA mediated inhibition in the CNS (similar to benzodiazepines) and inhibits NMDA-type glutamate receptors
- alcohol withdrawal is thought to be lead to the opposite (decreased inhibitory GABA and increased NMDA glutamate transmission)

Features
- symptoms start at 6-12 hours
- peak incidence of seizures at 36 hours
- peak incidence of delirium tremens is at 72 hours

Management
- benzodiazepines
- carbamazepine also effective in treatment of alcohol withdrawal
- phenytoin is said not to be as effective in the treatment of alcohol withdrawal seizures

Question 134 of 220

A 62-year-old man presents four weeks after initiating metformin for type 2 diabetes mellitus. His body mass index is 27.5 kg/m^2. Despite slowly titrating the dose up to 500mg tds he has experienced significant diarrhoea. He has tried reducing the dose back down to 500mg bd but his symptoms persisted. What is the most appropriate action?

- A. Switch to pioglitazone 15mg od
- B. Switch to gliclazide 40mg od
- C. Start modified release metformin 500mg od with evening meal
- D. Add loperamide as required
- E. Arrange colonoscopy

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- ✓ C. Start modified release metformin 500mg od with evening meal
- D. Add loperamide as required
- E. Arrange colonoscopy

If a patient is intolerant to standard metformin then modified release preparations should be tried

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action
- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects
- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis* with severe liver disease or renal failure

Contraindications**
- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 135 of 220

Which one of the following symptom is least associated with salicylate overdose?

- A. Tremor
- B. Tinnitus
- C. Hyperventilation
- D. Seizures
- E. Nausea

Question 135 of 220

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Salicylate overdose

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

Features
- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

Treatment
- general (ABC, charcoal)
- urinary alkalinization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

Indications for haemodialysis in salicylate overdose
- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure
- pulmonary oedema
- seizures
- coma

*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production

Question 136 of 220

Which one of the following drugs is least likely to cause gynaecomastia?

- A. Spironolactone
- B. Sodium valproate
- C. Digoxin
- D. Cimetidine
- E. Anabolic steroids

Question 136 of 220

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- C. Digoxin
- D. Cimetidine
- E. Anabolic steroids

Whilst sodium valproate may rarely causes gynaecomastia it is much more common after taking the other listed drugs.

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia
- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

Drug causes of gynaecomastia
- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia
- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

Question 137 of 220

A patient presents to the Emergency Department following the development of an urticarial skin rash following the introduction of a new drug. Which one of the following is most likely to be responsible?

- A. Omeprazole
- B. Sodium valproate
- C. Aspirin
- D. Paracetamol
- E. Simvastatin

Question 137 of 220

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- ✓ C. Aspirin
- D. Paracetamol
- E. Simvastatin

Aspirin is a common cause of urticaria

Although all medications can potentially cause urticaria it is commonly seen secondary to aspirin

Drug causes of urticaria

The following drugs commonly cause urticaria:

- aspirin
- penicillins
- NSAIDs
- opiates

Question 138 of 220

Which one of the following unwanted effects is most likely to occur in patients taking gliclazide?

- A. Peripheral neuropathy
- B. Cholestasis
- C. Photosensitivity
- D. Syndrome of inappropriate ADH secretion
- E. Increased appetite and weight gain

Question 138 of 220

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- C. Photosensitivity
- D. Syndrome of inappropriate ADH secretion
- ✓ E. Increased appetite and weight gain

All of the above may be seen in patients taking sulfonylureas but increased appetite in most commonly seen

Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present.

Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- increased appetite and weight gain

Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- photosensitivity
- peripheral neuropathy

Sulfonylureas should be avoided in breast feeding and pregnancy

Question 139 of 220

A 19-year-old man presents to the Emergency Department 5 hours ingesting 20g of paracetamol. N-acetyl cysteine is started straight away. What is the mechanism of action of N-acetyl cysteine?

- A. Replenishes glutathione
- B. Inhibits P450 mixed function oxidases
- C. Replenishes glucuronic acid
- D. Promotes formation of N-acetyl-B-benzoquinone imine
- E. Neutralises mercapturic acid

Question 139 of 220

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Paracetamol overdose: metabolic pathways

The liver normally conjugates paracetamol with glucuronic acid/sulphate. During an overdose the conjugation system becomes saturated leading to oxidation by P450 mixed function oxidases*. This produces a toxic metabolite (N-acetyl-B-benzoquinone imine)

Normally glutathione acts as a defence mechanism by conjugating with the toxin forming the non-toxic mercapturic acid. If glutathione stores run-out, the toxin forms covalent bonds with cell proteins, denaturing them and leading to cell death. This occurs not only in hepatocytes but also in the renal tubules

N-acetyl cysteine is used in the management of paracetamol overdose as it is a precursor of glutathione and hence can increase hepatic glutathione production

*this explains why there is a lower threshold for treating patients who take P450 inducing medications e.g. phenytoin or rifampicin

Question 140 of 220

A 34-year-old man who is known to have glucose-6-phosphate dehydrogenase deficiency presents with symptoms of a urinary tract infection. He is prescribed an antibiotic. A few days later he becomes unwell and is noticed by his partner to be pale and jaundiced. What drug is mostly likely to have been prescribed?

- A. Co-amoxiclav
- B. Trimethoprim
- C. Ciprofloxacin
- D. Cefalexin
- E. Erythromycin

Question 140 of 220

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- ✓ C. Ciprofloxacin
- D. Cefalexin
- E. Erythromycin

The sulfamethoxazole in co-trimoxazole causes haemolysis in G6PD, not the trimethoprim

G6PD deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in a X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Features
- neonatal jaundice is often seen
- intravascular haemolysis
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

Some drugs causing haemolysis
- anti-malarials: primaquine
- ciprofloxacin
- sulphonamides

Some drugs thought to be safe
- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Question 141 of 220

A 67-year-old female is prescribed simvastatin for hyperlipidaemia. Which one of the following may potentially interact with her medication?

- A. Orange juice
- B. Apple juice
- C. Grapefruit juice
- D. Cranberry juice
- E. Carrot juice

Question 141 of 220

A 67-year-old female is prescribed simvastatin for hyperlipidaemia. Which one of the following may potentially interact with her medication?

- A. Orange juice
- B. Apple juice
- ✓ C. Grapefruit juice
- D. Cranberry juice
- E. Carrot juice

Grapefruit juice is a potent inhibitor of the cytochrome P450 enzyme CYP3A4

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 142 of 220

Which one of the following statements regarding raloxifene in the management of osteoporosis is incorrect?

- A. Has been shown to prevent bone loss and to reduce the risk of vertebral fractures
- B. Is a selective oestrogen receptor modulator
- C. May worsen menopausal symptoms
- D. Increases risk of thromboembolic events
- E. Increases the risk of breast cancer

Question 142 of 220

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- ✓ E. Increases the risk of breast cancer

Question 143 of 220

A 47-year-old lorry driver presents following the development of a widespread urticarial rash. This is associated with pruritus. What is the most appropriate medication to help relieve the itch?

- A. Cetirizine
- B. Loratadine
- C. Chlorphenamine
- D. Ranitidine
- E. Alimemazine

Question 143 of 220

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- ✓ B. Loratadine
- C. Chlorphenamine
- D. Ranitidine
- E. Alimemazine

The obvious concern in a lorry driver is drowsiness. Of the non-sedating antihistamines there is some evidence that cetirizine causes more drowsiness than loratadine

Antihistamines

Antihistamines are of value in the treatment of allergic rhinitis and urticaria. Of the non-sedating antihistamines there is some evidence that cetirizine may cause more drowsiness than other drugs in the class

Question 144 of 220

What is the mechanism of action of ciclosporin?

- A. Monoclonal antibody against IL-2 receptor
- B. Interferes with purine synthesis
- C. Inhibits inosine monophosphate dehydrogenase
- D. Decreases IL-2 release by inhibiting calcineurin
- E. Mercaptopurine antagonist

Question 144 of 220

What is the mechanism of action of ciclosporin?

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- B. Interferes with purine synthesis
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- E. Mercaptopurine antagonist

Ciclosporin - decreases IL-2 release by inhibiting calcineurin

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin
- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications
- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 145 of 220

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

- A. Photosensitivity rash
- B. Agranulocytosis
- C. Hypokalaemia
- D. Pancreatitis
- E. Hirsuitism

Question 145 of 220

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

- A. Photosensitivity rash
- B. Agranulocytosis
- C. Hypokalaemia
- D. Pancreatitis
- ✓ E. Hirsuitism

Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide currently is in hypertension (part of the effect is due to vasodilation)

Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects

- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

Question 146 of 220

A 44-year-old man asks for advice. He is due to go on a long bus journey but suffers from debilitating motion sickness. Which one of the following medications is most likely to prevent motion sickness?

- A. Cyclizine
- B. Chlorpromazine
- C. Metoclopramide
- D. Prochlorperazine
- E. Domperidone

Question 146 of 220

A 44-year-old man asks for advice. He is due to go on a long bus journey but suffers from debilitating motion sickness. Which one of the following medications is most likely to prevent motion sickness?

- ✓ A. Cyclizine
- B. Chlorpromazine
- C. Metoclopramide
- D. Prochlorperazine
- E. Domperidone

Motion sickness - hyoscine > cyclizine > promethazine

Motion sickness

Motion sickness describes the nausea and vomiting which occurs when an apparent discrepancy exists between visually perceived movement and the vestibular systems sense of movement

Management

- the BNF recommends hyoscine (e.g. transdermal patch) as being the most effective treatment. Use is limited due to side-effects
- non-sedating antihistamines such as cyclizine or cinnarizine are recommended in preference to sedating preparation such as promethazine

Question 147 of 220

A 23-year-old female is commenced on varenicline to help her stop smoking. Which one of the following adverse effects is most likely to occur?

- A. Vivid dreams
- B. Nausea
- C. Constipation
- D. Insomnia
- E. Drug-induced lupus

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- ✓ B. Nausea
- C. Constipation
- D. Insomnia
- E. Drug-induced lupus

Whilst all of the above adverse effects may occur nausea is the most common

Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Question 148 of 220

A 36-year-old former intravenous drug user is to commence treatment for hepatitis C with interferon-alpha and ribavirin. Which adverse effects of interferon-alpha treatment are most likely to occur?

- A. Diarrhoea and transient rise in ALT
- B. Cough and haemolytic anaemia
- C. Flu-like symptoms and transient rise in ALT
- D. Haemolytic anaemia and flu-like symptoms
- E. Depression and flu-like symptoms

Question 148 of 220

A 36-year-old former intravenous drug user is to commence treatment for hepatitis C with interferon-alpha and ribavirin. Which adverse effects of interferon-alpha treatment are most likely to occur?

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- B. Cough and haemolytic anaemia
- C. Flu-like symptoms and transient rise in ALT
- D. Haemolytic anaemia and flu-like symptoms
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Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha
- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

IFN-beta
- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

IFN-gamma
- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

Question 149 of 220

A 76-year-old man presents with lower urinary tract symptoms. Following a digital rectal examination and prostate specific antigen test a diagnosis of benign prostatic hyperplasia is made and finasteride is started. What is the mechanism of action of this drug?

- A. Alpha-1 antagonist
- B. 5-alpha receptor antagonist
- C. Testosterone receptor antagonist
- D. Alpha-1 agonists
- E. Inhibits conversion of testosterone to dihydrotestosterone

Question 149 of 220

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- B. 5-alpha receptor antagonist
- C. Testosterone receptor antagonist
- D. Alpha-1 agonists
- ✓ E. Inhibits conversion of testosterone to dihydrotestosterone

Finasteride: 5 alpha-reductase inhibitor - inhibits conversion of testosterone to dihydrotestosterone

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

Risk factors
- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:
- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

Management options
- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin
- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride
- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

Question 150 of 220

A 62-year-old man is reviewed in diabetes clinic. His glycaemic control is poor despite weight loss, adherence to a diabetic diet and his current diabetes medications. He has no other past medical history of note. Which one of the following medications would increase insulin sensitivity?

- A. Repaglinide
- B. Tolbutamide
- C. Pioglitazone
- D. Acarbose
- E. Gliclazide

Question 150 of 220

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- B. Tolbutamide
- ✓ C. Pioglitazone
- D. Acarbose
- E. Gliclazide

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 151 of 220

Which of the following is least likely to be a precipitating factor in digoxin toxicity?

- A. Hypernatraemia
- B. Hypocalcaemia
- C. Hypokalaemia
- D. Hypothermia
- E. Hypomagnesaemia

Question 151 of 220

Which of the following is least likely to be a precipitating factor in digoxin toxicity?

- A. Hypernatraemia
- ✓ B. Hypocalcaemia
- C. Hypokalaemia
- D. Hypothermia
- E. Hypomagnesaemia

Hyper-, not hypocalcaemia may be a precipitating factor in digoxin toxicity

Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now used mainly in the management of atrial fibrillation.

Actions
- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the Na^+/K^+ ATPase pump

Digoxin toxicity

Features
- generally unwell, lethargy, nausea & vomiting, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors
- classically: hypokalaemia*
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion)

Management
- Digibind
- correct arrhythmias
- monitor K^+

*hyperkalaemia may also worsen digoxin toxicity

Question 152 of 220

What is the mode of action of bisphosphonates?

- A. Promotes osteoblasts
- B. Promotes calcium absorption
- C. Antagonist of PTH
- D. Inhibit osteoclasts
- E. Promotes phosphate excretion

Question 152 of 220

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- E. Promotes phosphate excretion

Bisphosphonates inhibit osteoclasts

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses
- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metatases

Adverse effects
- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw

The BNF suggests the following counselling for patients taking oral bisphosphonates
- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

Question 153 of 220

A 54-year-old man with a history of ischaemic heart disease is currently taking atorvastatin 40mg at night. A repeat lipid profile is ordered:

Total cholesterol	3.9 mmol/l
HDL	0.7 mmol/l
LDL	2.6 mmol/l
Triglycerides	1.2 mmol/l

What would be the most effective way of increasing HDL levels?

- A. Add nicotinic acid
- B. Add ezetimibe
- C. Switch atorvastatin to pravastatin
- D. Add bezafibrate
- E. Add colestyramine

Question 153 of 220

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Nicotinic acid increases HDL levels

Nicotinic acid

Nicotinic acid is used in the treatment of patients with hyperlipidaemia, although its use is limited by side-effects. As well as lowering cholesterol and triglyceride concentrations it also raises HDL levels

Adverse effects

- flushing
- impaired glucose tolerance
- myositis

Question 154 of 220

Thrombocytopenia is associated with each of the following drugs except:

- A. Abciximab
- B. Quinine
- C. Warfarin
- D. Penicillin
- E. Sodium valproate

Question 154 of 220

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Drug-induced thrombocytopenia

Drug-induced thrombocytopenia (probable immune mediated)

- quinine
- abciximab
- NSAIDS
- diuretics: furosemide
- antibiotics: penicillins, sulphonamides, rifampicin
- anticonvulsants: carbamazepine, valproate
- heparin

Question 155 of 220

A 14-year-old girl is taken to the Emergency Department, after being found lying on her bed next to an empty bottle of pills prescribed for her mother. On examination she is agitated, has a clenched jaw and her eyes are deviated upwards. Which drug is she most likely to have consumed?

- A. Phenytoin
- B. Metoclopramide
- C. Amitriptyline
- D. Carbamazepine
- E. Nifedipine

Question 155 of 220

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- C. Amitriptyline
- D. Carbamazepine
- E. Nifedipine

This is a classic description of an oculogyric crisis, a form of extrapyramidal disorder

Oculogyric crisis

An oculogyric crisis is a dystonic reaction to certain drugs or medical conditions

Features
- restlessness, agitation
- involuntary upward deviation of the eyes

Causes
- phenothiazines
- haloperidol
- metoclopramide
- postencephalitic Parkinson's disease.

Question 156 of 220

Each one of the following is a feature of mercury poisoning, except:

- A. Paraesthesia
- B. Epistaxis
- C. Renal tubular acidosis
- D. Visual field defects
- E. Hearing loss

Question 156 of 220

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- A. Paraesthesia
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- C. Renal tubular acidosis
- D. Visual field defects
- E. Hearing loss

Mercury poisoning

Features
- paraesthesia
- visual field defects
- hearing loss
- irritability
- renal tubular acidosis

Question 157 of 220

A 36-year-old man with difficult to control epilepsy is reviewed in clinic. He is currently taking phenytoin but presents due to fatigue. A full blood count is performed:

Hb 10.1 g/dl

MCV 121 fl

Plt 234 * 10^9/l

WCC 4.6 *10^9/l

What is the most likely cause for his tiredness?

- A. Iron deficiency
- B. Vitamin B12 deficiency
- C. Liver dysfunction secondary to phenytoin
- D. Haemolytic anaemia secondary to phenytoin
- E. Folate deficiency

Question 157 of 220

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- ✓ E. Folate deficiency

Phenytoin: side-effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute
- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic
- common: gingival hyperplasia, hirsuitism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic
- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic
- associated with cleft palate and congenital heart disease

*although not listed in the BNF

Question 158 of 220

What is the mechanism of action of tacrolimus?

- A. Mercaptopurine antagonist
- B. Interferes with purine synthesis
- C. Inhibits inosine monophosphate dehydrogenase
- D. Monoclonal antibody against IL-2 receptor
- E. Decreases IL-2 release by inhibiting calcineurin

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Tacrolimus

Tacrolimus is a macrolide used as an immunosuppressant to prevent transplant rejection. It has a very similar action to ciclosporin:

Action of ciclosporin

- decreases clonal proliferation of T cells by reducing IL-2 release
- binds to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

The action of tacrolimus differs in that it binds to a protein called FKBP rather than cyclophilin

Tacrolimus is more potent than ciclosporin and hence the incidence of organ rejection is less. However, nephrotoxicity and impaired glucose tolerance is more common

Question 159 of 220

A 33-year-old woman is prescribed varenicline to help her quit smoking. What is the mechanism of action of varenicline?

- A. Norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- B. Dopamine agonist
- C. Dopamine antagonist
- D. Selective serotonin reuptake inhibitor
- E. Nicotinic receptor partial agonist

Question 159 of 220

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Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Question 160 of 220

Which of the following drugs is most likely to cause impaired glucose tolerance?

- A. Bromocriptine
- B. Interferon-alpha
- C. Strontium
- D. Imipramine
- E. Montelukast

Question 160 of 220

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- ✓ B. Interferon-alpha
- C. Strontium
- D. Imipramine
- E. Montelukast

Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

Question 161 of 220

A 29-year-old woman is admitted to the Emergency Department with carbon monoxide poisoning. High-flow oxygen is applied on arrival. Which one of the following is not an indication for hyperbaric oxygen therapy?

- A. A carboxyhaemoglobin concentration of 16%
- B. Arrhythmia
- C. Seizures
- D. Loss of consciousness when initially found by paramedics
- E. Pregnancy

Question 161 of 220

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- D. Loss of consciousness when initially found by paramedics
- E. Pregnancy

Heavy smokers may have a carboxyhaemoglobin concentration of 10-15%

Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity
- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels
- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management
- 100% oxygen
- hyperbaric oxygen

Indications for hyperbaric oxygen*
- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

Question 162 of 220

A 34-year-old man with a history of migraine finds that paracetamol taken at the recommend dose often fails to relieve his acute attacks. He drinks 12 units of alcohol per week and smokes 15 cigarettes per day.

What factor is likely to contribute to this problem?

- A. Bacterial overgrowth
- B. Delayed gastric emptying
- C. P450 enzyme induction
- D. First pass metabolism
- E. P450 enzyme inhibition

Question 162 of 220

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Patients with migraine experience delayed gastric emptying during acute attacks. For this reason analgesics are often combined prokinetic agents such as metoclopramide. Paracetamol metabolism would not be significantly affected by changes in P450 enzyme activity (e.g. through smoking or drinking)

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment

Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis

Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 163 of 220

Which one of the following may reduce the effects of adenosine?

- A. Dipyridamole
- B. Diltiazem
- C. Clopidogrel
- D. Amiodarone
- E. Aminophylline

Question 163 of 220

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- C. Clopidogrel
- D. Amiodarone
- ✓ E. Aminophylline

Adenosine
- dipyridamole enhances effect
- aminophylline reduces effect

Adenosine

The effects of adenosine are enhanced by dipyridamole (anti-platelet agent) and blocked by theophyllines. It should be avoided in asthmatics due to possible bronchospasm

Adverse effects
- chest pain
- bronchospasm
- can enhance conduction down accessory pathways, resulting in increased ventricular rate (e.g. WPW syndrome)

Question 164 of 220

Which of the following drugs is least likely to cause cholestasis?

- A. Anabolic steroids
- B. Erythromycin
- C. Prochlorperazine
- D. Halothane
- E. Flucloxacillin

Question 164 of 220

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Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 165 of 220

A 30-year-old woman who is 7 weeks pregnant presents with dysuria and urinary frequency. A urine dipstick is positive for nitrites and leucocytes. Of the options given, what is the most suitable antibiotic to use?

- A. Ciprofloxacin
- B. Cefalexin
- C. Trimethoprim + folic acid 5mg
- D. Doxycycline
- E. Nitrofurantoin

Question 165 of 220

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- ✓ B. Cefalexin
- C. Trimethoprim + folic acid 5mg
- D. Doxycycline
- E. Nitrofurantoin

Amoxicillin is also recommended in this situation.

Urinary tract infection in adults: management

Lower urinary tract infections in women (cystitis)
- local antibiotic guidelines should be followed if available
- Clinical Knowledge Summaries (CKS) recommend trimethoprim or nitrofurantoin for 3 days

Lower urinary tract infections in pregnancy
- asymptomatic bacteriuria is screened for on the booking visit and should be treated with an antibiotic for 7 days (sensitivities should already be available)
- for acute lower urinary tract infections consider amoxicillin or an oral cephalosporin for 7 days*

For patients with sign of acute pyelonephritis hospital admission should be considered
- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum cephalosporin or a quinolone for 10-14 days
- Clinical Knowledge Summaries recommend ciprofloxacin for 7 days or co-amoxiclav for 14 days

*CKS also mention the use of trimethoprim and nitrofurantoin. Trimethoprim is a folate antagonist and concerns have been raised regarding the potential risk of neural tube defects. Manufacturers advise to avoid. Whilst short-term trimethoprim use is unlikely to cause folate deficiency it would seem reasonable to use an antibiotic such as amoxicillin first-line. Nitrofurantoin should be avoided at term because of the risk of neonatal haemolysis

Question 166 of 220

A 24-year-old woman presents following a sudden, acute onset of pain at the back of the ankle whilst jogging, during which she heard a cracking sound. Which one of the following medications may have contributed to this injury?

- A. Metronidazole
- B. Nitrofurantoin
- C. Fluconazole
- D. Ciprofloxacin
- E. Terbinafine

Question 166 of 220

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- ✓ D. Ciprofloxacin
- E. Terbinafine

This patient has classical signs of Achilles tendon rupture. Tendon damage is a well documented complication of quinolone therapy. It appears to be an idiosyncratic reaction, with the actual median duration of treatment being 8 days before problems occur

Quinolones

Quinolones are a group of antibiotics which work by inhibiting DNA synthesis and are bactericidal in nature. Examples include:

- ciprofloxacin
- levofloxacin

Adverse effects

- lower seizure threshold in patients with epilepsy
- tendon damage (including rupture) - the risk is increased in patients also taking steroids

Question 167 of 220

A patient is given ondansetron for chemotherapy related nausea. What is the most likely side-effect?

- A. Constipation
- B. Dry mouth
- C. Insomnia
- D. Visual disturbance
- E. Pruritus

Question 167 of 220

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- C. Insomnia
- D. Visual disturbance
- E. Pruritus

Whilst all the above may occur constipation is most common

5HT3 antagonists

5HT3 antagonists are antiemetics used mainly in the management of chemotherapy related nausea

Examples
- ondansetron
- granisetron

Question 168 of 220

A 27-year-old woman is started on risperidone for schizophrenia. Which receptor does risperidone have the highest affinity for?

- A. Dopamine D1 receptor
- B. Serotonin 5-HT2A receptor
- C. Alpha-adrenoceptor
- D. Histamine H1 receptor
- E. Dopamine D2 receptor

Question 168 of 220

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- C. Alpha-adrenoceptor
- D. Histamine H1 receptor
- E. Dopamine D2 receptor

This question is tough and very small print. Risperidone is an atypical antipsychotic agent that displays 5-HT2A receptor antagonism. The receptor affinity (Ki) values are 0.4 and 3.13 nM for 5-HT2A and D2 receptors respectively

Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics
- weight gain
- olanzapine and risperidone are associated with an increased risk of stroke in elderly patients
- clozapine is associated with agranulocytosis (see below)

Examples of atypical antipsychotics
- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine
- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Question 169 of 220

A 71-year-old man is prescribed digoxin for new onset atrial fibrillation. His doctor explains that the full effect will not be seen for one week. Which one of the following is responsible for this delayed effect?

- A. Clearance
- B. Volume of distribution
- C. Absorption
- D. First pass metabolism
- E. Half-life

Question 169 of 220

A 71-year-old man is prescribed digoxin for new onset atrial fibrillation. His doctor explains that the full effect will not be seen for one week. Which one of the following is responsible for this delayed effect?

- A. Clearance
- B. Volume of distribution
- C. Absorption
- D. First pass metabolism
- ✓ E. Half-life

The half-life of digoxin is around 36-48 hours. This results in a delay before steady plasma levels are seen

Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now used mainly in the management of atrial fibrillation.

Actions
- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the Na^+/K^+ ATPase pump

Digoxin toxicity

Features
- generally unwell, lethargy, nausea & vomiting, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors
- classically: hypokalaemia*
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion)

Management
- Digibind
- correct arrhythmias
- monitor K^+

*hyperkalaemia may also worsen digoxin toxicity

Question 170 of 220

A 43-year-old man presents with known acute intermittent porphyria is brought to the Emergency Department by the police due to an acute psychosis. What is the most suitable drug for sedation?

- A. Chloral hydrate
- B. Diazepam
- C. Phenobarbitone
- D. Chlorpromazine
- E. Primidone

Question 170 of 220

A 43-year-old man presents with known acute intermittent porphyria is brought to the Emergency Department by the police due to an acute psychosis. What is the most suitable drug for sedation?

- A. Chloral hydrate
- B. Diazepam
- C. Phenobarbitone
- ✓ D. Chlorpromazine
- E. Primidone

Chlorpromazine is considered safe to use in patients with acute intermittent porphyria. The other drugs are classified as unsafe

Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack
- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use
- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin

Question 171 of 220

A 54-year-old man is investigated for recurrent episodes of abdominal pain associated with weakness of his arms and legs. Which one of the following urine tests would best indicate lead toxicity?

- A. Haemoglobinuria
- B. Coproporphyrin
- C. Porphobilinogen
- D. Uroporphyrin
- E. Ham's test

Question 171 of 220

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- D. Uroporphyrin
- E. Ham's test

Lead poisoning

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs

Features
- abdominal pain
- peripheral neuropathy (mainly motor)
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

Investigations
- microcytic anaemia
- blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)

Management - various chelating agents are currently used:
- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol

Question 172 of 220

Which one of the following side-effects is not recognised in patients taking sodium valproate?

- A. Alopecia
- B. Weight gain
- C. Hepatitis
- D. Induction P450 system
- E. Teratogenicity

Question 172 of 220

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- C. Hepatitis
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- E. Teratogenicity

Sodium valproate causes inhibition of the P450 system

Sodium valproate

Sodium valproate is used in the management epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity

Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- teratogenic

Question 173 of 220

Each of the following drugs are known to inhibit cytochrome P450, except:

- A. Ketoconazole
- B. Ciprofloxacin
- C. Erythromycin
- D. Clopidogrel
- E. Amiodarone

Question 173 of 220

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P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include
- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include
- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Question 174 of 220

A 45-year-old female with a history of bipolar disorder presents with an acute confusional state. Which one of the following drugs is most likely to precipitate lithium toxicity?

- A. Sodium valproate
- B. Atenolol
- C. Aminophylline
- D. Sodium bicarbonate
- E. Bendroflumethiazide

Question 174 of 220

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C. Aminophylline

D. Sodium bicarbonate

✓ E. Bendroflumethiazide

Both sodium bicarbonate and aminophylline may reduce plasma concentrations of lithium. Sodium valproate is not listed in the BNF as interacting with lithium

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:
- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects
- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 175 of 220

A 62-year-old female is reviewed in the nurse-led heart failure clinic. Despite current treatment with furosemide, bisoprolol, enalapril and spironolactone she remains breathless on minimal exertion. On examination the chest is clear to auscultation and there is minimal ankle oedema

Recent results are as follows:

ECG	Sinus rhythm, rate 84 bpm
Chest x-ray	Cardiomegaly, clear lung fields
Echo	Ejection fraction 35%

What additional medication would best help her symptoms?

- A. Bosentan
- B. Isosorbide mononitrate
- C. Diltiazem
- D. Ivabradine
- E. Digoxin

Question 175 of 220

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- B. Isosorbide mononitrate
- C. Diltiazem
- D. Ivabradine
- ✓ E. Digoxin

Digoxin may be useful in this situation whether the patient is in atrial fibrillation or not. Whilst it has not been shown to be of prognostic benefit it may help reduce symptoms. In the United States a large proportion of patients with heart failure take digoxin for this reason. Another option to consider in such a patient would be a biventricular pacemaker (cardiac resynchronization therapy)

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

Whilst spironolactone has been shown to improve prognosis in patients with chronic heart failure, no long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide

NICE produced guidelines on management in 2003, key points include:

- all patients should be given an ACE inhibitor unless contradictions exist
- once an ACE inhibitor has been introduced a beta-blocker should be started regardless of whether the patient is still symptomatic
- offer annual influenza vaccine
- offer pneumococcal vaccine

Digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

Question 176 of 220

Which one of the following drugs does not characteristically undergo extensive first-pass metabolism?

- A. Propranolol
- B. Glyceryl trinitrate
- C. Diazepam
- D. Aspirin
- E. Verapamil

Question 176 of 220

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- E. Verapamil

Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are need orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil

Questions concerning zero-order kinetics and acetylator status are also common in the MRCP

Zero-order kinetics

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

Acetylator status

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Question 177 of 220

A 65-year-old female with metastatic breast cancer is reviewed in clinic. Her husband reports that she is increasingly confused and occasionally appears to talk to relatives that are not in the room. Following investigations for reversible causes, what is the most appropriate management?

- A. Subcutaneous midazolam
- B. Oral lithium
- C. Oral haloperidol
- D. Oral diazepam
- E. Oral quetiapine

Question 177 of 220

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- ✓ C. Oral haloperidol
- D. Oral diazepam
- E. Oral quetiapine

Oral haloperidol is the most appropriate treatment here. If the patient was in the terminal phase and agitated then subcutaneous midazolam would be indicated

Palliative care prescribing: agitation and confusion

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness (for example a patient on the Care of the Dying pathway) then agitation or restlessness is best treated with midazolam

Question 178 of 220

A 44-year-old woman with oestrogen receptor positive breast cancer comes for review, three months after starting tamoxifen. Which one of the following adverse effects is most likely to occur in this patient?

- A. Myalgia
- B. Cataracts
- C. Alopecia
- D. Hot flushes
- E. Cervical cancer

Question 178 of 220

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- ✓ D. Hot flushes
- E. Cervical cancer

Alopecia and cataracts are listed in the BNF as possible side-effects. They are however not as prevalent as hot flushes, which are very common in pre-menopausal women

Tamoxifen

Tamoxifen is a selective estrogen receptor modulator (SERM) which acts as an oestrogen receptor antagonist and partial agonist. It is used in the management of oestrogen receptor positive breast cancer

Adverse effects

- menstrual disturbance: vaginal bleeding, amenorrhoea
- hot flushes
- venous thromboembolism
- endometrial cancer

Raloxifene is a pure oestrogen receptor antagonist, and carries a lower risk of endometrial cancer

Question 179 of 220

A 54-year-old man is diagnosed with type 2 diabetes mellitus. A decision is made to start simvastatin 40mg. What is the ideal time to advise patients to take this medication?

- A. After breakfast
- B. Last thing in the evening
- C. After evening meal
- D. Just before evening meal
- E. First thing in the morning

Question 179 of 220

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Taking simvastatin at night improves efficacy

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months

**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 180 of 220

A 31-year-old female with a history of epilepsy consults you following an uneventful pregnancy. Which one of the following drugs would it be safe to continue during breast feeding?

- A. Phenytoin
- B. Carbamazepine
- C. Lamotrigine
- D. Sodium valproate
- E. All of the above

Question 180 of 220

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- C. Lamotrigine
- D. Sodium valproate
- ✓ E. All of the above

Breast feeding is acceptable with nearly all anti-epileptic drugs

The BNF states 'breast-feeding is acceptable with all antiepileptic drugs, taken in normal doses, with the possible exception of barbiturates'

Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects

Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- phenytoin: associated with cleft palate

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

Question 181 of 220

Which one of the following is least associated with an increased risk of hepatotoxicity following a paracetamol overdose?

- A. History of alcohol dependence
- B. Carbamazepine use
- C. Anorexia nervosa
- D. Chronic renal failure
- E. HIV

Question 181 of 220

Which one of the following is least associated with an increased risk of hepatotoxicity following a paracetamol overdose?

- A. History of alcohol dependence
- B. Carbamazepine use
- C. Anorexia nervosa
- ✓ D. Chronic renal failure
- E. HIV

Paracetamol overdose: risk factors

The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose:

- chronic alcohol excess
- patients on P450 enzyme inducers (rifampicin, phenytoin, carbamazepine)
- anorexia nervosa: decreased glutathione stores
- HIV

Question 182 of 220

What is the most appropriate time to take blood samples for therapeutic monitoring of phenytoin levels?

- A. At any time
- B. 12 hours after last dose
- C. 6 hours after last dose
- D. 4 hours after last dose
- E. Immediately before next dose

Question 182 of 220

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- D. 4 hours after last dose
- ✓ E. Immediately before next dose

Therapeutic drug monitoring

Lithium
- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

Ciclosporin
- trough levels immediately before dose

Digoxin
- at least 6 hrs post-dose

Phenytoin
- trough levels immediately before dose

Question 183 of 220

In the Vaughan Williams classification of antiarrhythmics disopyramide is an example of a:

- A. Class Ia agent
- B. Class Ib agent
- C. Class Ic agent
- D. Class II agent
- E. Class IV agent

Question 183 of 220

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- B. Class Ib agent
- C. Class Ic agent
- D. Class II agent
- E. Class IV agent

Antiarrhythmics: Vaughan Williams classification

The Vaughan Williams classification of antiarrhythmics is still widely used although it should be noted that a number of common drugs are not included in the classification e.g. adenosine, atropine, digoxin and magnesium

Class	Example	Mechanism of action
Ia	Disopyramide	Block sodium channels
Ib	Lidocaine	Block sodium channels
Ic	Flecainide	Block sodium channels
II	Propranolol	Beta-adrenoceptor antagonists
III	Amiodarone	Block potassium channels
IV	Verapamil	Calcium channel blockers

Question 184 of 220

Which one of the following medications is least associated with the development of methaemoglobinaemia?

- A. Phenytoin
- B. Sulphonamides
- C. Dapsone
- D. Sodium nitroprusside
- E. Primaquine

Question 184 of 220

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- C. Dapsone
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Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes
- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes
- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features
- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO2 but decreased oxygen saturation

Management
- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

Question 185 of 220

A 69-year-old man who takes warfarin for atrial fibrillation asks for advice. He is due to have a tooth extraction at the dentist and is unsure what to do with regards to his 'blood-thinning' tablets. There is no other past medical history of note. The last INR was taken two weeks ago and reported as 2.8 with his target INR being 2.0-3.0. What is the most appropriate advice?

- A. Admit to hospital + switch to subcutaneous low-molecular weight heparin prior to extraction
- B. Switch to aspirin prior to extraction
- C. Check INR 72 hours before procedure, proceed if INR < 4.0
- D. Check INR 72 hours before procedure, proceed if INR < 2.5
- E. Admit to hospital + switch to intravenous heparin prior to extraction

Question 185 of 220

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- D. Check INR 72 hours before procedure, proceed if INR < 2.5
- E. Admit to hospital + switch to intravenous heparin prior to extraction

Dentistry in warfarinised patients - check INR 72 hours before procedure, proceed if INR < 4.0

The BNF gives specific advice with regards to this, in the section 'Prescribing in dental practice'. If a patient has a history of an unstable INR then it should be checked within 24 hours of the dental procedure.

Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C

Factors that may potentiate warfarin
- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

Side-effects
- haemorrhage
- teratogenic
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

Question 186 of 220

Which one of the following dopamine receptor agonists used in the management of Parkinson's disease is least associated with pulmonary, retroperitoneal and pericardial fibrosis?

- A. Pergolide
- B. Lisuride
- C. Bromocriptine
- D. Cabergoline
- E. Ropinirole

Question 186 of 220

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- D. Cabergoline
- ✓ E. Ropinirole

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment

Dopamine receptor agonists
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Levodopa
- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors
- e.g. selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine
- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors
- e.g. entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics
- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 187 of 220

Which one of the following is not a recognised adverse effect of phenytoin use?

- A. Slurred speech
- B. Nystagmus
- C. Gynaecomastia
- D. Diplopia
- E. Ataxia

Question 187 of 220

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Phenytoin: side-effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute
- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic
- common: gingival hyperplasia, hirsuitism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic
- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic
- associated with cleft palate and congenital heart disease

*although not listed in the BNF

Question 188 of 220

A 71-year-old woman who takes warfarin for atrial fibrillation presents with bruising on her hands and arms. A blood test is arranged:

Hb 14.7 g/dl

Plt 198 * 10^9/l

WBC 5.3 * 10^9/l

INR 7.1

What is the most appropriate management?

- A. Stop warfarin + restart when INR < 3.0
- B. Intravenous vitamin K 0.5mg + stop warfarin + restart when INR < 5.0
- C. Stop warfarin + restart when INR < 5.0
- D. Stop warfarin + restart when INR < 5.0 + give low-molecular weight heparin until warfarin restarted
- E. Oral vitamin K 5mg + stop warfarin + restart when INR < 3.0

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- D. Stop warfarin + restart when INR < 5.0 + give low-molecular weight heparin until warfarin restarted
- E. Oral vitamin K 5mg + stop warfarin + restart when INR < 3.0

Reversal of anticoagulation is not indicated as the INR is less than 8.0 and there is no evidence of bleeding.

Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding

Major bleeding	Stop warfarin Vitamin K 5mg IV Prothrombin complex concentrate - if not available then FFP*
INR > 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0 If risk factors for bleeding then give vitamin K 0.5mg IV or 5mg po. Risk factors include: • age > 70 years • first year of warfarin therapy • history of gastrointestinal bleeding • hypertension • alcohol excess Dose can be repeated after 24 hours if INR still high
INR 6.0 - 8.0 **No bleeding or minor bleeding**	Stop warfarin, restart when INR < 5.0

*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

Question 189 of 220

Which one of the following statements regarding amiodarone-induced thyrotoxicosis (AIT) is correct?

A. AIT type 2 should be treated with corticosteroids

B. Amiodarone should be continued in the majority of patients

C. Carbimazole is contraindicated in AIT type 1

D. Goitre is usually present in AIT type 2

E. AIT type 1 is due to a amiodarone-related destructive thyroiditis

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- C. Carbimazole is contraindicated in AIT type 1
- D. Goitre is usually present in AIT type 2
- E. AIT type 1 is due to a amiodarone-related destructive thyroiditis

Amiodarone and the thyroid gland

Around 1 in 6 patients taking amiodarone develop thyroid dysfunction

Amiodarone-induced hypothyroidism

The pathophysiology of amiodarone-induced hypothyroidism (AIH) is thought to be due to the high iodine content of amiodarone causing a Wolff-Chaikoff effect*

Amiodarone may be continued if this is desirable

Amiodarone-induced thyrotoxicosis

Amiodarone-induced thyrotoxicosis (AIT) may be divided into two types:

	AIT type 1	AIT type 2
Pathophysiology	Excess iodine-induced thyroid hormone synthesis	Amiodarone-related destructive thyroiditis
Goitre	Present	Absent
Management	Carbimazole or potassium perchlorate	Corticosteroids

Unlike in AIH, amiodarone should be stopped if possible in patients who develop AIT

*an autoregulatory phenomenon where thyroxine formation is inhibited due to high levels of circulating iodide

Question 190 of 220

A confused 45-year-old man is admitted to the Emergency Department. He tells staff he has drank two bottles of antifreeze. On examination his pulse is 120 bpm and blood pressure is 140/90 mmHg. Arterial blood gases show an uncompensated metabolic acidosis. He is transferred to the high dependency unit and ethanol is given via a nasogastric tube. What is the mechanism of action of ethanol in this patient?

- A. Binds to glycolic acid
- B. Inhibits aldehyde dehydrogenase
- C. Inhibits alcohol dehydrogenase
- D. Competes with ethylene glycol for alcohol dehydrogenase
- E. Binds to glycoaldehyde

Question 190 of 220

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Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

Question 191 of 220

A 14-year-old is seen in the Emergency Department. She was diagnosed with having migraines three years ago and requests advice about options for treating an acute attack. Which one of the following medications is it least suitable to recommend?

- A. Aspirin
- B. Paracetamol + metoclopramide
- C. Paracetamol + codeine
- D. Ibuprofen
- E. Paracetamol

Question 191 of 220

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- C. Paracetamol + codeine
- D. Ibuprofen
- E. Paracetamol

Avoid aspirin in children < 16 years as risk of Reye's syndrome

Aspirin should be avoided in children due to the risk of Reye's syndrome.

Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. SIGN released guidelines on migraine management in 2008

Acute treatment

Standard analgesia
- first-line therapy
- e.g. paracetamol, ibuprofen, aspirin
- may be poorly absorbed, often combined with anti-emetic e.g. metoclopramide* to relieve associated nausea

Triptans
- second-line therapy
- specific 5-HT1 agonists - opposes vasodilation

Ergotamine
- alpha-blocker and a partial 5-HT1 agonist
- now rarely used due to high incidence of adverse effects (e.g. nausea and vomiting)
- listed in the BNF as 'less suitable for prescribing'

Prophylaxis

Prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients

First-line
- beta-blockers: propranolol 80-240mg od

Also recommended in the SIGN guidelines
- sodium valproate
- topiramate (CKS recommend this is used under specialist supervision)
- gabapentin
- amitriptyline
- venlafaxine

The SIGN guidelines also suggest that stress management and acupuncture may be useful

5-HT2 antagonists
- pizotifen: used less commonly now due to adverse effects (weight gain and drowsiness)
- methysergide: very rarely used as associated with retroperitoneal fibrosis

*caution should be exercised with young patients as acute dystonic reactions may develop

Question 192 of 220

A 55-year-old diabetic man presents to clinic concerned about erectile dysfunction. What is the mechanism of action of sildenafil?

- A. Phosphodiesterase type V inhibitor
- B. Nitric oxide synthetase inhibitor
- C. Nitric oxide donor
- D. Non-selective phosphodiesterase inhibitor
- E. Phosphodiesterase type IV inhibitor

Question 192 of 220

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- E. Phosphodiesterase type IV inhibitor

Sildenafil is a phosphodiesterase type V inhibitor

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications
- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Adverse effects
- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects

Question 193 of 220

A 45-year-old man develops toxic epidermal necrolysis following a change in his epilepsy medication. He is systemically unwell and is admitted to ITU for supportive care. What is the most appropriate treatment?

- A. Intravenous immunoglobulin
- B. Cyclophosphamide
- C. Supportive care only
- D. Pulsed methylprednisolone
- E. Plasmapheresis

Question 193 of 220

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- D. Pulsed methylprednisolone
- E. Plasmapheresis

Toxic epidermal necrolysis

Toxic epidermal necrolysis (TEN) is a potentially life-threatening skin disorder that is most commonly seen secondary to a drug reaction. In this condition the skin develops a scalded appearance over an extensive area. Some authors consider TEN to be the severe end of a spectrum of skin disorders which includes erythema multiforme and Stevens-Johnson syndrome

Features
- systemically unwell e.g. pyrexia, tachycardic
- positive Nikolsky's sign: the epidermis separates with mild lateral pressure

Drugs known to induce TEN
- phenytoin
- sulphonamides
- allopurinol
- penicillins
- carbamazepine
- NSAIDs

Management
- stop precipitating factor
- supportive care, often in intensive care unit
- intravenous immunoglobulin has been shown to be effective and is now commonly used first-line
- other treatment options include: immunosuppressive agents (ciclosporin and cyclophosphamide), plasmapheresis

Question 194 of 220

A 55-year-old man is prescribed sibutramine to try and help him lose weight. He currently has a body mass index of 34 kg/m^2. After initiating therapy what is the most important type of monitoring to perform?

- A. Visual acuity
- B. Liver function tests
- C. Anxiety and depression levels
- D. QT interval on ECG
- E. Blood pressure

Question 194 of 220

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- C. Anxiety and depression levels
- D. QT interval on ECG
- ✓ E. Blood pressure

Obesity: therapeutic options

The management of obesity consists of a step-wise approach:
- conservative: diet, exercise
- medical
- surgical

Orlistat is a pancreatic lipase inhibitor used in the management of obesity. Adverse effects include faecal urgency/incontinence and flatulence. A lower dose version is now available without prescription ('Alli'). NICE have defined criteria for the use of orlistat. It should only be prescribed as part of an overall plan for managing obesity in adults who have:
- BMI of 28 kg/m^2 or more with associated risk factors, or
- BMI of 30 kg/m^2 or more
- continued weight loss e.g. 5% at 3 months
- orlistat is normally used for < 1 year

Sibutramine
- centrally acting appetite suppressant (inhibits uptake of serotonin and noradrenaline at hypothalamic sites that regular food intake)
- adverse effects include hypertension (monitor blood pressure and pulse during treatment), constipation, headache, dry mouth, insomnia and anorexia
- contraindicated in psychiatric illness, hypertension, IHD, stroke, arrhythmias

Rimonabant, a specific CB1 cannabinoid receptor antagonist, was withdrawn in October 2008 after the European Medicines Agency warned of serious psychiatric problems including suicide

Question 195 of 220

Which one of the following statements regarding the management of pregnant women with severe pre-eclampsia and eclampsia is incorrect?

- A. Intravenous fluids should be given to prevent renal failure
- B. Magnesium sulphate treatment should continue for 24 hours post-partum
- C. Problems are only seen after 20 weeks gestation
- D. Reflexes should be monitored during magnesium sulphate infusion
- E. Magnesium sulphate is given to both prevent and treat seizures

Question 195 of 220

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- C. Problems are only seen after 20 weeks gestation
- D. Reflexes should be monitored during magnesium sulphate infusion
- E. Magnesium sulphate is given to both prevent and treat seizures

Severe pre-eclampsia - restrict fluids

Pulmonary and cerebral oedema are important causes of morbidity and mortality in severe pre-eclampsia

Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

Question 196 of 220

A 72-year-old man with metastatic small cell lung cancer is admitted to the local hospice for symptom control. His main problem at the moment is intractable hiccups. What is the most appropriate management?

- A. Chlorpromazine
- B. Codeine phosphate
- C. Diazepam
- D. Methadone
- E. Phenytoin

Question 196 of 220

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- C. Diazepam
- D. Methadone
- E. Phenytoin

Hiccups in palliative care - chlorpromazine or haloperidol

Haloperidol may also be used

Palliative care prescribing: hiccups

Management of hiccups

- chlorpromazine is licensed for the treatment of intractable hiccups
- haloperidol, gabapentin and baclofen are also used

Question 197 of 220

A 45-year-old man with a known history of seafood allergy is admitted to the Emergency Department. He developed an itchy skin rash whilst having dinner at a restaurant. On examination he has widespread urticaria but no facial or neck swelling. His respiratory rate is 30 per minute with oxygen sats of 99% on room air. The blood pressure is 168/90 mmHg and the pulse 104 bpm. Intravenous hydrocortisone and chlorpheniramine are given. What is the most appropriate next step in management?

- A. Inhaled adrenaline
- B. Observe
- C. Subcutaneous adrenaline
- D. Intravenous adrenaline
- E. Intramuscular adrenaline

Question 197 of 220

A 45-year-old man with a known history of seafood allergy is admitted to the Emergency Department. He developed an itchy skin rash whilst having dinner at a restaurant. On examination he has widespread urticaria but no facial or neck swelling. His respiratory rate is 30 per minute with oxygen sats of 99% on room air. The blood pressure is 168/90 mmHg and the pulse 104 bpm. Intravenous hydrocortisone and chlorpheniramine are given. What is the most appropriate next step in management?

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- D. Intravenous adrenaline
- E. Intramuscular adrenaline

Giving adrenaline is not without its risks, but very few severe adverse effects are seen with intramuscular adrenaline The 2005 ALS guidelines suggest giving adrenaline if there is stridor, wheeze, respiratory distress or clinical signs of shock.

We've had much feedback regarding this question, with many *Candida*tes stating they would give IM adrenaline in a real life situation. It is the opinion of the authors that the question is testing *Candida*tes knowledge of the ALS protocol and hence we would recommend giving the above answer in an exam situation. What do you think? Let us know

It could of course be argued that a raised respiratory rate and tachycardia are early signs of shock in a young person, but these may be secondary to anxiety

What do you think? - let us know.

Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications
- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection
- local infiltration of phentolamine

Question 198 of 220

A 55-year-old man presents with multiple erythematous target lesions two days after starting a new medication. Which one of the following drugs is most likely to have been started?

- A. Levetiracetam
- B. Olanzapine
- C. Carbamazepine
- D. Fluoxetine
- E. Diazepam

Question 198 of 220

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- B. Olanzapine
- ✓ C. Carbamazepine
- D. Fluoxetine
- E. Diazepam

This patient appears to have erythema multiforme which is a known complication of carbamazepine use

Erythema multiforme

Erythema multiforme
- target lesions (typically worse on peripheries e.g. palms and soles)
- severe = Stevens-Johnson syndrome (blistering and mucosal involvement)

Causes
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- viruses: herpes simplex virus, Orf
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. systemic lupus erythematosus
- sarcoidosis
- malignancy

Question 199 of 220

A 70-year-old woman is reviewed. She sustained a fracture of her wrist one year ago, following which a DEXA scan was performed. This showed a T-score of -2.8 SD. Calcium and vitamin D supplementation was started along with oral alendronate. This however was stopped due to oesophagitis. In accordance with NICE guidelines, what is the most suitable next management step?

- A. Start hormone replacement therapy
- B. Start raloxifene
- C. Start teriparatide
- D. Switch to risedronate
- E. Refer for hip protectors

Question 199 of 220

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- A. Start hormone replacement therapy
- B. Start raloxifene
- C. Start teriparatide
- ✓ D. Switch to risedronate
- E. Refer for hip protectors

Question 200 of 220

Which of the following drugs is considered most likely to precipitate an attack of acute intermittent porphyria?

- A. Morphine
- B. Aspirin
- C. Atenolol
- D. Metformin
- E. Oral contraceptive pill

Question 200 of 220

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- A. Morphine
- B. Aspirin
- C. Atenolol
- D. Metformin
- ✓ E. Oral contraceptive pill

Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack
- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use
- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin

Question 201 of 220

Which one of the following is not a recognised side-effect of sildenafil?

- A. Blue discolouration of vision
- B. Tinnitus
- C. Flushing
- D. Nasal congestion
- E. Non-arteritic anterior ischaemic optic neuropathy

Question 201 of 220

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- A. Blue discolouration of vision
- ✓ B. Tinnitus
- C. Flushing
- D. Nasal congestion
- E. Non-arteritic anterior ischaemic optic neuropathy

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications
- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Adverse effects
- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects

Question 202 of 220

Each of the following are true regarding tricyclic overdose, except:

- A. Anticholinergic features are prominent early on
- B. Metabolic acidosis is a common complication
- C. ECG changes include prolongation of the QT interval
- D. Dialysis is indicated in severe toxicity
- E. QRS duration > 160ms is associated with ventricular arrhythmias

Question 202 of 220

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B. Metabolic acidosis is a common complication

C. ECG changes include prolongation of the QT interval

✓ D. Dialysis is indicated in severe toxicity

E. QRS duration > 160ms is associated with ventricular arrhythmias

Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to A&E departments

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:
- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:
- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated with ventricular arrhythmias

Management
- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. quinidine) and class Ic antiarrhythmics (e.g. flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

Question 203 of 220

Which one of the following drugs is least associated with pancytopaenia?

- A. Carbamazepine
- B. Carbimazole
- C. Lithium
- D. Gold
- E. Chloramphenicol

Question 203 of 220

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- ✓ C. Lithium
- D. Gold
- E. Chloramphenicol

Lithium is not commonly associated with pancytopaenia

Drug-induced pancytopaenia

Drug causes of pancytopaenia
- cytotoxics
- antibiotics: trimethoprim, chloramphenicol
- anti-rheumatoid: gold, penicillamine
- carbimazole*
- anti-epileptics: carbamazepine
- sulphonylureas: tolbutamide

*causes both agranulocytosis and pancytopaenia

Question 204 of 220

Where is the site of action of bendroflumethiazide?

- A. Proximal convoluted tubules
- B. Ascending loop of Henle
- C. Descending loop of Henle
- D. Distal convoluted tubules
- E. Macula densa

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Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide currently is in hypertension (part of the effect is due to vasodilation)

Common adverse effects
- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects
- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

Question 205 of 220

Which one of the following features is least associated with ecstasy poisoning?

- A. Rhabdomyolysis
- B. Hyperthermia
- C. Ataxia
- D. Hypertension
- E. Hypernatraemia

Question 205 of 220

Which one of the following features is least associated with ecstasy poisoning?

- A. Rhabdomyolysis
- B. Hyperthermia
- C. Ataxia
- D. Hypertension
- ✓ E. Hypernatraemia

Hyponatraemia may be seen secondary to water intoxication

Ecstasy poisoning

Ecstasy (MDMA, 3,4-Methylenedioxymethamphetamine) use became popular in the 1990's during the emergence of dance music culture

Clinical features
- neurological: agitation, anxiety, confusion, ataxia
- cardiovascular: tachycardia, hypertension
- water intoxication
- hyperthermia
- rhabdomyolysis

Management
- supportive
- dantrolene may be used for hyperthermia if simple measures fail

Question 206 of 220

Which of the following cytotoxic agents is most associated with ototoxicity?

- A. Vincristine
- B. Bleomycin
- C. Cisplatin
- D. Doxorubicin
- E. Cyclophosphamide

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 207 of 220

Which one of the following side-effects is most associated with ciclosporin use?

- A. Hepatotoxicity
- B. Bone marrow toxicity
- C. Red cell aplasia
- D. Haemorrhagic cystitis
- E. Tinnitus

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- C. Red cell aplasia
- D. Haemorrhagic cystitis
- E. Tinnitus

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications

- Crohn's disease
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- following organ transplantation
- pure red cell aplasia

Question 208 of 220

You are considering prescribing varenicline to a 45-year-old man who is trying to stop smoking. Which one of the following conditions is most likely to contradict the prescription of varenicline?

- A. Previous or current central nervous system tumour
- B. Past history of deliberate self-harm
- C. Hypertension
- D. Epilepsy
- E. Obesity

Question 208 of 220

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C. Hypertension

D. Epilepsy

E. Obesity

Varenicline should be used with caution in patients with a history of depression. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline.

Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Question 209 of 220

Which of the following is true regarding the pathophysiology of paracetamol overdose?

- A. Paracetamol is normally exclusively metabolised by the P450 system
- B. Paracetamol overdose leads to an excessive build up of mercapturic acid
- C. Conjugation of paracetamol becomes saturated in overdose
- D. Glutathione levels increase following paracetamol overdose leading to hepatocellular death
- E. N-acetyl cysteine acts by antagonising glutathione

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Paracetamol overdose: metabolic pathways

The liver normally conjugates paracetamol with glucuronic acid/sulphate. During an overdose the conjugation system becomes saturated leading to oxidation by P450 mixed function oxidases*. This produces a toxic metabolite (N-acetyl-B-benzoquinone imine)

Normally glutathione acts as a defence mechanism by conjugating with the toxin forming the non-toxic mercapturic acid. If glutathione stores run-out, the toxin forms covalent bonds with cell proteins, denaturing them and leading to cell death. This occurs not only in hepatocytes but also in the renal tubules

N-acetyl cysteine is used in the management of paracetamol overdose as it is a precursor of glutathione and hence can increase hepatic glutathione production

*this explains why there is a lower threshold for treating patients who take P450 inducing medications e.g. phenytoin or rifampicin

Question 210 of 220

A patient who was commenced on a simvastatin six months ago presents with generalised muscles aches. Which one of the following is not a risk factor for statin-induced myopathy?

- A. Female gender
- B. Large fall in LDL-cholesterol
- C. Low body mass index
- D. Advanced age
- E. History of diabetes mellitus

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- C. Low body mass index
- D. Advanced age
- E. History of diabetes mellitus

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the BNF advise performing liver function tests (LFTs) before and within 1-3 months of starting a statin and therefore at intervals of 6 months for 1 year*. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk = 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering**

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*this is the BNF advice, the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months
**current NICE guidelines do not recommend a target cholesterol in primary prevention

Question 211 of 220

Which of the following anti-retroviral drugs is a known inducer of cytochrome P450?

- A. Nevirapine
- B. Ritonavir
- C. Saquinavir
- D. Nelfinavir
- E. Zidovudine

Question 211 of 220

Which of the following anti-retroviral drugs is a known inducer of cytochrome P450?

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- B. Ritonavir
- C. Saquinavir
- D. Nelfinavir
- E. Zidovudine

HIV: anti-retrovirals - P450 interaction
- nevirapine (a NNRTI): induces P450
- protease inhibitors: inhibits P450

Like other protease inhibitors, ritonavir is a potent inhibitor of the P450 system

HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)
- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)
- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Question 212 of 220

A 34-year-old man with a history of bipolar disorder is admitted with acute confusion. Lithium levels confirm the clinical diagnosis of lithium toxicity. A decision is made to give sodium bicarbonate. What is the mechanism of action of sodium bicarbonate in this situation?

- A. Reduce gastrointestinal tract absorption
- B. Myocardial stabaliser
- C. Neutralises lithium ions
- D. Central nervous system membrane stabaliser
- E. Increases urine alkalinity

Question 212 of 220

A 34-year-old man with a history of bipolar disorder is admitted with acute confusion. Lithium levels confirm the clinical diagnosis of lithium toxicity. A decision is made to give sodium bicarbonate. What is the mechanism of action of sodium bicarbonate in this situation?

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- B. Myocardial stabaliser
- C. Neutralises lithium ions
- D. Central nervous system membrane stabaliser
- ✓ E. Increases urine alkalinity

Increasing the alkalinity of the urine promotes lithium excretion. The preferred treatment in severe cases would be haemodialysis

Lithium

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys

Mechanism of action - not fully understood, two theories:
- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects
- nausea/vomiting, diarrhoea
- fine tremor
- polyuria
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity
- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management
- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Question 213 of 220

Which one of the following is not a recognised side-effects of dopamine receptor agonists?

- A. Postural hypotension
- B. Daytime somnolence
- C. Galactorrhoea
- D. Nausea
- E. Hallucinations

Question 213 of 220

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- B. Daytime somnolence
- ✓ C. Galactorrhoea
- D. Nausea
- E. Hallucinations

Dopamine receptor agonists

Indications
- Parkinson's disease
- prolactinoma/galactorrhoea
- cyclical breast disease
- acromegaly

Currently accepted practice in the management of patients with Parkinson's disease is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, L-dopa is sometimes used as an initial treatment

Overview
- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

Adverse effects
- nausea/vomiting
- postural hypotension
- hallucinations
- daytime somnolence

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 214 of 220

Which of the following antibiotics is predominately bacteriostatic?

- A. Metronidazole
- B. Penicillins
- C. Isoniazid
- D. Sulphonamides
- E. Aminoglycosides

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Antibiotics: bactericidal vs. bacteriostatic

Bactericidal antibiotics
- penicillins
- cephalosporins
- aminoglycosides
- nitrofurantoin
- metronidazole
- quinolones
- rifampicin
- isoniazid

Bacteriostatic antibiotics
- chloramphenicol
- macrolides
- tetracyclines
- sulphonamides
- trimethoprim

Question 215 of 220

What is the mechanism of action of vildagliptin?

- A. Incretin inhibitor
- B. Dipeptidyl peptidase-4 (DPP-4) inhibitor
- C. Alpha-glucosidase inhibitor
- D. Glucagon inhibitor
- E. Glucagon-like peptide-1 (GLP-1) mimetic

Question 215 of 220

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Gliptins = Dipeptidyl peptidase-4 (DPP-4) inhibitors

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)
- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide
- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)
- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors
- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 216 of 220

A 56 year old man is treated with doxorubicin for transition cell carcinoma of the bladder. Which one of the following adverse effects is most characteristically associated with this drug?

- A. Ototoxicity
- B. Pulmonary fibrosis
- C. Peripheral neuropathy
- D. Cardiomyopathy
- E. Haemorrhagic cystitis

Question 216 of 220

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- E. Haemorrhagic cystitis

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 217 of 220

What is the most appropriate dose of adrenaline to give during a cardiac arrest?

- A. 1ml 1:100,000 IV
- B. 10ml 1:1,000 IV
- C. 0.5ml 1:1,000 IM
- D. 1ml 1:10,000 IV
- E. 10ml 1:10,000 IV

Question 217 of 220

What is the most appropriate dose of adrenaline to give during a cardiac arrest?

- A. 1ml 1:100,000 IV
- B. 10ml 1:1,000 IV
- C. 0.5ml 1:1,000 IM
- D. 1ml 1:10,000 IV
- ✓ E. 10ml 1:10,000 IV

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

10ml of the 1:10,000 preparation contains 1mg of adrenaline

Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications
- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses
- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection
- local infiltration of phentolamine

Question 218 of 220

Which of the following drugs is least likely to cause cholestasis?

- A. Erythromycin
- B. Nitrofurantoin
- C. Methyldopa
- D. Gliclazide
- E. Oral contraceptive pill

Question 218 of 220

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Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 219 of 220

A 33-year-old woman who is known to have familial hypercholesterolaemia comes for review. She is planning to have children and asks for advice regarding medication as she currently takes atorvastatin 80mg on. What is the most appropriate advice?

- A. Switch to atorvastatin 10mg
- B. Continue current drug at same dose
- C. Stop atorvastatin before trying to conceive
- D. Switch to ezetimibe
- E. Switch to simvastatin 40mg

Question 219 of 220

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- E. Switch to simvastatin 40mg

Statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the hepatic proteins involved in clearance of LDL-cholesterol from the circulation

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Question 220 of 220

Which of the following antibiotics act by inhibiting protein synthesis?

- A. Cephalosporins
- B. Gentamicin
- C. Rifampicin
- D. Trimethoprim
- E. Flucloxacillin

Question 220 of 220

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Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation
- penicillins
- cephalosporins

Inhibit protein synthesis
- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis
- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis
- rifampicin

Question 1 of 116

A 24-year-old female presents with episodic wheezing and shortness of breath for the past 4 months. She has smoked for the past 8 years and has a history of eczema. Examination of her chest is unremarkable. Spirometry is arranged and is reported as normal. What is the most appropriate management of her symptoms?

- A. Peak flow diary
- B. Trial of lansoprazole
- C. Baseline FEV1 repeated following inhaled corticosteroids
- D. Arrange a chest x-ray
- E. Trial of salbutamol inhaler

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✓ E. Trial of salbutamol inhaler

Asthma diagnosis - if high probability of asthma - start treatment

The new British Thoracic Society guidelines take a more practical approach to diagnosing asthma. If a patient has typical symptoms of asthma a trial of treatment is recommended. Normal spirometry when the patient is well does not exclude a diagnosis of asthma. The smoking history is unlikely to be relevant at her age.
What is not necessarily clear is whether all patients should have spirometry prior to starting treatment - how do you interpret the guidelines?

Asthma: diagnosis in adults

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning • History of atopic disorder • Wheeze heard on auscultation • Unexplained peripheral blood eosinophilia	• Prominent dizziness, light-headedness, peripheral tingling • Chronic productive cough in the absence of wheeze or breathlessness • Repeatedly normal physical examination • Significant smoking history (i.e. > 20 pack-years) • Normal PEF or spirometry when symptomatic

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % = [(Highest – Lowest PEFR) / Highest PEFR] x 100
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant

Question 2 of 116

Which of the following factors is least useful in assessing patients with a poor prognosis in community-acquired pneumonia?

- A. Mini-mental score of 6/10
- B. Urea of 11.4 mmol/l
- C. C-reactive protein of 154
- D. Respiratory rate of 30
- E. Aged 75 years old

Question 2 of 116

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- B. Urea of 11.4 mmol/l
- ✓ C. C-reactive protein of 154
- D. Respiratory rate of 30
- E. Aged 75 years old

The C-reactive protein is the least useful of the above in predicting mortality in patients with community-acquired pneumonia. The rest of the answers are part of the CURB-65 criteria

Pneumonia: prognostic factors

CURB-65 criteria of severe pneumonia

- Confusion (abbreviated mental test score < 8/10)
- Urea > 7 mmol/L
- Respiratory rate = 30 / min
- BP: systolic < 90 or diastolic < 60 mmHg
- age > 65 years

Patients with 3 or more (out of 5) of the above criteria are regarded as having a severe pneumonia

Other factors associated with a poor prognosis include:

- presence of coexisting disease
- hypoxaemia (pO2 < 8 kPa) independent of FiO2

Question 3 of 116

A 27-year-old woman is reviewed in the asthma clinic. She currently uses salbutamol inhaler 100mcg prn combined with beclometasone dipropionate inhaler 400mcg bd. Despite this she is having frequent exacerbations of her asthma and recently required a course of prednisolone. What is the most appropriate next step in management?

- A. Add a leukotriene receptor antagonist
- B. Add tiotropium
- C. Add salmeterol
- D. Start to take the salbutamol regularly, 2 puffs qds
- E. Switch beclometasone to fluticasone

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Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: • good response to LABA - continue LABA • benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) • no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: • increasing inhaled steroid up to 2000 mcg/day* • addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet
Step 5	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Question 4 of 116

Which one of the following is a contraindication to surgical resection in lung cancer?

- A. Haemoptysis
- B. FEV 1.9 litres
- C. Histology shows squamous cell cancer
- D. Vocal cord paralysis
- E. Calcium = 2.84 mmol/L

Question 4 of 116

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- ✓ D. Vocal cord paralysis
- E. Calcium = 2.84 mmol/L

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

Paralysis of a vocal cord implies extracapsular spread to mediastinal nodes and is an indication of inoperability.

Lung cancer: non-small cell management

Management

- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

Surgery contraindications

- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

Question 5 of 116

Which one of the following is responsible for farmer's lung?

- A. Aspergillus clavatus
- B. Micropolyspora faeni
- C. Thermo*Actinomyces* candidus
- D. Mycobacterium avium
- E. Avian proteins

Question 5 of 116

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- D. Mycobacterium avium
- E. Avian proteins

Micropolyspora faeni causes farmer's lung, a type of EAA

Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase

Examples

- bird fanciers' lung (avian proteins)
- farmers lung (spores of Micropolyspora faeni)
- malt workers' lung (Aspergillus clavatus)
- mushroom workers' lung (thermophilic actinomycetes*)

Presentation

- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

Investigation

- CXR: upper lobe fibrosis
- BAL: lymphocytosis
- blood: NO eosinophilia

*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as Micropolyspora faeni

Question 6 of 116

A 45-year-old female develops pleuritic chest pain following a hysterectomy 10 days ago. Low-molecular weight heparin is given initially and CTPA confirms a pulmonary embolism. There is no previous history of venous thromboembolism. How long should the patient be warfarinised for?

- A. Not suitable for anticoagulation
- B. At least 4 weeks
- C. At least 3 months
- D. At least 6 months
- E. 12 months

Question 6 of 116

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- B. At least 4 weeks
- ✓ C. At least 3 months
- D. At least 6 months
- E. 12 months

As this patient has a temporary risk factor for a thromboembolic event the recommended period of anticoagulation is 3 months.

Pulmonary embolism: management

Unfortunately there is a lack of clear guidelines on the optimal length of anticoagulation following a pulmonary embolism. The 2003 British Thoracic Society guidelines which advocate a shorter duration of treatment are not widely followed. The following is based on the 2005 British Committee for Standards in Haematology (BCSH) guidelines and Clinical Knowledge Summaries.

Initial anticoagulation with heparin

- low molecular weight heparin (LMWH), rather than unfractionated heparin (UFH), should be used routinely in patients with suspected pulmonary embolism. This reflects the equal efficacy and safety of LMWHs as well as their ease of use
- exceptions include patients with a massive PE or in situations where rapid reversal of anticoagulation may be necessary

Ongoing anticoagulation with warfarin

- target INR 2.0 - 3.0, length of treatment:
- calf DVT: at least 6 weeks
- proximal DVT or PE where there is transient risk factors: at least 3 months
- idiopathic venous thromboembolism or permanent risk factors: at least 6 months

Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. Hypotension). Other invasive approaches should be considered where appropriate facilities exist

Question 7 of 116

A 70-year-old man who is known to have chronic obstructive pulmonary disease (COPD) is admitted to the Medical Admissions Unit with a suspected infective exacerbation of COPD. What should the target oxygen saturations be until blood gases are available?

- A. >98%
- B. 94-98%
- C. 88-92%
- D. 92-94%
- E. > 95% first 48 hours, > 90% rest of admission

Question 7 of 116

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- ✓ C. 88-92%
- D. 92-94%
- E. > 95% first 48 hours, > 90% rest of admission

Oxygen therapy

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

Oxygen saturation targets

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

Management of COPD patients

- prior to the availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO_2 is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

Question 8 of 116

Which one of the following causes of lung fibrosis predominately affect the upper zones?

- A. Bleomycin
- B. Rheumatoid arthritis
- C. Cryptogenic fibrosis alveolitis
- D. Methotrexate
- E. Extrinsic allergic alveolitis

Question 8 of 116

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- ✓ E. Extrinsic allergic alveolitis

Lung fibrosis

It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis. It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones

- extrinsic allergic alveolitis
- coal worker's pneumoconiosis/progressive massive fibrosis
- silicosis
- sarcoidosis
- ankylosing spondylitis (rare)
- histiocytosis
- tuberculosis

Fibrosis predominately affecting the lower zones

- cryptogenic fibrosing alveolitis
- most connective tissue disorders (except ankylosing spondylitis)
- drug-induced: amiodarone, bleomycin, methotrexate
- asbestosis

Question 9 of 116

A 46-year-old female with a history of rheumatoid arthritis is investigated due to progressive shortness of breath. She is currently treated with methotrexate and ibuprofen. The following results are obtained from spirometry:

FEV1/FVC 45%

What is the most likely cause of the dyspnoea?

- A. Bronchiolitis obliterans
- B. Methotrexate pneumonitis
- C. Pulmonary fibrosis
- D. Caplan's syndrome
- E. Lung cancer

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- D. Caplan's syndrome
- E. Lung cancer

The spirometry reveals an obstructive picture which would be in keeping with bronchiolitis obliterans

Rheumatoid arthritis: respiratory manifestations

A variety of respiratory problems may be seen in patients with rheumatoid arthritis:

- pulmonary fibrosis
- pleural effusion
- pulmonary nodules
- bronchiolitis obliterans
- complications of drug therapy e.g. methotrexate pneumonitis
- pleurisy
- Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure
- infection (possibly atypical) secondary to immunosuppression

Question 10 of 116

A 45-year-old man is noted to have bilateral hilar lymphadenopathy on chest x-ray. Which one of the following is the least likely cause?

- A. Amyloidosis
- B. Sarcoidosis
- C. Histoplasmosis
- D. Tuberculosis
- E. Berylliosis

Question 10 of 116

A 45-year-old man is noted to have bilateral hilar lymphadenopathy on chest x-ray. Which one of the following is the least likely cause?

- ✓ A. Amyloidosis
- B. Sarcoidosis
- C. Histoplasmosis
- D. Tuberculosis
- E. Berylliosis

Amyloidosis is not commonly associated with bilateral hilar lymphadenopathy

Bilateral hilar lymphadenopathy

The most common causes of bilateral hilar lymphadenopathy are sarcoidosis and tuberculosis

Other causes include:

- lymphoma/other malignancy
- pneumoconiosis e.g. berylliosis
- fungi e.g. histoplasmosis, coccidioidomycosis

Question 11 of 116

A chest x-ray of a patient with sarcoidosis shows bilateral hilar lymphadenopathy but is otherwise normal. What chest x-ray stage does this correspond to?

- A. Stage 0
- B. Stage 1
- C. Stage 2
- D. Stage 3
- E. Stage 4

Question 11 of 116

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- ✓ B. Stage 1
- C. Stage 2
- D. Stage 3
- E. Stage 4

Sarcoidosis CXR
- 1 = BHL
- 2 = BHL + infiltrates
- 3 = infiltrates
- 4 = fibrosis

Sarcoidosis: investigation

There is no one diagnostic test for sarcoidosis and hence diagnosis is still largely clinical. ACE levels have a sensitivity of 60% and specificity of 70% and are therefore not reliable in the diagnosis of sarcoidosis although they may have a role in monitoring disease activity. Routine bloods may show hypercalcaemia (seen in 10% if patients) and a raised ESR

A chest x-ray may show the following changes:
- stage 0 = normal
- stage 1 = bilateral hilar lymphadenopathy (BHL)
- stage 2 = BHL + interstitial infiltrates
- stage 3 = diffuse interstitial infiltrates only
- stage 4 = diffuse fibrosis

Other investigations*
- spirometry: may show a restrictive defect
- tissue biopsy: non-caseating granulomas
- gallium-67 scan - not used routinely

*the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection

Question 12 of 116

A 41-year-old female presents with 3 day history of a dry cough and shortness of breath. This was preceded by flu-like symptoms. On examination there is a symmetrical, erythematous rash with 'target' lesions over the whole body. What is the likely organism causing the symptoms?

- A. *Pseudomonas*
- B. *Staphylococcus aureus*
- C. Mycoplasma pneumoniae
- D. *Chlamydia* pneumoniae
- E. *Legionella pneumophilia*

Question 12 of 116

A 41-year-old female presents with 3 day history of a dry cough and shortness of breath. This was preceded by flu-like symptoms. On examination there is a symmetrical, erythematous rash with 'target' lesions over the whole body. What is the likely organism causing the symptoms?

- A. *Pseudomonas*
- B. *Staphylococcus aureus*
- ✓ C. Mycoplasma pneumoniae
- D. *Chlamydia* pneumoniae
- E. *Legionella pneumophilia*

Pneumococcus may also cause erythema multiforme

Mycoplasma pneumoniae

Mycoplasma pneumoniae is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

Features

- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

Complications

- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

Diagnosis

- Mycoplasma serology

Management

- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative

Question 13 of 116

Which one of the following types of lung cancer is most associated with cavitating lesions?

- A. Carcinoid
- B. Large cell
- C. Small cell
- D. Squamous cell
- E. Adenocarcinoma

Question 13 of 116

Which one of the following types of lung cancer is most associated with cavitating lesions?

- A. Carcinoid
- B. Large cell
- C. Small cell
- ✓ D. Squamous cell
- E. Adenocarcinoma

Whilst the other types of lung cancer may cause cavitating lesions, it is most commonly seen in squamous cell cancer

CXR: cavitating lung lesion

Differential

- tuberculosis
- lung cancer (especially squamous cell)
- abscess (Staph aureus, Klebsiella and *Pseudomonas*)
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis

Question 14 of 116

A 62-year-old female with a 40 pack year history of smoking is investigated for a chronic cough associated with haemoptysis. Bronchoscopy reveals a small 1 cm tumour confined to the right main bronchus. A biopsy taken shows small cell lung cancer. What is the most appropriate management?

- A. Laser therapy
- B. Chemotherapy
- C. Surgery
- D. Radiotherapy
- E. Interferon-alpha

Question 14 of 116

A 62-year-old female with a 40 pack year history of smoking is investigated for a chronic cough associated with haemoptysis. Bronchoscopy reveals a small 1 cm tumour confined to the right main bronchus. A biopsy taken shows small cell lung cancer. What is the most appropriate management?

- A. Laser therapy
- ✓ B. Chemotherapy
- C. Surgery
- D. Radiotherapy
- E. Interferon-alpha

Surgery plays little role in the management of small cell lung cancer, with chemotherapy being the mainstay of treatment

Lung cancer: small cell

Features

- usually central
- arise from APUD* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome
- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

Management

- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- radiotherapy: only used for debulking
- chemotherapy: good response to combination chemotherapy, may extend life by approximately 4 months

*an acronym for

- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

Question 15 of 116

A 24-year-old male with no past medical history presents to the Emergency Department with pleuritic chest pain. There is no history of a productive cough and he is not short of breath. Chest x-ray shows a right-sided pneumothorax with a 1 cm rim of air and no mediastinal shift. What is the most appropriate management?

- A. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
- B. Discharge with outpatient chest x-ray
- C. Aspiration
- D. Intercostal drain insertion
- E. Admit for 48 hours observation

Question 15 of 116

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- C. Aspiration
- D. Intercostal drain insertion
- E. Admit for 48 hours observation

It would of course be prudent to give advice about what he should do if his symptoms worsen and also suggest routine follow-up with his GP

Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

Primary pneumothorax
Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails then repeat aspiration should be considered
- if this fails then a chest drain should be inserted

Secondary pneumothorax
Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted. If aspiration fails a chest drain should be inserted. All patients should be admitted for at least 24 hours

Iatrogenic pneumothorax
Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Question 16 of 116

A 65-year-old female with a history of chronic obstructive pulmonary disease (COPD) is reviewed in the Emergency Department. She has presented with a sudden worsening of her dyspnoea associated with haemoptysis. What is the most suitable initial imaging investigation to exclude a pulmonary embolism?

- A. Ventilation-perfusion scan
- B. Echocardiogram
- C. Pulmonary angiography
- D. Computed tomographic pulmonary angiography
- E. MRI thorax

Question 16 of 116

A 65-year-old female with a history of chronic obstructive pulmonary disease (COPD) is reviewed in the Emergency Department. She has presented with a sudden worsening of her dyspnoea associated with haemoptysis. What is the most suitable initial imaging investigation to exclude a pulmonary embolism?

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- B. Echocardiogram
- C. Pulmonary angiography
- ✓ D. Computed tomographic pulmonary angiography
- E. MRI thorax

It is still common in UK hospitals, despite guidelines, for a ventilation-perfusion scan to be done first-line

Pulmonary embolism: investigation

The British Thoracic Society (BTS) published guidelines in 2003 on the management of patients with suspected pulmonary embolism (PE)

Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

Some other points

Clinical probability scores based on risk factors and history and now widely used to help decide on further investigation/management

D-dimers

- sensitivity = 95-98%, but poor specificity

V/Q scan

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

CTPA

- peripheral emboli affecting subsegmental arteries may be missed

Pulmonary angiography

- the gold standard
- significant complication rate compared to other investigations

Question 17 of 116

A 74-year-old woman with thyroid cancer is admitted due to shortness of breath. What is the best investigation to assess for possible compression of the upper airways?

- A. Arterial blood gases
- B. Forced vital capacity
- C. Transfer factor
- D. Peak expiratory flow rate
- E. Flow volume loop

Question 17 of 116

A 74-year-old woman with thyroid cancer is admitted due to shortness of breath. What is the best investigation to assess for possible compression of the upper airways?

- A. Arterial blood gases
- B. Forced vital capacity
- C. Transfer factor
- D. Peak expiratory flow rate
- ✓ E. Flow volume loop

Flow volume loop is the investigation of choice for upper airway compression

Flow volume loop

A normal flow volume loop is often described as a 'triangle on top of a semi circle'

Flow volume loops are the most suitable way of assessing compression of the upper airway

Question 18 of 116

You are reviewing the results from investigations requested at the previous respiratory clinic. A 40-year-old man is being investigated for increasing shortness of breath. The notes show he has smoked for the past 25 years. Pulmonary function tests reveal the following:

FEV1 1.4 L

FVC 1.7 L

FEV1/FVC 82%

Which one of the following is the most likely explanation?

- A. Asthma
- B. Bronchiectasis
- C. Kyphoscoliosis
- D. Chronic obstructive pulmonary disease
- E. Laryngeal malignancy

Question 18 of 116

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- A. Asthma
- B. Bronchiectasis
- ✓ C. Kyphoscoliosis
- D. Chronic obstructive pulmonary disease
- E. Laryngeal malignancy

These results show a restrictive picture, which may result from a number of conditions including kyphoscoliosis. The other answers cause an obstructive picture.

Pulmonary function tests

Pulmonary function tests can be used to determine whether a respiratory disease is obstructive or restrictive. The table below summarises the main findings and gives some example conditions:

Obstructive lung disease	**Restrictive lung disease**
FEV1 - significantly reduced FVC - reduced or normal FEV1% (FEV1/FVC) - reduced	FEV1 - reduced FVC - significantly reduced FEV1% (FEV1/FVC) - normal or increased
Asthma COPD Bronchiectasis Bronchiolitis obliterans	Pulmonary fibrosis Asbestosis Sarcoidosis Acute respiratory distress syndrome Infant respiratory distress syndrome Kyphoscoliosis Neuromuscular disorders

Question 19 of 116

A 31-year-old woman is referred to the acute medical unit with a 4 day history of polyarthritis and a low-grade pyrexia. Examination reveals shin lesions which the patient states are painful. Chest x-ray shows a bulky mediastinum. What is the most likely diagnosis?

- A. Loffler's syndrome
- B. Lofgren's syndrome
- C. Systemic lupus erythematous
- D. Gonococcal arthritis
- E. Reiter's syndrome

Question 19 of 116

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- ✓ B. Lofgren's syndrome
- C. Systemic lupus erythematous
- D. Gonococcal arthritis
- E. Reiter's syndrome

Loffler's syndrome is a cause of pulmonary eosinophilia thought to be caused by parasites such as Ascaris lumbricoides

Lofgren's syndrome

Lofgren's syndrome is an acute form sarcoidosis characterised by bilateral hilar lymphadenopathy (BHL), erythema nodosum, fever and polyarthralgia.

It typically occurs in young females and carries an excellent prognosis

Question 20 of 116

A 24-year-old female comes for review. She was diagnosed with asthma two years ago and is currently using a salbutamol inhaler 100mcg prn combined with beclometasone dipropionate inhaler 200mcg bd. Despite this her asthma is not well controlled. On examination her chest is clear and she has a good inhaler technique. What is the most appropriate next step in management?

- A. Increase beclometasone dipropionate to 400mcg bd
- B. Switch steroid to fluticasone propionate
- C. Trial of leukotriene receptor antagonist
- D. Add salmeterol
- E. Add tiotropium

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B. Switch steroid to fluticasone propionate

C. Trial of leukotriene receptor antagonist

✓ D. Add salmeterol

E. Add tiotropium

The British Thoracic Society recommend adding a long-acting B2 agonist if there is an inadequate response to the addition of inhaled steroid. The inhaled steroid dose should be increased if there is an inadequate response to the long-acting B2 agonist.

Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: • good response to LABA - continue LABA • benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) • no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: • increasing inhaled steroid up to 2000 mcg/day* • addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet
Step 5	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone
Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles
Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Question 21 of 116

Each one of the following may result in bronchiectasis, except:

- A. Kartagener's syndrome
- B. Amyloidosis
- C. Selective IgA deficiency
- D. Lung cancer
- E. Allergic bronchopulmonary aspergillosis

Question 21 of 116

Each one of the following may result in bronchiectasis, except:

- A. Kartagener's syndrome
- ✓ B. Amyloidosis
- C. Selective IgA deficiency
- D. Lung cancer
- E. Allergic bronchopulmonary aspergillosis

Amyloidosis does not cause bronchiectasis per se, but may be seen in bronchiectasis as a consequence of chronic inflammation and infection

Bronchiectasis: causes

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. There are a wide variety of causes are listed below:

Causes

- post-infective: tuberculosis, measles, pertussis, pneumonia
- cystic fibrosis
- bronchial obstruction e.g. lung cancer/foreign body
- immune deficiency: selective IgA, hypogammaglobulinaemia
- allergic bronchopulmonary aspergillosis (ABPA)
- ciliary dyskinetic syndromes: Kartagener's syndrome, Young's syndrome
- yellow nail syndrome

Question 22 of 116

Which one of the following interventions is most likely to increase survival in patients with COPD?

- A. Home nebulisers
- B. Prophylactic antibiotic therapy
- C. Pulmonary rehabilitation
- D. Long-term steroid therapy
- E. Long-term oxygen therapy

Question 22 of 116

Which one of the following interventions is most likely to increase survival in patients with COPD?

- A. Home nebulisers
- B. Prophylactic antibiotic therapy
- C. Pulmonary rehabilitation
- D. Long-term steroid therapy
- ✓ E. Long-term oxygen therapy

After smoking cessation, long-term oxygen therapy is one of the few interventions that has been shown to improve survival in COPD

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%
- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness
- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics
- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale
- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 23 of 116

A 54-year-old man is investigated for a chronic cough. A chest x-ray arranged by his GP shows a suspicious lesion in the right lung. He has no past history of note and is a life-long non-smoker. An urgent bronchoscopy is arranged which is normal. What is the most likely diagnosis?

- A. Lung sarcoma
- B. Squamous cell lung cancer
- C. Lung adenocarcinoma
- D. Small cell lung cancer
- E. Lung carcinoid

Question 23 of 116

A 54-year-old man is investigated for a chronic cough. A chest x-ray arranged by his GP shows a suspicious lesion in the right lung. He has no past history of note and is a life-long non-smoker. An urgent bronchoscopy is arranged which is normal. What is the most likely diagnosis?

- A. Lung sarcoma
- B. Squamous cell lung cancer
- ✓ C. Lung adenocarcinoma
- D. Small cell lung cancer
- E. Lung carcinoid

Lung adenocarcinoma
- most common type in non-smokers
- peripheral lesion

The clues are the absence of a smoking history and normal bronchoscopy, which suggests a peripherally located lesion.

Lung cancer: non-small cell

There are three main subtypes of non-small cell lung cancer:

Squamous cell cancer
- typically central
- associated with ectopic PTH secretion --> hypercalcaemia
- strongly associated with finger clubbing
- hypertrophic pulmonary osteoarthropathy (HPOA)

Adenocarcinoma
- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers
- typically located on the lung periphery

Large cell lung carcinoma

Question 24 of 116

A 24-year-old woman who is 34 weeks pregnant presents with pleuritic chest pain and shortness of breath. She has noticed some pain in her left calf for the past 3 days and on examination she has clinical signs consistent with a left calf deep vein thrombosis. What is the most appropriate investigation?

- A. D-dimer
- B. Compression duplex Doppler
- C. Computed tomographic pulmonary angiography
- D. Venogram
- E. Ventilation-perfusion scan

Question 24 of 116

A 24-year-old woman who is 34 weeks pregnant presents with pleuritic chest pain and shortness of breath. She has noticed some pain in her left calf for the past 3 days and on examination she has clinical signs consistent with a left calf deep vein thrombosis. What is the most appropriate investigation?

- A. D-dimer
- ✓ B. Compression duplex Doppler
- C. Computed tomographic pulmonary angiography
- D. Venogram
- E. Ventilation-perfusion scan

Confirming a DVT is the first step as this may provide indirect evidence of a pulmonary embolism. As both conditions require anticoagulation this may negate the need for further radiation exposure.

Pregnancy: DVT/PE investigation

Guidelines were published in 2007 by the Royal College of Obstetricians. Key points include:

- chest x-ray should be performed in all patients

- compression duplex Doppler should be performed if the chest x-ray is normal - this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure

- the decision to perform a V/Q or CTPA should be taken at a local level after discussion with the patient and radiologist
- CTPA exposes the fetus to about 10-30% of the radiation dose of a V/Q scan
- V/Q scanning exposes the maternal breast tissue to less radiation than a CTPA

D-dimer is of no use in the investigation of thromboembolism as it raised in pregnancy

Question 25 of 116

Which one of the following markers is most useful for monitoring the progression of patients with chronic obstructive pulmonary disease?

- A. FEV1/FVC ratio
- B. Lifestyle questionnaire
- C. Oxygen saturations
- D. FEV1
- E. Number of exacerbations per year

Question 25 of 116

Which one of the following markers is most useful for monitoring the progression of patients with chronic obstructive pulmonary disease?

- A. FEV1/FVC ratio
- B. Lifestyle questionnaire
- C. Oxygen saturations
- ✓ D. FEV1
- E. Number of exacerbations per year

COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50–79%	Stage 2 - Moderate
< 0.7	30–49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

**symptoms should be present to diagnose COPD in these patients

Question 26 of 116

A 24-year-old female with a history of anxiety is taken to the Emergency Department following an acute onset of shortness of breath. On examination the chest is clear to auscultation but the respiratory rate is raised at 40 breaths per minute. A diagnosis of hyperventilation secondary to anxiety is suspected. Which of the following arterial blood gas results (taken on room air) are consistent with this?

- A. pH = 7.56; pCO2 = 2.9 kPa; pO2 = 10.1 kPa
- B. pH = 7.24; pCO2 = 8.4 kPa; pO2 = 12.7 kPa
- C. pH = 7.34; pCO2 = 2.7 kPa; pO2 = 15.4 kPa
- D. pH = 7.54; pCO2 = 2.4 kPa; pO2 = 14.1 kPa
- E. pH = 7.54; pCO2 = 4.9 kPa; pO2 = 13.3 kPa

Question 26 of 116

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- C. pH = 7.34; pCO2 = 2.7 kPa; pO2 = 15.4 kPa
- ✓ D. pH = 7.54; pCO2 = 2.4 kPa; pO2 = 14.1 kPa
- E. pH = 7.54; pCO2 = 4.9 kPa; pO2 = 13.3 kPa

Hyperventilation will result in carbon dioxide being 'blown off', causing an alkalosis.

Whilst the gases in answer A show a respiratory alkalosis the hypoxia could not be explained by hyperventilation

Respiratory alkalosis

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

Question 27 of 116

Which one of the following paraneoplastic features is least commonly seen in patients with squamous cell lung cancer?

- A. Lambert-Eaton syndrome
- B. Hyperthyroidism
- C. Hypertrophic pulmonary osteoarthropathy
- D. Hypercalcaemia
- E. Clubbing

Question 27 of 116

Which one of the following paraneoplastic features is least commonly seen in patients with squamous cell lung cancer?

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- B. Hyperthyroidism
- C. Hypertrophic pulmonary osteoarthropathy
- D. Hypercalcaemia
- E. Clubbing

Paraneoplastic features of lung cancer
- squamous cell: PTHrp, clubbing, HPOA
- small cell: ADH, ACTH, Lambert-Eaton syndrome

Lambert-Eaton syndrome occurs almost exclusively in small cell lung cancer

Lung cancer: paraneoplastic features

Small cell
- ADH
- ACTH - not typical, hypertension, hyperglycaemia, hypokalaemia, alkalosis and muscle weakness are more common than buffalo hump etc
- Lambert-Eaton syndrome

Squamous cell
- PTH-rp
- clubbing
- hypertrophic pulmonary osteoarthropathy (HPOA)
- hyperthyroidism due to ectopic TSH

Adenocarcinoma
- gynaecomastia

Question 28 of 116

A 24-year-old heroin addict is admitted following an overdose. He is drowsy and has a respiratory rate of 6 / min. Which of the following arterial blood gas results (taken on room air) are most consistent with this?

- A. pH = 7.49; pCO2 = 4.9 kPa; pO2 = 10.1 kPa
- B. pH = 7.52; pCO2 = 2.9 kPa; pO2 = 13.1 kPa
- C. pH = 7.31; pCO2 = 7.4 kPa; pO2 = 8.1 kPa
- D. pH = 7.55; pCO2 = 3.4 kPa; pO2 = 14.3 kPa
- E. pH = 7.32; pCO2 = 3.4 kPa; pO2 = 8.3 kPa

Question 28 of 116

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- D. pH = 7.55; pCO2 = 3.4 kPa; pO2 = 14.3 kPa
- E. pH = 7.32; pCO2 = 3.4 kPa; pO2 = 8.3 kPa

This patient is likely to have developed a respiratory acidosis secondary to hypoventilation.

Respiratory acidosis

Respiratory acidosis may be caused by a number of conditions

- COPD
- decompensation in other respiratory conditions e.g. Life-threatening asthma / pulmonary oedema
- sedative drugs: benzodiazepines, opiate overdose

Question 29 of 116

Which one of the following is least associated with Kartagener's syndrome?

- A. Male subfertility
- B. Recurrent sinusitis
- C. Malabsorption
- D. Dextrocardia
- E. Bronchiectasis

Question 29 of 116

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- A. Male subfertility
- B. Recurrent sinusitis
- ✓ C. Malabsorption
- D. Dextrocardia
- E. Bronchiectasis

Kartagener's syndrome

Kartagener's syndrome (also known as primary ciliary dyskinesia) was first described in 1933 and most frequently occurs in examinations due to its association with dextrocardia (e.g. 'quiet heart sounds', 'small volume complexes in lateral leads')

Features

- dextrocardia or complete situs inversus
- bronchiectasis
- recurrent sinusitis
- subfertility (secondary to diminished sperm motility and defective ciliary action in the fallopian tubes)

Question 30 of 116

A 19-year-old man presents as he is concerned he may be asthmatic. Which one of the following points in the history would make this diagnosis less likely?

- A. Smoking since age of 16 years
- B. Peripheral tingling during episodes of dyspnoea
- C. Peripheral blood eosinophilia
- D. Chest tightness whilst exercising
- E. History of eczema

Question 30 of 116

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- D. Chest tightness whilst exercising
- E. History of eczema

The British Thoracic Society suggest peripheral tingling is one of the factors which makes a diagnosis of asthma less likely. His smoking history does not preclude a diagnosis of asthma

Asthma: diagnosis in adults

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning • History of atopic disorder • Wheeze heard on auscultation • Unexplained peripheral blood eosinophilia	• Prominent dizziness, light-headedness, peripheral tingling • Chronic productive cough in the absence of wheeze or breathlessness • Repeatedly normal physical examination • Significant smoking history (i.e. > 20 pack-years) • Normal PEF or spirometry when symptomatic

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % = [(Highest – Lowest PEFR) / Highest PEFR] x 100
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant

Question 31 of 116

A 55-year-old man is referred to the medical admissions unit. He recently returned from a holiday in Italy and has failed to respond to a course of co-amoxiclav for a suspected lower respiratory tract infection. Chest x-ray shows bilateral infiltrates. Bloods are as follows:

Na^+	122 mmol/l
K^+	4.3 mmol/l
Urea	8.4 mmol/l
Creatinine	130 µmol/l

What is the likely diagnosis?

- A. Goodpasture's syndrome
- B. Legionella pneumonia
- C. *Pneumocystis carinii* pneumonia
- D. Pulmonary eosinophilia
- E. Mycoplasma pneumonia

Question 31 of 116

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- C. *Pneumocystis carinii* pneumonia
- D. Pulmonary eosinophilia
- E. Mycoplasma pneumonia

Legionella

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophilia*. It is typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays. Person-to-person transmission is not seen

Features
- flu-like symptoms
- dry cough
- lymphopenia
- hyponatraemia
- deranged LFTs

Diagnosis
- urinary antigen

Management
- treat with erythromycin

Question 32 of 116

A 49-year-old male with a past history of alcohol excess presents to the Emergency Department due to fever and shortness of breath. Chest x-ray reveals a cavitating lesion in the right middle zone. What is the most likely causative organism?

- A. Klebsiella
- B. Bartonella
- C. Pneumococcus
- D. *Coxiella burnetii*
- E. *Haemophilus influenzae*

Question 32 of 116

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- D. *Coxiella burnetii*
- E. *Haemophilus influenzae*

Klebsiella pneumonia (Friedlander's pneumonia) typically occurs in middle-aged alcoholic men. Chest x-ray features may include abscess formation in the middle/upper lobes and empyema. The mortality approaches 30-50%

CXR: cavitating lung lesion

Differential

- tuberculosis
- lung cancer (especially squamous cell)
- abscess (Staph aureus, Klebsiella and *Pseudomonas*)
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis

Question 33 of 116

A 62-year-old man who is investigated for haemoptysis is found to have squamous cell lung cancer. Which one of the following is a contraindication to surgery?

- A. Pleural effusion
- B. Superior vena caval obstruction
- C. Haemoptysis
- D. Hypercalcaemia
- E. Enlarged mediastinal lymph nodes

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- D. Hypercalcaemia
- E. Enlarged mediastinal lymph nodes

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

If one of the options was 'malignant pleural effusion', rather than just 'pleural effusion' (which may be reactive), then this would also be a contraindication

Lung cancer: non-small cell management

Management
- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

Surgery contraindications
- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

Question 34 of 116

A 44-year-old man who is known to be HIV positive presents with shortness-of-breath. Which one of the following features is most characteristic of *Pneumocystis carinii* pneumonia?

- A. Usually occurs when the CD4 count is 200-300/mm³
- B. Absence of fever
- C. Productive cough
- D. Oxygen saturations usually improve after short period of exertion
- E. Normal chest auscultation

Question 34 of 116

A 44-year-old man who is known to be HIV positive presents with shortness-of-breath. Which one of the following features is most characteristic of *Pneumocystis carinii* pneumonia?

- A. Usually occurs when the CD4 count is 200-300/mm³
- B. Absence of fever
- C. Productive cough
- D. Oxygen saturations usually improve after short period of exertion
- ✓ E. Normal chest auscultation

HIV: Pneumocystis jiroveci pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as Pneumocystis jiroveci, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- Pneumocystis jiroveci is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm³ should receive PCP prophylaxis

Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if pO2 < 9.3kPa then steroids reduce risk of respiratory failure by 50% and death by a third)

Question 35 of 116

A 62-year-old female is admitted with a suspected infective exacerbation of COPD. A chest x-ray shows no evidence of consolidation. What is the most likely causative organism?

- A. *Pseudomonas aeruginosa*
- B. *Haemophilus influenzae*
- C. *Staphylococcus aureus*
- D. *Streptococcus pneumoniae*
- E. *Moraxella catarrhalis*

Question 35 of 116

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- A. *Pseudomonas aeruginosa*
- ✓ B. *Haemophilus influenzae*
- C. *Staphylococcus aureus*
- D. *Streptococcus pneumoniae*
- E. *Moraxella catarrhalis*

COPD: acute management

The most common bacterial organisms that cause infective exacerbations of COPD are:

- *Haemophilus influenzae* (most common cause)
- *Streptococcus pneumoniae*
- *Moraxella catarrhalis*

Respiratory viruses account for around 30% of exacerbations, with the human rhinovirus being the most important pathogen.

Question 36 of 116

A 20-year-old man who has a family history of alpha-1 antitrypsin deficiency has genetic testing. The following results are received:

A1AT genotype PiMZ

What is the most likely outcome?

- A. Weekly intravenous alpha1-antitrypsin protein concentrates in later life
- B. Mild emphysema controlled with bronchodilator therapy
- C. Death within 5-10 years
- D. Lung transplantation in later life
- E. No evidence of lung disease

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- C. Death within 5-10 years
- D. Lung transplantation in later life
- ✓ E. No evidence of lung disease

Heterozygote patients such as those with the PiMZ genotype have alpha-1 antitrypsin levels approximately 35% of normal. They therefore have a low risk of developing clinically evident lung disease.

Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver

Genetics
- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

Features
- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

Investigations
- A1AT concentrations

Management
- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

*trusted sources are split on which is a more accurate description

Question 37 of 116

A 67-year-old female is referred to the acute medical unit with an infective exacerbation of COPD. Despite maximal medical therapy the arterial blood gases continue to show type II respiratory failure. You are asked to consider non-invasive ventilation. At what pH is the patient most likely to receive benefit from non-invasive ventilation?

- A. pH 7.13
- B. pH 7.18
- C. pH 7.23
- D. pH 7.29
- E. pH 7.37

Question 37 of 116

A 67-year-old female is referred to the acute medical unit with an infective exacerbation of COPD. Despite maximal medical therapy the arterial blood gases continue to show type II respiratory failure. You are asked to consider non-invasive ventilation. At what pH is the patient most likely to receive benefit from non-invasive ventilation?

- A. pH 7.13
- B. pH 7.18
- C. pH 7.23
- ✓ D. pH 7.29
- E. pH 7.37

The evidence surrounding the use of NIV in COPD shows that patients with a pH in the range of 7.25-7.35 achieve the most benefit. If the pH is < 7.25 then invasive ventilation should be considered if appropriate

Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H2O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H20 whilst BTS suggest 12-15 cm H2O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

Question 38 of 116

A 35-year-old female with sarcoidosis is started on a course of prednisolone. Which one of the following is a suitable indication for commencing steroid therapy in such patients?

- A. Bilateral hilar lymphadenopathy
- B. Arthralgia
- C. Hypercalcaemia
- D. Serum ACE > 120 u/l
- E. Erythema nodosum

Question 38 of 116

A 35-year-old female with sarcoidosis is started on a course of prednisolone. Which one of the following is a suitable indication for commencing steroid therapy in such patients?

- A. Bilateral hilar lymphadenopathy
- B. Arthralgia
- ✓ C. Hypercalcaemia
- D. Serum ACE > 120 u/l
- E. Erythema nodosum

Sarcoidosis: management

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent

Indications for steroids

- hypercalcaemia
- worsening lung function
- eye, heart or neuro involvement

Question 39 of 116

A 52-year-old woman with a history of breast cancer is admitted with acute dyspnoea. Her respiratory rate on admission is 42 / min and her oxygen saturations are 87% on room air. A pulmonary embolism is suspected and she is transferred to the high dependency unit after being treated with oxygen and enoxaparin. Which one of the following would be strongest indication for thrombolysis?

- A. Extensive deep venous thrombosis
- B. Hypotension
- C. Patient choice following informed consent
- D. Hypoxaemia despite high flow oxygen
- E. ECG showing right ventricular strain

Question 39 of 116

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- D. Hypoxaemia despite high flow oxygen
- E. ECG showing right ventricular strain

Massive PE + hypotension - thrombolyse

Pulmonary embolism: management

Unfortunately there is a lack of clear guidelines on the optimal length of anticoagulation following a pulmonary embolism. The 2003 British Thoracic Society guidelines which advocate a shorter duration of treatment are not widely followed. The following is based on the 2005 British Committee for Standards in Haematology (BCSH) guidelines and Clinical Knowledge Summaries.

Initial anticoagulation with heparin

- low molecular weight heparin (LMWH), rather than unfractionated heparin (UFH), should be used routinely in patients with suspected pulmonary embolism. This reflects the equal efficacy and safety of LMWHs as well as their ease of use
- exceptions include patients with a massive PE or in situations where rapid reversal of anticoagulation may be necessary

Ongoing anticoagulation with warfarin

- target INR 2.0 - 3.0, length of treatment:
- calf DVT: at least 6 weeks
- proximal DVT or PE where there is transient risk factors: at least 3 months
- idiopathic venous thromboembolism or permanent risk factors: at least 6 months

Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. Hypotension). Other invasive approaches should be considered where appropriate facilities exist

Question 40 of 116

A 24-year-old male is admitted with acute severe asthma. Treatment is initiated with 100% oxygen, nebulised salbutamol and ipratropium bromide nebulisers and IV hydrocortisone. Despite initial treatment there is no improvement. What is the next step in management?

- A. IV aminophylline
- B. IV magnesium sulphate
- C. IV salbutamol
- D. Non-invasive ventilation
- E. IV adrenaline

Question 40 of 116

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- A. IV aminophylline
- ✓ B. IV magnesium sulphate
- C. IV salbutamol
- D. Non-invasive ventilation
- E. IV adrenaline

Current guidelines do not support the routine use of non-invasive ventilation in asthmatics.

Asthma: acute severe

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
• PEF > 50% best or predicted • Speech normal • RR < 25 / min • Pulse < 110 bpm	• PEF 33 - 50% best or predicted • Can't complete sentences • RR > 25/min • Pulse > 110 bpm	• PEF < 33% best or predicted • Oxygen sats < 92% • Silent chest, cyanosis or feeble respiratory effort • Bradycardia, dysrhythmia or hypotension • Exhaustion, confusion or coma

British Thoracic Society guidelines 2003 (updated 2004)

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

Question 41 of 116

You are reviewing the management of a number of patients with chronic obstructive pulmonary disease (COPD). Which one of the following factors should prompt an assessment for long-term oxygen therapy?

- A. FEV1 54% of predicted
- B. Haemoglobin of 18.4 g/dl
- C. Body mass index 18.8 kg / m^2
- D. Oxygen saturations of 93% on room air
- E. FEV1/FVC of 0.47

Question 41 of 116

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- E. FEV1/FVC of 0.47

COPD: long-term oxygen therapy

The 2010 NICE guidelines on COPD clearly define which patients should be assessed for and offered long-term oxygen therapy (LTOT). Patients who receive LTOT should breathe supplementary oxygen for at least 15 hours a day.

Assess patients if any of the following:

- very severe airflow obstruction (FEV1 < 30% predicted). Assessment should be 'considered' for patients with severe airflow obstruction (FEV1 30-49% predicted)
- cyanosis
- polycythaemia
- peripheral oedema
- raised jugular venous pressure
- oxygen saturations less than or equal to 92% on room air

Assessment is done by measuring arterial blood gases on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.

Offer LTOT to patients with a pO2 of < 7.3 kPa or to those with a pO2 of 7.3 - 8 kPa and one of the following:

- secondary polycythaemia
- nocturnal hypoxaemia
- peripheral oedema
- pulmonary hypertension

Question 42 of 116

Each one of the following predisposes to the development of obstructive sleep apnoea, except:

- A. Acromegaly
- B. Chronic obstructive pulmonary disease
- C. Amyloidosis
- D. Obesity
- E. Hypothyroidism

Question 42 of 116

Each one of the following predisposes to the development of obstructive sleep apnoea, except:

- A. Acromegaly
- ✓ B. Chronic obstructive pulmonary disease
- C. Amyloidosis
- D. Obesity
- E. Hypothyroidism

Sleep apnoea causes include obesity and macroglossia

The Sleep Heart Health Study showed that when these two conditions do coexist, this is the result of chance alone

Obstructive sleep apnoea/hypopnoea syndrome

Predisposing factors
- obesity
- macroglossia: acromegaly, hypothyroidism, amyloidosis
- large tonsils
- Marfan's syndrome

Consequence
- daytime somnolence
- hypertension

SIGN guidelines for the diagnosis and management of patients with OSAHS were published in 2003

Assessment of sleepiness
- Epworth Sleepiness Scale - questionnaire completed by patient +/- partner
- Multiple Sleep Latency Test (MSLT) - measures the time to fall asleep in a dark room (using EEG criteria)

Diagnostic tests
- sleep studies - ranging from monitoring of pulse oximetry at night to full polysomnography where a wide variety of physiological factors are measured including EEG, respiratory airflow, thoraco-abdominal movement, snoring and pulse oximetry

Management
- weight loss
- CPAP is first line for moderate or severe OSAHS
- intra-oral devices (e.g. mandibular advancement) may be used if CPAP is not tolerated or for patients with mild OSAHS where there is no daytime sleepiness
- limited evidence to support use of pharmacological agents

Question 43 of 116

A 45-year-old woman who is a known asthmatic comes for review. In the past two years she has had around six exacerbations of asthma requiring oral steroids. Her current medication includes salbutamol 2 puffs prn, salmeterol 50mcg bd and beclometasone 200 mcg 1 puff bd. You note from the records that her BMI is 31 kg/m^2, she is a non-smoker and has a good inhaler technique. What is the most appropriate next step in management?

- A. Increase beclometasone to 200 mcg 2 puffs bd
- B. Referral to a dietician
- C. Add oral theophylline
- D. Add oral montelukast
- E. Add inhaled tiotropium

Question 43 of 116

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Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: • good response to LABA - continue LABA • benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) • no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: • increasing inhaled steroid up to 2000 mcg/day* • addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet
Step 5	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone
Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles
Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Question 44 of 116

A 39-year-old man presents with shortness of breath following one week of flu-like symptoms. He also has a non-productive cough but no chest pain. A chest x-ray shows bilateral consolidation and examination reveals erythematous lesions on his limbs and trunk. Which one of the following investigations is most likely to be diagnostic?

- A. Cold agglutins
- B. Sputum culture
- C. Urinary antigen for Legionella
- D. Serology for Mycoplasma
- E. Blood culture

Question 44 of 116

A 39-year-old man presents with shortness of breath following one week of flu-like symptoms. He also has a non-productive cough but no chest pain. A chest x-ray shows bilateral consolidation and examination reveals erythematous lesions on his limbs and trunk. Which one of the following investigations is most likely to be diagnostic?

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- ✓ D. Serology for Mycoplasma
- E. Blood culture

Mycoplasma? - serology is diagnostic

The flu-like symptoms, bilateral consolidation and erythema multiforme point to a diagnosis of Mycoplasma. The most appropriate diagnostic test is Mycoplasma serology

Mycoplasma pneumoniae

Mycoplasma pneumoniae is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

Features
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

Complications
- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

Diagnosis
- Mycoplasma serology

Management
- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative

Question 45 of 116

A 60-year-old woman who has recently been diagnosed with chronic obstructive pulmonary disease (COPD) presents for review. She is still occasionally breathless despite using a short-acting muscarinic antagonist (SAMA) as required. Her FEV1 is 45% of predicted and she has managed to stop smoking. Of the following options, which one is the most appropriate next step in management?

- A. Switch to a combined short-acting beta2-agonist and muscarinic antagonist inhaler (e.g. Combivent)
- B. Long-acting beta2-agoinst
- C. Long-acting beta2-agoinst + inhaled corticosteroid (ICS) in a combination inhaler
- D. Inhaled corticosteroid
- E. Use the SAMA regularly (e.g. 2 puffs qds)

Question 45 of 116

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- B. Long-acting beta2-agoinst
- ✓ C. Long-acting beta2-agoinst + inhaled corticosteroid (ICS) in a combination inhaler
- D. Inhaled corticosteroid
- E. Use the SAMA regularly (e.g. 2 puffs qds)

Another option here is a long-acting muscarinic antagonist (LAMA), for example tiotropium. Please see the 2010 NICE guidelines for more details.

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy

- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%

- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 46 of 116

A 31-year-old female with no past medical history of note is admitted to hospital with dyspnoea and fever. She has recently returned from holiday in Turkey. A clinical diagnosis of pneumonia is made. On examination she is noted to have an ulcerated lesion on her upper lip consistent with reactivation of herpes simplex. Which organism is most associated with this examination finding?

- A. *Legionella pneumophilia*
- B. Staphylococcal aureus
- C. *Streptococcus pneumoniae*
- D. *Pneumocystis carinii*
- E. Mycoplasma pneumoniae

Question 46 of 116

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- D. *Pneumocystis carinii*
- E. Mycoplasma pneumoniae

Streptococcus pneumoniae commonly causes reactivation of the herpes simplex virus resulting in 'cold sores'

Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- Staphylococcal aureus
- atypical pneumonias (e.g. Due to Mycoplasma pneumoniae)
- viruses

Klebsiella pneumoniae is classically in alcoholics

Streptococcus pneumoniae **(pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

Question 47 of 116

A preliminary diagnosis of extrinsic allergic alveolitis in a 55-year-old man. Which one of the following features would most support this diagnosis?

- A. Clubbing
- B. Eosinophilia
- C. Cyanosis
- D. Fibrosis in the upper zones
- E. History of working in the steel industry

Question 47 of 116

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- ✓ D. Fibrosis in the upper zones
- E. History of working in the steel industry

A history of working in the steel industry and eosinophilia are not features of extrinsic allergic alveolitis. Clubbing and cyanosis are non-specific

Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase

Examples
- bird fanciers' lung (avian proteins)
- farmers lung (spores of Micropolyspora faeni)
- malt workers' lung (Aspergillus clavatus)
- mushroom workers' lung (thermophilic actinomycetes*)

Presentation
- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

Investigation
- CXR: upper lobe fibrosis
- BAL: lymphocytosis
- blood: NO eosinophilia

*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as Micropolyspora faeni

Question 48 of 116

A 65-year-old woman with a history of chronic obstructive pulmonary disease (COPD) is admitted to the Emergency Department with breathlessness. This is her first admission with an exacerbation of COPD. Blood gases taken on room air shortly after admission are as follows:

pH 7.38

pCO2 4.9 kPa

pO2 8.8 kPa

What should her target oxygen saturations be?

- A. 94-98%
- B. 88-92%
- C. 92-94%
- D. >98%
- E. > 95% first 48 hours, > 90% rest of admission

Question 48 of 116

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- B. 88-92%
- C. 92-94%
- D. >98%
- E. > 95% first 48 hours, > 90% rest of admission

When managing patients with COPD, once the pCO2 is known to be normal the target oxygen saturations should be 94-98%.

Oxygen therapy

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

Oxygen saturation targets

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

Management of COPD patients

- prior to the availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO2 is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

Question 49 of 116

A 54-year-old man is admitted with suspected pulmonary embolism. He has no past medical history of note. Blood pressure is 120/80 mmHg with a pulse of 90/min. The chest x-ray is normal. Following treatment with low-molecular weight heparin, what is the most appropriate initial lung imaging investigation to perform?

- A. Pulmonary angiography
- B. Echocardiogram
- C. MRI thorax
- D. Ventilation-perfusion scan
- E. Computed tomographic pulmonary angiography

Question 49 of 116

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- D. Ventilation-perfusion scan
- ✓ E. Computed tomographic pulmonary angiography

CTPA is the first line investigation for PE according to current BTS guidelines

This is a difficult question to answer as both computed tomographic pulmonary angiography (CTPA) and ventilation-perfusion scanning are commonly used in UK clinical practice. The 2003 British Thoracic Society (BTS) guidelines, however, recommended that CTPA is now used as the initial lung imaging modality of choice. Pulmonary angiography is of course the 'gold standard' but this is not what the question asks for

Pulmonary embolism: investigation

The British Thoracic Society (BTS) published guidelines in 2003 on the management of patients with suspected pulmonary embolism (PE)

Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

Some other points

Clinical probability scores based on risk factors and history and now widely used to help decide on further investigation/management

D-dimers

- sensitivity = 95-98%, but poor specificity

V/Q scan

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

CTPA

- peripheral emboli affecting subsegmental arteries may be missed

Pulmonary angiography

- the gold standard
- significant complication rate compared to other investigations

Question 50 of 116

Which of the following features is associated with a good prognosis in sarcoidosis?

- A. Insidious onset
- B. Splenomegaly
- C. Disease in black people
- D. Stage III features on CXR
- E. Erythema nodosum

Question 50 of 116

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- B. Splenomegaly
- C. Disease in black people
- D. Stage III features on CXR
- ✓ E. Erythema nodosum

Erythema nodosum is associated with a good prognosis in sarcoidosis

Sarcoidosis: prognostic features

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people

Factors associated with poor prognosis

- insidious onset, symptoms > 6 months
- absence of erythema nodosum
- extrapulmonary manifestations: e.g. lupus pernio, splenomegaly
- CXR: stage III-IV features
- black people

Question 51 of 116

Which one the following statements regarding asbestos is not correct?

- A. Pleural plaques are premalignant
- B. Asbestosis typically affects the lower zones
- C. Crocidolite (blue) asbestos is the most dangerous form
- D. Severity of asbestosis is related to the length of exposure
- E. Mesothelioma may develop following minimal exposure

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Asbestos and the lung

Asbestos can cause a variety of lung disease from benign pleural plaques to mesothelioma.

Pleural plaques
Pleural plaques are benign and do not undergo malignant change. They are the most common form of asbestos related lung disease and generally occur after a latent period of 20-40 years.

Pleural thickening
Asbestos exposure may cause diffuse pleural thickening in a similar pattern to that seen following an empyema or haemothorax. The underlying pathophysiology is not fully understood.

Asbestosis
The severity of asbestosis is related to the length of exposure. This is in contrast to mesothelioma where even very limited exposure can cause disease. The latent period is typically 15-30 years. Asbestosis typically causes lower lobe fibrosis. As with other forms of lung fibrosis the most common symptoms are shortness-of-breath and reduced exercise tolerance.

Mesothelioma
Mesothelioma is a malignant disease of the pleura. Crocidolite (blue) asbestos is the most dangerous form.

Possible features
- progressive shortness-of-breath
- chest pain
- pleural effusion

Patients are usually offered palliative chemotherapy and there is also a limited role for surgery and radiotherapy. Unfortunately the prognosis is very poor, with a median survival from diagnosis of 8-14 months.

Lung cancer
Asbestos exposure is a risk factor for lung cancer and also has a synergistic effect with cigarette smoke.

Question 52 of 116

A 43-year-old man is admitted due to shortness of breath and is noted to have a cavitating lesion on his chest x-ray. Which one of the following conditions is not part of the differential diagnosis?

- A. Lung cancer
- B. Pulmonary embolism
- C. Wegener's granulomatosis
- D. Churg-Strauss syndrome
- E. Tuberculosis

Question 52 of 116

A 43-year-old man is admitted due to shortness of breath and is noted to have a cavitating lesion on his chest x-ray. Which one of the following conditions is not part of the differential diagnosis?

- A. Lung cancer
- B. Pulmonary embolism
- C. Wegener's granulomatosis
- ✓ D. Churg-Strauss syndrome
- E. Tuberculosis

CXR: cavitating lung lesion

Differential

- tuberculosis
- lung cancer (especially squamous cell)
- abscess (Staph aureus, Klebsiella and *Pseudomonas*)
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis

Question 53 of 116

Each one of the following is a known cause of occupational asthma, except:

- A. Isocyanates
- B. Cadmium
- C. Soldering flux resin
- D. Flour
- E. Platinum salts

Question 53 of 116

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Asthma: occupational

Causes
- isocyanates
- platinum salts
- soldering flux resin
- glutaraldehyde
- flour
- epoxy resins
- proteolytic enzymes

Diagnosis
- specific recommendations are made in the 2007 joint British Thoracic Society and SIGN guidelines
- serial measurements of peak expiratory flow are recommended at work and away from work

Question 54 of 116

A 57-year-old female presents to the Emergency Department with shortness of breath and pleuritic chest pain. She has no past medical history of note and enjoys good health. Investigations reveal a non-massive pulmonary embolism. What is the recommended length of warfarinisation for this patient?

- A. 6 weeks
- B. 3 months
- C. 6 months
- D. 12 months
- E. Life-long

Question 54 of 116

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- B. 3 months
- ✓ C. 6 months
- D. 12 months
- E. Life-long

There are no transient risk factors for venous thromboembolism therefore the patient should be anticoagulated for 6 months.

Pulmonary embolism: management

Unfortunately there is a lack of clear guidelines on the optimal length of anticoagulation following a pulmonary embolism. The 2003 British Thoracic Society guidelines which advocate a shorter duration of treatment are not widely followed. The following is based on the 2005 British Committee for Standards in Haematology (BCSH) guidelines and Clinical Knowledge Summaries.

Initial anticoagulation with heparin

- low molecular weight heparin (LMWH), rather than unfractionated heparin (UFH), should be used routinely in patients with suspected pulmonary embolism. This reflects the equal efficacy and safety of LMWHs as well as their ease of use
- exceptions include patients with a massive PE or in situations where rapid reversal of anticoagulation may be necessary

Ongoing anticoagulation with warfarin

- target INR 2.0 - 3.0, length of treatment:
- calf DVT: at least 6 weeks
- proximal DVT or PE where there is transient risk factors: at least 3 months
- idiopathic venous thromboembolism or permanent risk factors: at least 6 months

Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. Hypotension). Other invasive approaches should be considered where appropriate facilities exist

Question 55 of 116

You review a 60-year-old woman in the COPD clinic. She was diagnosed with COPD four years ago and is currently maintained on a salbutamol inhaler as required and a tiotropium inhaler regularly. She has recently managed to give up smoking and her latest FEV1 was 42% of predicted. Despite her current therapy she is have frequent exacerbations. What is the most appropriate next step in her management?

- A. Salmeterol inhaler
- B. Combined salmeterol + fluticasone inhaler
- C. Long term oxygen therapy
- D. Betamethasone inhaler
- E. Oral aminophylline

Question 55 of 116

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- D. Betamethasone inhaler
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Following the 2010 NICE guidelines the next step in management would be a combined long-acting beta2-agoinst (LABA) with an inhaled corticosteroid (ICS).

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy

- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%

- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 56 of 116

A 58-year-old man is investigated for a chronic cough and is found to have lung cancer. He enquires whether it may be work related. Which one of the following is most likely to increase his risk of developing lung cancer?

- A. Isocyanates
- B. Soldering flux resin
- C. Passive smoking
- D. Coal dust
- E. Polyvinyl chloride

Question 56 of 116

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Whilst many chemicals have been implicated in the development of lung cancer passive smoking is the most likely cause. Up to 15% of lung cancers in patients who do not smoke are thought to be caused by passive smoking

Lung cancer: risk factors

Smoking
- increases risk of lung ca by a factor of 10

Other factors
- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

Factors that are NOT related
- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Question 57 of 116

You review a 27-year-old woman in the Emergency Department who has been admitted with an acute exacerbation of her asthma. Which one of the following features is most likely to indicate a life-threatening attack?

- A. Failure to improve after nebulised salbutamol 5mg
- B. Cannot complete sentences
- C. Oxygen saturations of 94% on room air
- D. Peak flow of 30% best or predicted
- E. Respiratory rate of 42 / min

Question 57 of 116

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- ✓ D. Peak flow of 30% best or predicted
- E. Respiratory rate of 42 / min

Asthma: acute severe

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
• PEF > 50% best or predicted • Speech normal • RR < 25 / min • Pulse < 110 bpm	• PEF 33 - 50% best or predicted • Can't complete sentences • RR > 25/min • Pulse > 110 bpm	• PEF < 33% best or predicted • Oxygen sats < 92% • Silent chest, cyanosis or feeble respiratory effort • Bradycardia, dysrhythmia or hypotension • Exhaustion, confusion or coma

British Thoracic Society guidelines 2003 (updated 2004)

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

Question 58 of 116

A 62-year-old man with a history of recurrent lower respiratory tract infections is diagnosed as having bilateral bronchiectasis following a high resolution CT scan. Which one of the following is most important in controlling his symptoms?

- A. Inhaled corticosteroids
- B. Prophylactic antibiotics
- C. Surgery
- D. Postural drainage
- E. Mucolytic therapy

Question 58 of 116

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- B. Prophylactic antibiotics
- C. Surgery
- ✓ D. Postural drainage
- E. Mucolytic therapy

Symptom control in non-CF bronchiectasis - inspiratory muscle training + postural drainage

Bronchiectasis: management

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. After assessing for treatable causes (e.g. immune deficiency) management is as follows:

- physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
- postural drainage
- antibiotics for exacerbations + long-term rotating antibiotics in severe cases
- bronchodilators in selected cases
- immunisations
- surgery in selected cases (e.g. Localised disease)

Most common organisms isolated from patients with bronchiectasis:

- *Haemophilus influenzae* (most common)
- *Pseudomonas aeruginosa*
- Klebsiella spp.
- *Streptococcus pneumoniae*

Question 59 of 116

A 30-year-old female with a past history of asthma presents to the Emergency Department with shortness of breath. Chest x-ray shows a right-sided pneumothorax with a 1.5cm rim of air and no mediastinal shift. What is the most appropriate management?

- A. Admit for 48 hours observation
- B. Intercostal drain insertion
- C. Aspiration
- D. Discharge
- E. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line

Question 59 of 116

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A. Admit for 48 hours observation

B. Intercostal drain insertion

✓ C. Aspiration

D. Discharge

E. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line

This should be treated as a secondary pneumothorax as the patient has a history of asthma

Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails then repeat aspiration should be considered
- if this fails then a chest drain should be inserted

Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted. If aspiration fails a chest drain should be inserted. All patients should be admitted for at least 24 hours

Iatrogenic pneumothorax

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Question 60 of 116

Which one of the following causes of lung fibrosis predominately affect the lower zones?

- A. Methotrexate
- B. Sarcoidosis
- C. Coal worker's pneumoconiosis
- D. Ankylosing spondylitis
- E. Extrinsic allergic alveolitis

Question 60 of 116

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- C. Coal worker's pneumoconiosis
- D. Ankylosing spondylitis
- E. Extrinsic allergic alveolitis

Lung fibrosis

It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis. It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones

- extrinsic allergic alveolitis
- coal worker's pneumoconiosis/progressive massive fibrosis
- silicosis
- sarcoidosis
- ankylosing spondylitis (rare)
- histiocytosis
- tuberculosis

Fibrosis predominately affecting the lower zones

- cryptogenic fibrosing alveolitis
- most connective tissue disorders (except ankylosing spondylitis)
- drug-induced: amiodarone, bleomycin, methotrexate
- asbestosis

Question 61 of 116

Which of the following is not a recognised cause of pulmonary eosinophilia?

- A. Churg-Strauss syndrome
- B. Sulphonamides
- C. Extrinsic allergic alveolitis
- D. Loffler's syndrome
- E. Allergic bronchopulmonary aspergillosis

Question 61 of 116

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Pulmonary eosinophilia

Causes of pulmonary eosinophilia
- Churg-Strauss syndrome
- allergic bronchopulmonary aspergillosis (ABPA)
- Loffler's syndrome
- eosinophilic pneumonia
- hypereosinophilic syndrome
- tropical pulmonary eosinophilia
- drugs: nitrofurantoin, sulphonamides
- less common: Wegener's granulomatosis

Loffler's syndrome
- transient CXR shadowing and blood eosinophilia
- thought to be due to parasites such as Ascaris lumbricoides causing an alveolar reaction
- presents with a fever, cough and night sweats which often last for less than 2 weeks.
- generally a self-limiting disease

Tropical pulmonary eosinophilia
- associated with Wuchereria bancrofti infection

Question 62 of 116

Which one of the following is least associated with bronchiectasis?

- A. Hypogammaglobulinaemia
- B. Allergic bronchopulmonary aspergillosis
- C. Measles
- D. Cystic fibrosis
- E. Sarcoidosis

Question 62 of 116

Which one of the following is least associated with bronchiectasis?

- A. Hypogammaglobulinaemia
- B. Allergic bronchopulmonary aspergillosis
- C. Measles
- D. Cystic fibrosis
- ✓ E. Sarcoidosis

Traction bronchiectasis may be seen in some rare cases of stage IV pulmonary sarcoidosis but this is the least strong association of the five options

Bronchiectasis: causes

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. There are a wide variety of causes are listed below:

Causes

- post-infective: tuberculosis, measles, pertussis, pneumonia
- cystic fibrosis
- bronchial obstruction e.g. lung cancer/foreign body
- immune deficiency: selective IgA, hypogammaglobulinaemia
- allergic bronchopulmonary aspergillosis (ABPA)
- ciliary dyskinetic syndromes: Kartagener's syndrome, Young's syndrome
- yellow nail syndrome

Question 63 of 116

A 63-year-old man presents to the respiratory out-patients department with shortness of breath. Investigations reveal a fibrosing lung disease. A sputum sample however is positive for acid-fast bacilli. Which of the following may have predisposed him to developing tuberculosis?

- A. Cadmium
- B. Coal dust
- C. White asbestos fibres
- D. Blue asbestos fibres
- E. Silica

Question 63 of 116

A 63-year-old man presents to the respiratory out-patients department with shortness of breath. Investigations reveal a fibrosing lung disease. A sputum sample however is positive for acid-fast bacilli. Which of the following may have predisposed him to developing tuberculosis?

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- D. Blue asbestos fibres
- ✓ E. Silica

Silicosis

Silicosis is a risk factor for developing TB (silica is toxic to macrophages)

Features
- fibrosing lung disease
- 'egg-shell' calcification of hilar lymph nodes

Question 64 of 116

Which type of hypersensitivity reaction predominates in the acute phase of extrinsic allergic alveolitis?

- A. Type I
- B. Type II
- C. Type III
- D. Type IV
- E. Type V

Question 64 of 116

Which type of hypersensitivity reaction predominates in the acute phase of extrinsic allergic alveolitis?

- A. Type I
- B. Type II
- ✓ C. Type III
- D. Type IV
- E. Type V

Although it is known that the pathogenesis of extrinsic allergic alveolitis involves a type IV (delayed) hypersensitivity reaction, a type III hypersensitivity reaction is thought to predominate, especially in the acute phase

Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase

Examples
- bird fanciers' lung (avian proteins)
- farmers lung (spores of Micropolyspora faeni)
- malt workers' lung (Aspergillus clavatus)
- mushroom workers' lung (thermophilic actinomycetes*)

Presentation
- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

Investigation
- CXR: upper lobe fibrosis
- BAL: lymphocytosis
- blood: NO eosinophilia

*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as Micropolyspora faeni

Question 65 of 116

Which one of the following is not part of the diagnostic criteria of acute respiratory distress syndrome (ARDS)?

- A. Bilateral infiltrates on CXR
- B. Non-cardiogenic
- C. pO2/FiO2 < 200 mmHg
- D. Respiratory rate > 24/min
- E. Acute onset

Question 65 of 116

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- E. Acute onset

ARDS

Basics
- acute respiratory distress syndrome
- caused by increased permeability of alveolar capillaries leading to fluid accumulation in alveoli i.e. non-cardiogenic pulmonary oedema

Criteria (American-European Consensus Conference)
- acute onset
- bilateral infiltrates on CXR
- non-cardiogenic (pulmonary artery wedge pressure needed if doubt)
- pO2/FiO2 < 200 mmHg

Causes
- infection: sepsis, pneumonia
- massive blood transfusion
- trauma
- smoke inhalation
- pancreatitis
- cardio-pulmonary bypass

Question 66 of 116

A 65-year-old man with a history of Parkinson's disease is referred to the respiratory clinic with shortness of breath. He has never smoked. Spirometry is performed:

	Percentage predicted
FEV1	71%
FVC	74%

Which one of the following drugs is most likely to be responsible?

- A. Levodopa
- B. Entacapone
- C. Ropinirole
- D. Selegiline
- E. Pergolide

Question 66 of 116

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- D. Selegiline
- ✓ E. Pergolide

This patient has developed pulmonary fibrosis (explaining the restrictive picture on spirometry) secondary to pergolide therapy

Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence

Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia, 'on-off' effect
- no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Question 67 of 116

A 45-year-old female with a 30 pack-year history of smoking is admitted to the Emergency Department with shortness of breath. Arterial blood gases taken on room air are as follows:

pH 7.49

pCO2 2.9 kPa

pO2 8.8 kPa

Which one of the following is the most likely diagnosis?

- A. Salicylate overdose
- B. Chronic obstructive pulmonary disease
- C. Pulmonary embolism
- D. Vomiting
- E. Anxiety

Question 67 of 116

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- ✓ C. Pulmonary embolism
- D. Vomiting
- E. Anxiety

Pulmonary embolism needs to be excluded. Even with a significant smoking history a reduced pO2 should not be attributed to anxiety. A salicylate overdose would not account for a reduced pO2, unless it is severe enough to have caused pulmonary oedema. This option is much less likely than a pulmonary embolism

Respiratory alkalosis

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

Question 68 of 116

A 38-year-old man is reviewed in the respiratory clinic complaining of episodic wheezing whilst playing rugby. There is no history of cough, atopy or smoking. He is generally fit and well and has no past medical history of note. Clinical examination is unremarkable. Following history and examination it is thought he has an intermediate probability of asthma. Which one of the following is the most appropriate next investigation?

- A. Spirometry
- B. Serial peak expiratory flow measurements
- C. Histamine stimulation test
- D. Methacholine stimulation test
- E. A trial of inhaled steroids with FEV1 measurements before and after

Question 68 of 116

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- D. Methacholine stimulation test
- E. A trial of inhaled steroids with FEV1 measurements before and after

Asthma - intermediate probability - do spirometry first-line

If the FEV1/FVC < 0.7 then a trial of treatment is appropriate. Otherwise further investigations should be performed

Asthma: diagnosis in adults

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning • History of atopic disorder • Wheeze heard on auscultation • Unexplained peripheral blood eosinophilia	• Prominent dizziness, light-headedness, peripheral tingling • Chronic productive cough in the absence of wheeze or breathlessness • Repeatedly normal physical examination • Significant smoking history (i.e. > 20 pack-years) • Normal PEF or spirometry when symptomatic

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % = [(Highest – Lowest PEFR) / Highest PEFR] x 100
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant

Question 69 of 116

A newborn female baby is diagnosed with cystic fibrosis following an episode of meconium ileus shortly after birth. Which one of the following is least likely to occur as a consequence of her underlying diagnosis?

- A. Delayed puberty
- B. Nasal polyps
- C. Diabetes mellitus
- D. Rectal prolapse
- E. Arthropathy

Question 69 of 116

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- B. Nasal polyps
- C. Diabetes mellitus
- D. Rectal prolapse
- ✓ E. Arthropathy

Arthropathy is not a common feature of cystic fibrosis

Cystic fibrosis: features

Presenting features

- neonatal period (around 20%): meconium ileus, less commonly prolonged jaundice
- recurrent chest infections (40%)
- malabsorption (30%): steatorrhoea, failure to thrive
- other features (10%): liver disease

Other features of cystic fibrosis

- short stature
- diabetes mellitus
- delayed puberty
- rectal prolapse (due to bulky stools)
- nasal polyps
- male infertility, female subfertility

Question 70 of 116

A 33-year-old man is seen in the respiratory clinic. He was referred with poorly control asthma and has recently had salmeterol added in addition to beclometasone dipropionate inhaler 200mcg bd and salbutamol prn. There has unfortunately been no response to adding the salmeterol. What is the most appropriate action?

A. Stop salmeterol + trial of leukotriene receptor antagonist

B. Continue salmeterol + increase beclometasone dipropionate inhaler to 400mcg bd

C. Continue salmeterol + trial of leukotriene receptor antagonist

D. Stop salmeterol + trial of oral theophylline

E. Stop salmeterol + increase beclometasone dipropionate inhaler to 400mcg bd

Question 70 of 116

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- C. Continue salmeterol + trial of leukotriene receptor antagonist
- D. Stop salmeterol + trial of oral theophylline
- ✓ E. Stop salmeterol + increase beclometasone dipropionate inhaler to 400mcg bd

Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: • good response to LABA - continue LABA • benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) • no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: • increasing inhaled steroid up to 2000 mcg/day* • addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet
Step 5	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Question 71 of 116

A 67-year-old man is referred to the respiratory clinic. He has a past history of tuberculosis as a child but is otherwise normally fit and well. Over the past two months he has had a cough, lost one stone in weight and had four episodes of haemoptysis. A chest x-ray shows a solid mass occupying the right upper zone. Investigation results include the following:

Aspergillus precipitin antibody	Positive

What is the most likely diagnosis?

- A. Lung abscess
- B. Invasive aspergillosis
- C. Aspergilloma
- D. Reactivation of primary tuberculosis
- E. Allergic bronchopulmonary aspergillosis

Question 71 of 116

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Aspergillus precipitin antibody Positive

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- B. Invasive aspergillosis
- ✓ C. Aspergilloma
- D. Reactivation of primary tuberculosis
- E. Allergic bronchopulmonary aspergillosis

Aspergilloma

An aspergilloma is a fungus ball which often colonises an existing lung cavity (e.g. secondary to TB, lung cancer or cystic fibrosis)

Usually asymptomatic but features may include
- cough
- haemoptysis (may be severe)

Investigations
- CXR containing a rounded opacity
- high titres Aspergillus precipitins

Question 72 of 116

Which one of the following is the most common type of lung cancer in the UK?

- A. Small cell
- B. Squamous cell
- C. Adenocarcinoma
- D. Large cell
- E. Carcinoid

Question 72 of 116

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- ✓ B. Squamous cell
- C. Adenocarcinoma
- D. Large cell
- E. Carcinoid

Tricky question. It is well known that the incidence of adenocarcinoma is rising in comparison to the other types of non-small cell lung cancer. Indeed, adenocarcinoma is now the most common type of lung cancer in the USA. In the UK however squamous cell cancer remains the most common subtype

Reference
Janssen-Heijnen, M.L. and J.W. Coebergh, The changing epidemiology of lung cancer in Europe. Lung Cancer, 2003. 41(3)

Lung cancer: types

Lung cancer
- squamous: c. 35%
- adenocarcinoma: c. 30%
- small (oat) cell: c. 15%
- large cell: c. 10%
- other c. 5%

Other tumours
- alveolar cell carcinoma: not related to smoking, ++sputum
- bronchial adenoma: mostly carcinoid

Question 73 of 116

A 52-year-old man with a history of alcohol dependence is admitted with fever and feeling generally unwell. An admission chest x-ray shows consolidation in the right upper lobe with early cavitation. What is the most likely causative organism?

- A. *Streptococcus pneumoniae*
- B. *Legionella pneumophilia*
- C. *Staphylococcus aureus*
- D. *Klebsiella pneumoniae*
- E. Mycoplasma pneumoniae

Question 73 of 116

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- B. *Legionella pneumophilia*
- C. *Staphylococcus aureus*
- ✓ D. *Klebsiella pneumoniae*
- E. Mycoplasma pneumoniae

Pneumonia in an alcoholic - Klebsiella

Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- Staphylococcal aureus
- atypical pneumonias (e.g. Due to Mycoplasma pneumoniae)
- viruses

Klebsiella pneumoniae is classically in alcoholics

Streptococcus pneumoniae **(pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

Question 74 of 116

A 56-year-old man is admitted with type II respiratory failure secondary to COPD but fails to respond to maximal medical therapy. It is decided that a trial of non-invasive ventilation in the form of bi-level pressure support should be given. What are the most appropriate initial settings for the ventilator?

- A. IPAP = 10 cm H2O; EPAP = 5 cm H2O
- B. IPAP = 15 cm H2O; EPAP = 15 cm H2
- C. IPAP = 50 cm H2O; EPAP = 20 cm H2O
- D. IPAP = 20 cm H2O; EPAP = 50 cm H2O
- E. IPAP = 5 cm H2O; EPAP = 12 cm H2O

Question 74 of 116

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- C. IPAP = 50 cm H2O; EPAP = 20 cm H2O
- D. IPAP = 20 cm H2O; EPAP = 50 cm H2O
- E. IPAP = 5 cm H2O; EPAP = 12 cm H2O

The 2008 Royal College of Physicians guidelines recommend an initial IPAP of 10 cm H20. The 2002 British Thoracic Society guidelines had previously advocated starting at 12-15 cm H20

Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H2O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H20 whilst BTS suggest 12-15 cm H2O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

Question 75 of 116

A 54-year-old woman with chronic obstructive pulmonary disease (COPD) is prescribed an inhaled corticosteroid. What is the main therapeutic benefit of inhaled corticosteroids in patients with COPD?

- A. Reduced severity of exacerbations
- B. Improved all cause mortality
- C. Reduced use of bronchodilators
- D. Slows decline in FEV1
- E. Reduced frequency of exacerbations

Question 75 of 116

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COPD - reason for using inhaled corticosteroids - reduced exacerbations

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%
- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness
- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics
- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale
- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 76 of 116

A 54-year-old woman with a 30-pack-year history of smoking presents due to increasing breathlessness. A diagnosis of chronic obstructive pulmonary disease (COPD) is suspected. Which of the following diagnostic criteria should be used when assessing a patient with suspected COPD?

- A. FEV1 > 70% of predicted value + FEV1/FVC < 60%
- B. FEV1/FVC < 70% + symptoms suggestive of COPD
- C. FEV1 < 80% of predicted value + FEV1/FVC < 70%
- D. FEV1 < 80% of predicted value + FEV1/FVC < 60%
- E. FEV1 < 70% of predicted value + FEV1/FVC > 70%

Question 76 of 116

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- C. FEV1 < 80% of predicted value + FEV1/FVC < 70%
- D. FEV1 < 80% of predicted value + FEV1/FVC < 60%
- E. FEV1 < 70% of predicted value + FEV1/FVC > 70%

Please see the 2010 NICE guidelines for further details. Patients can now be diagnosed with 'mild' COPD if their FEV1 predicted is > 80% if they have symptoms suggestive of COPD.

COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50–79%	Stage 2 - Moderate
< 0.7	30–49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

**symptoms should be present to diagnose COPD in these patients

Question 77 of 116

A 52-year-old male is admitted to hospital with a temperature of 38.2 C and a 3 days history of a productive cough. He has been generally unwell for the past 10 days with flu-like symptoms. On examination blood pressure is 96/60 mmHg and the heart rate is 102 / min. Chest x-ray shows bilateral lower zone consolidation. What is the most likely causative organism?

- A. *Moraxella catarrhalis*
- B. Mycoplasma pneumoniae
- C. Klebsiella
- D. *Staphylococcus aureus*
- E. *Chlamydia* pneumoniae

Question 77 of 116

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- B. Mycoplasma pneumoniae
- C. Klebsiella
- ✓ D. *Staphylococcus aureus*
- E. *Chlamydia* pneumoniae

Preceding influenza predisposes to *Staphylococcus aureus* pneumonia

Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- Staphylococcal aureus
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Streptococcus pneumoniae **(pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

Question 78 of 116

A 65-year-old man is admitted with fever and dyspnoea. A chest x-ray shows extensive shadowing in the right lower zone. Which one of the following is associated with a poor prognosis in patients with community-acquired pneumonia?

- A. Diastolic blood pressure 65 mmHg
- B. Sodium 131 mmol/l
- C. Urea 12 mmol/l
- D. White blood cell 27 * 10^9/l
- E. Respiratory rate 25/min

Question 78 of 116

A 65-year-old man is admitted with fever and dyspnoea. A chest x-ray shows extensive shadowing in the right lower zone. Which one of the following is associated with a poor prognosis in patients with community-acquired pneumonia?

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- B. Sodium 131 mmol/l
- ✓ C. Urea 12 mmol/l
- D. White blood cell 27 * 10^9/l
- E. Respiratory rate 25/min

Pneumonia: prognostic factors

CURB-65 criteria of severe pneumonia

- Confusion (abbreviated mental test score < 8/10)
- Urea > 7 mmol/L
- Respiratory rate = 30 / min
- BP: systolic < 90 or diastolic < 60 mmHg
- age > 65 years

Patients with 3 or more (out of 5) of the above criteria are regarded as having a severe pneumonia

Other factors associated with a poor prognosis include:

- presence of coexisting disease
- hypoxaemia (pO2 < 8 kPa) independent of FiO2

Question 79 of 116

Which one of the following interventions is most likely to increase survival in patients with COPD?

- A. Home nebulisers
- B. Tiotropium inhaler
- C. Long-term steroid therapy
- D. Smoking cessation
- E. Long-term oxygen therapy

Question 79 of 116

Which one of the following interventions is most likely to increase survival in patients with COPD?

- A. Home nebulisers
- B. Tiotropium inhaler
- C. Long-term steroid therapy
- ✓ D. Smoking cessation
- E. Long-term oxygen therapy

Whilst long-term oxygen therapy may increase survival in hypoxic patients, smoking cessation is the single most important intervention in patients with COPD

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%
- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness
- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics
- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale
- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 80 of 116

A 29-year-old man who is being investigated for haemoptysis and a chronic cough has a blood screen:

Hb 12.9 g/dl

Plt 248 * 10^9/l

WBC 5.4 * 10^9/l

ESR 11 mm/hr

Na^+ 138 mmol/l

K^+ 5.0 mmol/l

Bicarbonate 19 mmol/l

Urea 14.0 mmol/l

Creatinine 178 µmol/l

Urine dipstick shows blood ++. What is the most likely diagnosis?

- A. Wegener's granulomatosis
- B. Lung cancer with renal metastases
- C. Churg-Strauss syndrome
- D. Renal cancer with lung metastases
- E. Goodpasture's syndrome

Question 80 of 116

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- D. Renal cancer with lung metastases
- ✓ E. Goodpasture's syndrome

The age of the patient and normal ESR point to a diagnosis of Goodpasture's syndrome.

Goodpasture's syndrome

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

Features
- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

Factors which increase likelihood of pulmonary haemorrhage
- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons
- young males

Investigations
- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

Management
- plasma exchange
- steroids
- cyclophosphamide

Question 81 of 116

A 55-year-old man is diagnosed with non-small cell lung cancer. Which one of the following is a contraindication to surgery?

- A. Pleural effusion
- B. FEV1 of 1.3 litres
- C. Continuation of smoking
- D. Hypercalcaemia
- E. Stage T2N1

Question 81 of 116

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- A. Pleural effusion
- ✓ B. FEV1 of 1.3 litres
- C. Continuation of smoking
- D. Hypercalcaemia
- E. Stage T2N1

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

Lung cancer: non-small cell management

Management
- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

Surgery contraindications
- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

Question 82 of 116

Which one of the following is responsible for malt workers' lung?

- A. Aspergillus clavatus
- B. Avian proteins
- C. Mycobacterium avium
- D. Thermo*Actinomyces* candidus
- E. Micropolyspora faeni

Question 82 of 116

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- E. Micropolyspora faeni

Aspergillus clavatus causes malt workers' lung, a type of EAA

Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase

Examples
- bird fanciers' lung (avian proteins)
- farmers lung (spores of Micropolyspora faeni)
- malt workers' lung (Aspergillus clavatus)
- mushroom workers' lung (thermophilic actinomycetes*)

Presentation
- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

Investigation
- CXR: upper lobe fibrosis
- BAL: lymphocytosis
- blood: NO eosinophilia

*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as Micropolyspora faeni

Question 83 of 116

A 19-year-old male with no past medical history presents to the Emergency Department with anterior chest pain and shortness of breath. Blood pressure is 110/80 mmHg and his pulse is 84 bpm. The chest x-ray is reported as showing a 50% pneumothorax with no mid-line shift. What is the most appropriate management?

- A. Intercostal drain insertion
- B. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
- C. Discharge
- D. Admit for 48 hours observation and repeat chest x-ray
- E. Aspiration

Question 83 of 116

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- D. Admit for 48 hours observation and repeat chest x-ray
- ✓ E. Aspiration

Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

Primary pneumothorax
Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails then repeat aspiration should be considered
- if this fails then a chest drain should be inserted

Secondary pneumothorax
Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted. If aspiration fails a chest drain should be inserted. All patients should be admitted for at least 24 hours

Iatrogenic pneumothorax
Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Question 84 of 116

A 29-year-old man with HIV is admitted with shortness of breath. He ha recently emigrated from South Africa and has only just started taking anti-retroviral medication. Auscultation of his chest is unremarkable although chest x-ray shows bilateral pulmonary interstitial shadowing. What is the investigation of choice?

- A. Bronchoalveolar lavage
- B. CT thorax
- C. Transbronchial biopsy
- D. Sputum culture
- E. Blood culture

Question 84 of 116

A 29-year-old man with HIV is admitted with shortness of breath. He ha recently emigrated from South Africa and has only just started taking anti-retroviral medication. Auscultation of his chest is unremarkable although chest x-ray shows bilateral pulmonary interstitial shadowing. What is the investigation of choice?

- ✓ A. Bronchoalveolar lavage
- B. CT thorax
- C. Transbronchial biopsy
- D. Sputum culture
- E. Blood culture

This man likely has *Pneumocystis carinii* pneumonia. Definitive diagnosis is by bronchial alveolar lavage with silver staining

HIV: Pneumocystis jiroveci pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as Pneumocystis jiroveci, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- Pneumocystis jiroveci is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm³ should receive PCP prophylaxis

Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if pO2 < 9.3kPa then steroids reduce risk of respiratory failure by 50% and death by a third)

Question 85 of 116

Which one of the following is least associated with the development of COPD?

- A. Cadmium exposure
- B. Smoking
- C. Coal dust
- D. Isocyanates
- E. Alpha-1 antitrypsin deficiency

Question 85 of 116

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- A. Cadmium exposure
- B. Smoking
- C. Coal dust
- ✓ D. Isocyanates
- E. Alpha-1 antitrypsin deficiency

Isocyanates are more associated with occupational asthma

COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

Other causes

- cadmium (used in smelting)
- coal
- cotton
- cement
- grain

Question 86 of 116

What is the first line treatment in allergic bronchopulmonary aspergillosis?

- A. Itraconazole
- B. Nebulised pentamidine
- C. Fluconazole
- D. Cyclophosphamide
- E. Prednisolone

Question 86 of 116

What is the first line treatment in allergic bronchopulmonary aspergillosis?

- A. Itraconazole
- B. Nebulised pentamidine
- C. Fluconazole
- D. Cyclophosphamide
- ✓ E. Prednisolone

Allergic bronchopulmonary aspergillosis

Allergic bronchopulmonary aspergillosis results from an allergy to Aspergillus spores. In the exam questions often give a history of bronchiectasis and eosinophilia.

Features
- bronchoconstriction: wheeze, cough, dyspnoea
- bronchiectasis (proximal)

Investigations
- eosinophilia
- flitting CXR changes
- positive radioallergosorbent (RAST) test to Aspergillus
- positive IgG precipitins (not as positive as in aspergilloma)
- raised IgE

Management
- steroids
- itraconazole is sometimes introduced as a second line agent

Question 87 of 116

A 23-year-old female who is 28 weeks pregnant presents with shortness-of-breath and right-sided pleuritic chest pain. A diagnosis of pulmonary embolism is suspected. Which one of the following statements regarding the appropriate management is incorrect?

- A. Chest x-ray should be performed
- B. Positive compression duplex Doppler may negate the need for further investigation
- C. Ventilation-perfusion scanning exposes the fetus to less radiation than computed tomographic pulmonary angiography
- D. D-dimer levels are of no use
- E. Computed tomographic pulmonary angiography increases the lifetime risk of breast cancer in the pregnant women

Question 87 of 116

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- B. Positive compression duplex Doppler may negate the need for further investigation
- ✓ C. Ventilation-perfusion scanning exposes the fetus to less radiation than computed tomographic pulmonary angiography
- D. D-dimer levels are of no use
- E. Computed tomographic pulmonary angiography increases the lifetime risk of breast cancer in the pregnant women

Pregnancy: DVT/PE investigation

Guidelines were published in 2007 by the Royal College of Obstetricians. Key points include:

- chest x-ray should be performed in all patients

- compression duplex Doppler should be performed if the chest x-ray is normal - this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure

- the decision to perform a V/Q or CTPA should be taken at a local level after discussion with the patient and radiologist
- CTPA exposes the fetus to about 10-30% of the radiation dose of a V/Q scan
- V/Q scanning exposes the maternal breast tissue to less radiation than a CTPA

D-dimer is of no use in the investigation of thromboembolism as it raised in pregnancy

Question 88 of 116

A 35-year-old female presents with shortness of breath. The following blood gases are obtained on room air:

pH 7.54

pCO2 1.8 kPa

pO2 12.4 kPa

Which one of the following is the least likely cause?

- A. Opiate overdose
- B. Pulmonary embolism
- C. Pregnancy
- D. Encephalitis
- E. Anxiety

Question 88 of 116

A 35-year-old female presents with shortness of breath. The following blood gases are obtained on room air:

pH 7.54

pCO2 1.8 kPa

pO2 12.4 kPa

Which one of the following is the least likely cause?

- A. Opiate overdose
- B. Pulmonary embolism
- C. Pregnancy
- D. Encephalitis
- E. Anxiety

The question asks for the least likely cause of a respiratory alkalosis. Salicylate, not opiate, poisoning is associated with a respiratory alkalosis. Opiate overdose would lead to respiratory depression and hence a respiratory acidosis

Respiratory alkalosis

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

Question 89 of 116

You are reviewing a 40-year-old man who is known to have bronchiectasis. What organism is most likely to be isolated from his sputum?

- A. *Streptococcus pneumoniae*
- B. Klebsiella spp.
- C. *Haemophilus influenzae*
- D. Pneumocystis jiroveci
- E. *Pseudomonas aeruginosa*

Question 89 of 116

You are reviewing a 40-year-old man who is known to have bronchiectasis. What organism is most likely to be isolated from his sputum?

- A. *Streptococcus pneumoniae*
- B. Klebsiella spp.
- ✓ C. *Haemophilus influenzae*
- D. Pneumocystis jiroveci
- E. *Pseudomonas aeruginosa*

Bronchiectasis: management

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. After assessing for treatable causes (e.g. immune deficiency) management is as follows:

- physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
- postural drainage
- antibiotics for exacerbations + long-term rotating antibiotics in severe cases
- bronchodilators in selected cases
- immunisations
- surgery in selected cases (e.g. Localised disease)

Most common organisms isolated from patients with bronchiectasis:

- *Haemophilus influenzae* (most common)
- *Pseudomonas aeruginosa*
- Klebsiella spp.
- *Streptococcus pneumoniae*

Question 90 of 116

A 34-year-old steelworker presents complaining of episodic shortness of breath. This is particularly noted whilst at work where he describes feeling wheezy and having a tendency to cough. Which one of the following is the most appropriate diagnostic investigation?

- A. Patch testing
- B. High resolution computed tomography of thorax
- C. Serial peak flow measurements at work and at home
- D. Specific IgE measurements
- E. Skin prick test

Question 90 of 116

A 34-year-old steelworker presents complaining of episodic shortness of breath. This is particularly noted whilst at work where he describes feeling wheezy and having a tendency to cough. Which one of the following is the most appropriate diagnostic investigation?

- A. Patch testing
- B. High resolution computed tomography of thorax
- ✓ C. Serial peak flow measurements at work and at home
- D. Specific IgE measurements
- E. Skin prick test

Asthma: occupational

Causes

- isocyanates
- platinum salts
- soldering flux resin
- glutaraldehyde
- flour
- epoxy resins
- proteolytic enzymes

Diagnosis

- specific recommendations are made in the 2007 joint British Thoracic Society and SIGN guidelines
- serial measurements of peak expiratory flow are recommended at work and away from work

Question 91 of 116

A 63-year-old man is noted to have a pleural effusion on CXR. Which one of the following would typically cause a transudate?

- A. Pancreatitis
- B. Pneumonia
- C. Yellow nail syndrome
- D. Hypothyroidism
- E. Dressler's syndrome

Question 91 of 116

A 63-year-old man is noted to have a pleural effusion on CXR. Which one of the following would typically cause a transudate?

- A. Pancreatitis
- B. Pneumonia
- C. Yellow nail syndrome
- ✓ D. Hypothyroidism
- E. Dressler's syndrome

Pleural effusion

Exudate (> 30g/L protein)
- infection: pneumonia, TB, subphrenic abscess
- connective tissue disease: RA, SLE
- neoplasia: lung cancer, mesothelioma, metastases
- pancreatitis
- pulmonary embolism
- Dressler's syndrome
- yellow nail syndrome

Transudate (< 30g/L protein)
- heart failure
- hypoalbuminaemia (liver disease, nephrotic syndrome, malabsorption)
- hypothyroidism
- Meigs' syndrome

Question 92 of 116

A 77-year-old man with a history of type 2 diabetes mellitus is admitted to hospital with worsening shortness-of-breath. He started a course of amoxicillin given by his GP 5 days ago. On examination blood pressure is 88/60 mmHg with a respiratory rate of 36 / min. A chest x-ray reveals left lower lobe consolidation. Arterial blood gases on air are as follows:

pH 7.37

pCO2 5.5 kPa

pO2 9.1 kPa

What is the most suitable antibiotic therapy?

- A. Oral amoxicillin + erythromycin
- B. Intravenous ceftriaxone
- C. Intravenous co-amoxiclav + clarithromycin
- D. Intravenous vancomycin + clarithromycin
- E. Oral co-amoxiclav + erythromycin

Question 92 of 116

A 77-year-old man with a history of type 2 diabetes mellitus is admitted to hospital with worsening shortness-of-breath. He started a course of amoxicillin given by his GP 5 days ago. On examination blood pressure is 88/60 mmHg with a respiratory rate of 36 / min. A chest x-ray reveals left lower lobe consolidation. Arterial blood gases on air are as follows:

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What is the most suitable antibiotic therapy?

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- B. Intravenous ceftriaxone
- ✓ C. Intravenous co-amoxiclav + clarithromycin
- D. Intravenous vancomycin + clarithromycin
- E. Oral co-amoxiclav + erythromycin

This patient has a severe pneumonia as the CURB score is 3. He should therefore be treated with a combination of intravenous antibiotics as recommended by the British Thoracic Society guidelines.

Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- Staphylococcal aureus
- atypical pneumonias (e.g. Due to Mycoplasma pneumoniae)
- viruses

Klebsiella pneumoniae is classically in alcoholics

Streptococcus pneumoniae **(pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

Question 93 of 116

A 35-year-old patient with a history of asthma and epilepsy presents with haemoptysis and a worsening of his asthma. Blood tests reveal an eosinophilia and a positive pANCA. Which of the following drugs is most likely to have precipitated the likely diagnosis?

- A. Montelukast
- B. Phenytoin
- C. Sodium valproate
- D. Prednisolone
- E. Sodium cromoglycate

Question 93 of 116

A 35-year-old patient with a history of asthma and epilepsy presents with haemoptysis and a worsening of his asthma. Blood tests reveal an eosinophilia and a positive pANCA. Which of the following drugs is most likely to have precipitated the likely diagnosis?

- ✓ A. Montelukast
- B. Phenytoin
- C. Sodium valproate
- D. Prednisolone
- E. Sodium cromoglycate

This patient probably has Churg-Strauss syndrome, which is associated with the use of leukotriene receptor antagonists

Churg-Strauss syndrome

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis

Features
- asthma
- blood eosinophilia (e.g. > 10%)
- paranasal sinusitis
- mononeuritis multiplex
- pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

Question 94 of 116

A 49-year-old female is admitted to the Emergency Department with shortness of breath. On examination the pulse is 114 bpm with blood pressure 106/66 mmHg, temperature 37.7ºC and respiratory rate 30/min. Examination of the cardiorespiratory system is unremarkable with a peak expiratory flow rate of 400 l/min. Arterial blood gases on air reveal:

pH 7.41

pCO2 4.0 kPa

pO2 7.2 kPa

Following the initiation of oxygen therapy, what is the next most important step in management?

- A. IV aminophylline
- B. IV hydrocortisone
- C. Low molecular weight heparin
- D. IV fluids
- E. IV co-trimoxazole

Question 94 of 116

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- B. IV hydrocortisone
- ✓ C. Low molecular weight heparin
- D. IV fluids
- E. IV co-trimoxazole

Type 1 respiratory failure in a tachycardic, tachypnoeic female with an absence of chest signs points towards a diagnosis of pulmonary embolism.

Low-grade pyrexia is common in pulmonary embolism.

Pulmonary embolism: management

Unfortunately there is a lack of clear guidelines on the optimal length of anticoagulation following a pulmonary embolism. The 2003 British Thoracic Society guidelines which advocate a shorter duration of treatment are not widely followed. The following is based on the 2005 British Committee for Standards in Haematology (BCSH) guidelines and Clinical Knowledge Summaries.

Initial anticoagulation with heparin

- low molecular weight heparin (LMWH), rather than unfractionated heparin (UFH), should be used routinely in patients with suspected pulmonary embolism. This reflects the equal efficacy and safety of LMWHs as well as their ease of use
- exceptions include patients with a massive PE or in situations where rapid reversal of anticoagulation may be necessary

Ongoing anticoagulation with warfarin

- target INR 2.0 - 3.0, length of treatment:
- calf DVT: at least 6 weeks
- proximal DVT or PE where there is transient risk factors: at least 3 months
- idiopathic venous thromboembolism or permanent risk factors: at least 6 months

Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. Hypotension). Other invasive approaches should be considered where appropriate facilities exist

Question 95 of 116

A chest x-ray of a patient with sarcoidosis shows bilateral hilar lymphadenopathy accompanied with interstitial infiltrates. What chest x-ray stage does this correspond to?

- A. Stage 0
- B. Stage 1
- C. Stage 2
- D. Stage 3
- E. Stage 4

Question 95 of 116

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- A. Stage 0
- B. Stage 1
- ✓ C. Stage 2
- D. Stage 3
- E. Stage 4

Sarcoidosis CXR
- 1 = BHL
- 2 = BHL + infiltrates
- 3 = infiltrates
- 4 = fibrosis

Sarcoidosis: investigation

There is no one diagnostic test for sarcoidosis and hence diagnosis is still largely clinical. ACE levels have a sensitivity of 60% and specificity of 70% and are therefore not reliable in the diagnosis of sarcoidosis although they may have a role in monitoring disease activity. Routine bloods may show hypercalcaemia (seen in 10% if patients) and a raised ESR

A chest x-ray may show the following changes:
- stage 0 = normal
- stage 1 = bilateral hilar lymphadenopathy (BHL)
- stage 2 = BHL + interstitial infiltrates
- stage 3 = diffuse interstitial infiltrates only
- stage 4 = diffuse fibrosis

Other investigations*
- spirometry: may show a restrictive defect
- tissue biopsy: non-caseating granulomas
- gallium-67 scan - not used routinely

*the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection

Question 96 of 116

A 60-year-old female with a history of COPD presents to the Emergency Department with shortness of breath. Blood pressure is 120/80 mmHg and he pulse is 90 bpm. The chest x-ray shows a pneumothorax with a 2.5 cm rim of air and no mediastinal shift. What is the most appropriate management?

- A. Intercostal drain insertion
- B. Discharge
- C. Admit for 48 hours observation and repeat chest x-ray
- D. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
- E. Aspiration

Question 96 of 116

A 60-year-old female with a history of COPD presents to the Emergency Department with shortness of breath. Blood pressure is 120/80 mmHg and he pulse is 90 bpm. The chest x-ray shows a pneumothorax with a 2.5 cm rim of air and no mediastinal shift. What is the most appropriate management?

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- C. Admit for 48 hours observation and repeat chest x-ray
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Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

Primary pneumothorax
Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails then repeat aspiration should be considered
- if this fails then a chest drain should be inserted

Secondary pneumothorax
Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted. If aspiration fails a chest drain should be inserted. All patients should be admitted for at least 24 hours

Iatrogenic pneumothorax
Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Question 97 of 116

You are asked to interpret the post-bronchodilator spirometry results of a 56-year-old woman who has been complaining of progressive shortness-of-breath.

FEV1/FVC 0.60

FEV1% predicted 60%

What is the most appropriate interpretation of these results?

- A. Poor technique - repeat spirometry
- B. Asthma
- C. COPD (stage 1 - mild)
- D. COPD (stage 2 - moderate)
- E. Pulmonary fibrosis

Question 97 of 116

You are asked to interpret the post-bronchodilator spirometry results of a 56-year-old woman who has been complaining of progressive shortness-of-breath.

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FEV1% predicted 60%

What is the most appropriate interpretation of these results?

- A. Poor technique - repeat spirometry
- B. Asthma
- C. COPD (stage 1 - mild)
- ✓ D. COPD (stage 2 - moderate)
- E. Pulmonary fibrosis

COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50–79%	Stage 2 - Moderate
< 0.7	30–49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

**symptoms should be present to diagnose COPD in these patients

Question 98 of 116

You are reviewing a patient with chronic obstructive pulmonary disease (COPD) who remains breathless despite using a salbutamol inhaler as required. Their FEV1 is 60%. What are the two main options?

A. Long-acting beta2-agoinst (LABA) **or** inhaled corticosteroid

B. Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler **or** long-acting beta2-agoinst (LABA)

C. Long-acting beta2-agoinst (LABA) **or** LABA + inhaled corticosteroid (ICS) in a combination inhaler

D. Long-acting beta2-agoinst (LABA) **or** regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)

E. Long-acting beta2-agoinst (LABA) **or** long-acting muscarinic antagonist (LAMA)

Question 98 of 116

You are reviewing a patient with chronic obstructive pulmonary disease (COPD) who remains breathless despite using a salbutamol inhaler as required. Their FEV1 is 60%. What are the two main options?

- A. Long-acting beta2-agoinst (LABA) **or** inhaled corticosteroid
- B. Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler **or** long-acting beta2-agoinst (LABA)
- C. Long-acting beta2-agoinst (LABA) **or** LABA + inhaled corticosteroid (ICS) in a combination inhaler
- D. Long-acting beta2-agoinst (LABA) **or** regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)
- ✓ E. Long-acting beta2-agoinst (LABA) **or** long-acting muscarinic antagonist (LAMA)

COPD - still breathless despite using inhalers as required?
- FEV1 > 50%: LABA **or** LAMA
- FEV1 < 50%: LABA + ICS **or** LAMA

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%
- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness
- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics
- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale
- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 99 of 116

Which one of the following is the main criteria for determining whether a patient with chronic obstructive pulmonary disease (COPD) should be offered long-term oxygen therapy?

- A. Two arterial blood gases measurements with pO2 < 6.3 kPa
- B. One arterial blood gas measurement with pO2 < 7.7 kPa
- C. One arterial blood gas measurement with pO2 < 8.3 kPa
- D. One arterial blood gas measurement with pO2 < 8.0 kPa
- E. Two arterial blood gases measurements with pO2 < 7.3 kPa

Question 99 of 116

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- C. One arterial blood gas measurement with pO2 < 8.3 kPa
- D. One arterial blood gas measurement with pO2 < 8.0 kPa
- ✓ E. Two arterial blood gases measurements with pO2 < 7.3 kPa

COPD - LTOT if 2 measurements of pO2 < 7.3 kPa

COPD: long-term oxygen therapy

The 2010 NICE guidelines on COPD clearly define which patients should be assessed for and offered long-term oxygen therapy (LTOT). Patients who receive LTOT should breathe supplementary oxygen for at least 15 hours a day.

Assess patients if any of the following:

- very severe airflow obstruction (FEV1 < 30% predicted). Assessment should be 'considered' for patients with severe airflow obstruction (FEV1 30-49% predicted)
- cyanosis
- polycythaemia
- peripheral oedema
- raised jugular venous pressure
- oxygen saturations less than or equal to 92% on room air

Assessment is done by measuring arterial blood gases on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.

Offer LTOT to patients with a pO2 of < 7.3 kPa or to those with a pO2 of 7.3 - 8 kPa and one of the following:

- secondary polycythaemia
- nocturnal hypoxaemia
- peripheral oedema
- pulmonary hypertension

Question 100 of 116

A 25-year-old man is referred due to pain and swelling in his knees and ankles. On examination he has a painful, erythematous rash on his legs. The following results are obtained:

Rheumatoid factor	Negative
ESR	94 mm/hr
Chest x-ray	Hilar lymphadenopathy

What is the most likely outcome?

- A. Improvement following a course of prednisolone
- B. Scarring and ulceration of skin
- C. Spontaneous improvement
- D. Progressive arthritis
- E. Renal replacement therapy in 20 years time

Question 100 of 116

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- B. Scarring and ulceration of skin
- ✓ C. Spontaneous improvement
- D. Progressive arthritis
- E. Renal replacement therapy in 20 years time

The majority of patients with sarcoidosis get better without treatment

This man has an acute form of sarcoidosis. There are no indications for steroid therapy and his symptoms will resolve spontaneously in the majority of cases

Sarcoidosis: prognostic features

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people

Factors associated with poor prognosis

- insidious onset, symptoms > 6 months
- absence of erythema nodosum
- extrapulmonary manifestations: e.g. lupus pernio, splenomegaly
- CXR: stage III-IV features
- black people

Question 101 of 116

A 37-year-old woman who is being as an inpatient for Mycoplasma pneumonia is reviewed. Unfortunately she is unable to tolerate clarithromycin due to severe nausea. What is the most suitable alternative antibiotic?

- A. Linezolid
- B. Cefaclor
- C. Ampicillin
- D. Co-amoxiclav
- E. Doxycycline

Question 101 of 116

A 37-year-old woman who is being as an inpatient for Mycoplasma pneumonia is reviewed. Unfortunately she is unable to tolerate clarithromycin due to severe nausea. What is the most suitable alternative antibiotic?

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- B. Cefaclor
- C. Ampicillin
- D. Co-amoxiclav
- ✓ E. Doxycycline

Mycoplasma pneumoniae

Mycoplasma pneumoniae is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

Features
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

Complications
- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

Diagnosis
- Mycoplasma serology

Management
- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative

Question 102 of 116

A 62-year-old woman with recently diagnosed chronic obstructive pulmonary disease (COPD) presents for review. Her FEV1 is 65% of the predicted value. She has managed to give up smoking and was prescribed a salbutamol inhaler to use as required. Despite this she is still symptomatic and complains of wheeze and shortness of breath. What is the most appropriate next step?

- A. Add an inhaled corticosteroid
- B. Add a long-acting muscarinic antagonist inhaler
- C. Refer for consideration of long-term oxygen therapy
- D. Add oral theophylline
- E. Add a combination long-acting beta2-agonist and corticosteroid inhaler

Question 102 of 116

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- ✓ B. Add a long-acting muscarinic antagonist inhaler
- C. Refer for consideration of long-term oxygen therapy
- D. Add oral theophylline
- E. Add a combination long-acting beta2-agonist and corticosteroid inhaler

Following the 2010 NICE guidelines a long-acting beta2-agoinst (LABA) would be an alternative option.

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
- long-acting beta2-agoinst (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%
- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness
- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline
- NICE only recommends theophylline after trials of short an long-acting bronchodilators or to people who cannot used inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics
- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

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- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 103 of 116

A 30-year-old woman is admitted to the Emergency Department with an exacerbation of asthma. On arrival her peak flow is 30% of predicted, respiratory rate is 36/min and oxygen saturations are 98% on 100% high-flow oxygen. She is given back-to-back nebulisers, intravenous hydrocortisone and started on a magnesium infusion. Which one of the following would be the strongest indicator of a need for intubation and ventilation?

- A. PEFR 20% of predicted
- B. pH 7.33
- C. Patient preference after informed consent
- D. Respiratory rate of 50 / min
- E. Oxygen saturations of 95% on 100% high-flow oxygen

Question 103 of 116

A 30-year-old woman is admitted to the Emergency Department with an exacerbation of asthma. On arrival her peak flow is 30% of predicted, respiratory rate is 36/min and oxygen saturations are 98% on 100% high-flow oxygen. She is given back-to-back nebulisers, intravenous hydrocortisone and started on a magnesium infusion. Which one of the following would be the strongest indicator of a need for intubation and ventilation?

- A. PEFR 20% of predicted
- ✓ B. pH 7.33
- C. Patient preference after informed consent
- D. Respiratory rate of 50 / min
- E. Oxygen saturations of 95% on 100% high-flow oxygen

A falling pH likely represents carbon dioxide retention in a tiring patient as is an ominous sign in acute asthma. Performing serial peak flows in a patient with life-threatening asthma is neither practical nor desirable.

Asthma: acute severe

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
• PEF > 50% best or predicted • Speech normal • RR < 25 / min • Pulse < 110 bpm	• PEF 33 - 50% best or predicted • Can't complete sentences • RR > 25/min • Pulse > 110 bpm	• PEF < 33% best or predicted • Oxygen sats < 92% • Silent chest, cyanosis or feeble respiratory effort • Bradycardia, dysrhythmia or hypotension • Exhaustion, confusion or coma

British Thoracic Society guidelines 2003 (updated 2004)

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

Question 104 of 116

A 65-year-old life-long smoker with a significant past history of asbestos exposure is investigated for lung cancer. Given his history of both smoking and asbestos exposure, what is his increased risk of lung cancer?

- A. 5
- B. 10
- C. 50
- D. 500
- E. 1,000

Question 104 of 116

A 65-year-old life-long smoker with a significant past history of asbestos exposure is investigated for lung cancer. Given his history of both smoking and asbestos exposure, what is his increased risk of lung cancer?

- A. 5
- B. 10
- ✓ C. 50
- D. 500
- E. 1,000

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Lung cancer: risk factors

Smoking
- increases risk of lung ca by a factor of 10

Other factors
- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

Factors that are NOT related
- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Question 105 of 116

You are reviewing a man with haemoptysis in the rapid-access lung clinic. Which one of the following is the most significant risk factor for developing lung cancer?

- A. Cryptogenic fibrosing alveolitis
- B. Asbestos exposure for most of working life
- C. 10 year period of smoking 'crack' cocaine 20 years ago
- D. 30 pack-year history of smoking
- E. 20 year history of recreational cannabis use

Question 105 of 116

You are reviewing a man with haemoptysis in the rapid-access lung clinic. Which one of the following is the most significant risk factor for developing lung cancer?

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Lung cancer: risk factors

Smoking
- increases risk of lung ca by a factor of 10

Other factors
- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

Factors that are NOT related
- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Question 106 of 116

A 17-year-old male with a history of cystic fibrosis presents to clinic for annual review. What is the most appropriate advice regarding his diet?

- A. High calorie and low fat with pancreatic enzyme supplementation for every meal
- B. High calorie and low fat with pancreatic enzyme supplementation for evening meal
- C. Normal calorie and low fat with pancreatic enzyme supplementation for every meal
- D. High calorie and high fat with pancreatic enzyme supplementation for evening meal
- E. High calorie and high fat with pancreatic enzyme supplementation for every meal

Question 106 of 116

A 17-year-old male with a history of cystic fibrosis presents to clinic for annual review. What is the most appropriate advice regarding his diet?

- A. High calorie and low fat with pancreatic enzyme supplementation for every meal
- B. High calorie and low fat with pancreatic enzyme supplementation for evening meal
- C. Normal calorie and low fat with pancreatic enzyme supplementation for every meal
- D. High calorie and high fat with pancreatic enzyme supplementation for evening meal
- ✓ E. High calorie and high fat with pancreatic enzyme supplementation for every meal

Cystic fibrosis: management

Management of cystic fibrosis involves a multidisciplinary approach

Key points

- regular (at least twice daily) chest physiotherapy and postural drainage. Parents are usually taught to do this. Deep breathing exercises are also useful
- high calorie diet, including high fat intake*
- vitamin supplementation
- pancreatic enzyme supplements taken with meals
- heart and lung transplant

*this is now the standard recommendation - previously high calorie, low-fat diets have been recommended to reduce the amount of steatorrhoea

Question 107 of 116

A middle-aged woman is admitted to the Emergency Department with pleuritic chest pain ten days after having a hysterectomy. There is a clinical suspicion of pulmonary embolism. What is the most common chest x-ray finding in patients with pulmonary embolism?

- A. Right heart enlargement
- B. Normal
- C. Pleural effusion
- D. Linear atelectasis
- E. Dilatation of the pulmonary vessels proximal to the embolism

Question 107 of 116

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- C. Pleural effusion
- D. Linear atelectasis
- E. Dilatation of the pulmonary vessels proximal to the embolism

Pulmonary embolism - normal CXR

The vast majority of patients with a pulmonary embolism have a normal chest x-ray.

Pulmonary embolism: investigation

The British Thoracic Society (BTS) published guidelines in 2003 on the management of patients with suspected pulmonary embolism (PE)

Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

Some other points

Clinical probability scores based on risk factors and history and now widely used to help decide on further investigation/management

D-dimers

- sensitivity = 95-98%, but poor specificity

V/Q scan

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

CTPA

- peripheral emboli affecting subsegmental arteries may be missed

Pulmonary angiography

- the gold standard
- significant complication rate compared to other investigations

Question 108 of 116

You are reviewing a patient with chronic obstructive pulmonary disease (COPD) who remains breathless despite using an ipratropium bromide inhaler as required. Her FEV1 is 40%. What are the two main options?

- A. Long-acting beta2-agoinst (LABA) **or** inhaled corticosteroid
- B. Long-acting muscarinic antagonist (LAMA) **or** LABA + inhaled corticosteroid (ICS) in a combination inhaler
- C. Long-acting beta2-agoinst (LABA) **or** long-acting muscarinic antagonist (LAMA)
- D. Long-acting beta2-agoinst (LABA) **or** regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)
- E. Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler **or** long-acting beta2-agoinst (LABA)

Question 108 of 116

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D. Long-acting beta2-agoinst (LABA) **or** regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)

E. Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler **or** long-acting beta2-agoinst (LABA)

COPD - still breathless despite using inhalers as required?
- FEV1 > 50%: LABA **or** LAMA
- FEV1 < 50%: LABA + ICS **or** LAMA

COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

General management
- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

Bronchodilator therapy
- a short-acting beta2-agoinst (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%
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Oral theophylline
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- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD
- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Question 109 of 116

When assessing a patient with suspected chronic obstructive pulmonary disease, which one of the following is least relevant?

- A. Smoking history
- B. Chest x-ray
- C. Full blood count
- D. Peak expiratory flow
- E. Spirometry

Question 109 of 116

When assessing a patient with suspected chronic obstructive pulmonary disease, which one of the following is least relevant?

- A. Smoking history
- B. Chest x-ray
- C. Full blood count
- ✓ D. Peak expiratory flow
- E. Spirometry

Peak expiratory flow is of no value in the diagnosis of COPD

COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50–79%	Stage 2 - Moderate
< 0.7	30–49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

**symptoms should be present to diagnose COPD in these patients

Question 110 of 116

Each one of the following is a risk factor for lung cancer, except:

- A. Radon
- B. Cryptogenic fibrosing alveolitis
- C. Coal dust
- D. Asbestos
- E. Arsenic

Question 110 of 116

Each one of the following is a risk factor for lung cancer, except:

- A. Radon
- B. Cryptogenic fibrosing alveolitis
- ✓ C. Coal dust
- D. Asbestos
- E. Arsenic

Lung cancer: risk factors

Smoking
- increases risk of lung ca by a factor of 10

Other factors
- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

Factors that are NOT related
- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a 10 * 5 = 50 times increased risk

Question 111 of 116

You review a 28-year-old woman with no past medical history of note. For the past week she has being experiencing left sided pleuritic chest pain. Her GP treated her for pleurisy with amoxicillin but there has been no improvement in her symptoms. She denies any shortness of breath and oxygen saturations on room air are 98%. A chest x-ray shows a 20% pneumothorax on the left side. What is the most appropriate management?

- A. Observe for 24 hours before discharging with standard advice
- B. Insert a chest drain
- C. Discharge with standard advice
- D. Aspiration
- E. Observe for 48 hours then repeat chest x-ray

Question 111 of 116

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- ✓ C. Discharge with standard advice
- D. Aspiration
- E. Observe for 48 hours then repeat chest x-ray

Questions sometimes discuss the size of the pneumothorax in percentage terms rather than giving the interpleural distance. A variety of formulas have been proposed to convert between the two.

As a very general rule of thumb:

Average interpleural distance	Approximate size of pneumothorax
0.5 cm	10%
1 cm	15 %
2 cm	30%
3 cm	45%
4 cm	60%

A pneumothorax of 20% if therefore within the 2 cm limit suggested by the British Thoracic Society for observation, if the patient is not short of breath.

Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails then repeat aspiration should be considered
- if this fails then a chest drain should be inserted

Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted. If aspiration fails a chest drain should be inserted. All patients should be admitted for at least 24 hours

Iatrogenic pneumothorax

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Question 112 of 116

A 74-year-old woman has a chest x-ray organised by her GP due to a chronic cough. The chest x-ray shows a cavity in the left upper zone inside of which there is a solid mass. An aspergilloma is suspected. What is the most appropriate next test?

- A. Sputum culture
- B. Serology for Aspergillus precipitins
- C. Blood culture
- D. Bronchoscopy with biopsy
- E. Transthoracic fine needle biopsy

Question 112 of 116

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- C. Blood culture
- D. Bronchoscopy with biopsy
- E. Transthoracic fine needle biopsy

Aspergilloma

An aspergilloma is a fungus ball which often colonises an existing lung cavity (e.g. secondary to TB, lung cancer or cystic fibrosis)

Usually asymptomatic but features may include
- cough
- haemoptysis (may be severe)

Investigations
- CXR containing a rounded opacity
- high titres Aspergillus precipitins

Question 113 of 116

A 19-year-old with 'brittle asthma' is seen in clinic. Three weeks ago she started taking prednisolone 15mg od as her asthma was poorly controlled on beclometasone dipropionate 800 mcg bd., salmeterol, oral montelukast and salbutamol as required. What should happen with regards to inhaled steroids?

- A. Continue beclometasone dipropionate 800 mcg bd
- B. Stop inhaled steroids
- C. Increase beclometasone dipropionate to 1000 mcg bd
- D. Decrease beclometasone dipropionate to 400 mcg bd
- E. Use beclometasone dipropionate 200 mcg on an 'as required' basis with salbutamol

Question 113 of 116

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- E. Use beclometasone dipropionate 200 mcg on an 'as required' basis with salbutamol

Even when patients are on oral prednisolone they should continue high-dose inhaled corticosteroids

Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

Step 1	Inhaled short-acting B2 agonist as required
Step 2	Add inhaled steroid at 200-800 mcg/day* 400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
Step 3	1. Add inhaled long-acting B2 agonist (LABA) 2. Assess control of asthma: • good response to LABA - continue LABA • benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose) • no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline
Step 4	Consider trials of: • increasing inhaled steroid up to 2000 mcg/day* • addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet
Step 5	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets Maintain high dose inhaled steroid at 2000 mcg/day* Refer patient for specialist care

*beclometasone dipropionate or equivalent

Additional notes

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Question 114 of 116

What is the mode of inheritance of Alpha-1 antitrypsin deficiency?

- A. Mitochondrial
- B. X-linked recessive
- C. Polygenic
- D. Autosomal recessive
- E. Autosomal dominant

Question 114 of 116

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Alpha-1 antitrypsin deficiency - autosomal recessive / co-dominant

Alpha-1 antitrypsin deficiency is also sometimes listed as being an autosomal co-dominant condition. Unfortunately trusted sources vary - how would you classify A1AT?

Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver

Genetics
- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

Features
- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

Investigations
- A1AT concentrations

Management
- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

*trusted sources are split on which is a more accurate description

Question 115 of 116

Non-invasive ventilation (NIV) is least likely to be successful in which one of the following scenarios?

- A. COPD
- B. Chest wall deformity
- C. Obstructive sleep apnoea
- D. Weaning from tracheal intubation
- E. Bronchiectasis

Question 115 of 116

Non-invasive ventilation (NIV) is least likely to be successful in which one of the following scenarios?

A. COPD

B. Chest wall deformity

C. Obstructive sleep apnoea

D. Weaning from tracheal intubation

✓ E. Bronchiectasis

The British Thoracic Society recommend that whilst a trial of NIV may be undertaken in bronchiectasis it should not be used routinely as its effectiveness is likely to be limited by excessive secretions

Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H2O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H20 whilst BTS suggest 12-15 cm H2O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

Question 116 of 116

A 24-year-old man who has been discharged following admission for a spontaneous pneumothorax ask for advice about flying. During his stay in hospital the pneumothorax was aspirated and a check x-ray revealed no residual air. What is the earliest time he should fly?

- A. Immediately
- B. 24 hours
- C. 3 days
- D. 2 weeks
- E. 2 months

Question 116 of 116

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- B. 24 hours
- C. 3 days
- ✓ D. 2 weeks
- E. 2 months

Please see the text below for an explanation about the competing and changing guidelines.

Fitness to fly

The Civil Aviation Authority (CAA) has issued guidelines on air travel for people with medical conditions; please see the link provided.

Cardiovascular disease

- unstable angina, uncontrolled hypertension, uncontrolled cardiac arrhythmia, decompensated heart failure, severe symptomatic valvular disease: should not fly
- uncomplicated myocardial infarction: may fly after 7-10 days
- complicated myocardial infarction: after 4-6 weeks
- coronary artery bypass graft: after 10-14 days
- percutaneous coronary intervention: after 5 days

Respiratory disease

- pneumonia: should be 'clinically improved with no residual infection'
- pneumothorax: absolute contraindication, the CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air. The British Thoracic Society used to recommend not travelling by air for a period of 6 weeks but this has now been changed to 1 week post check x-ray

Pregnancy

- most airlines do not allow travel after 36 weeks for a single pregnancy and after 32 weeks for a multiple pregnancy
- most airlines require a certificate after 28 weeks confirming that the pregnancy is progressing normally

Surgery

- travel should be avoided for 10 days following abdominal surgery
- laparoscopic surgery: after 24 hours
- colonoscopy: after 24 hours
- following the application of a plaster cast, the majority of airlines restrict flying for 24 hours on flights of less than 2 hours or 48 hours for longer flights

Haematological disorders

- patients with a haemoglobin of greater than 8 g/dl may travel without problems (assuming there is no coexisting condition such as cardiovascular or respiratory disease)

Question 1 of 97

A 47-year-old man with a history of chronic sinusitis presents with shortness of breath to the Emergency Department. Initial investigations reveal:

Hb	10.4g/dl
Platelets	477 * 10^9/l
WCC	14.3 * 10^9/l
ESR	92 mm/h
Urea	20 mmol/l
Creatinine	198 µmol/l

Urine dipstick blood +++

What is the most likely diagnosis?

- A. Mixed cryoglobulinaemia
- B. Churg-Strauss syndrome
- C. Wegener's granulomatosis
- D. Haemolytic uraemic syndrome
- E. Henoch-Schonlein purpura

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- C. Wegener's granulomatosis
- D. Haemolytic uraemic syndrome
- E. Henoch-Schonlein purpura

The combination of pulmonary and renal involvement combined with a history of chronic sinusitis points towards a diagnosis of Wegener's granulomatosis

Wegener's granulomatosis

Wegener's granulomatosis is an autoimmune condition associated with a necrotizing granulomatous vasculitis, affecting both the upper and lower respiratory tract as well as the kidneys

Features
- upper respiratory tract: epistaxis, sinusitis, nasal crusting
- lower respiratory tract: dyspnoea, haemoptysis
- glomerulonephritis ('pauci-immune', 80% of patients)
- saddle-shape nose deformity
- also: vasculitic rash, eye involvement (e.g. proptosis), cranial nerve lesions

Investigations
- cANCA positive in > 90%, pANCA positive in 25%
- chest x-ray: wide variety of presentations, including cavitating lesions
- renal biopsy: crescenteric glomerulonephritis

Management
- steroids
- cyclophosphamide (90% response)
- plasma exchange
- median survival = 8-9 years

Question 2 of 97

A 50-year-old female with a history of rheumatoid presents with a suspected septic knee joint. A diagnostic aspiration is performed and sent to microbiology. Which of the following organisms is most likely to be responsible?

- A. *Staphylococcus aureus*
- B. *Staphylococcus epidermidis*
- C. *Escherichia coli*
- D. *Neisseria gonorrhoeae*
- E. *Streptococcus pneumoniae*

Question 2 of 97

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- B. *Staphylococcus epidermidis*
- C. *Escherichia coli*
- D. *Neisseria gonorrhoeae*
- E. *Streptococcus pneumoniae*

Septic arthritis - most common organism: *Staphylococcus aureus*

Septic arthritis

Overview
- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

Management
- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin + fusidic acid or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

Question 3 of 97

Which one of the following is least associated with Behcet's syndrome?

- A. Mouth ulcers
- B. Genital ulcers
- C. Conjunctivitis
- D. Deep vein thrombosis
- E. Aseptic meningitis

Question 3 of 97

Which one of the following is least associated with Behcet's syndrome?

- A. Mouth ulcers
- B. Genital ulcers
- C. Conjunctivitis
- D. Deep vein thrombosis
- E. Aseptic meningitis

Oral ulcers + genital ulcers + anterior uveitis = Behcet's

Mouth ulcers, genital ulcers, deep vein thrombosis and aseptic meningitis are all recognised features of Behcet's syndrome

Ocular involvement is the most feared complication of Behcet's syndrome. Conjunctivitis is seen rarely and is much less common than anterior uveitis. Other ocular problems seen include retinal vasculitis, iridocyclitis and chorioretinitis

Behcet's syndrome

Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

Epidemiology
- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5* and MICA6 allele
- c. 30% of patients have a positive family history

Features
- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis
- erythema nodosum, DVT

Diagnosis
- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

*more specifically HLA B51, a split antigen of HLA B5

Question 4 of 97

Low levels of which one of the following types of complement are associated with the development of systemic lupus erythematous?

- A. C4
- B. C5
- C. C6
- D. C7
- E. C8

Question 4 of 97

Low levels of which one of the following types of complement are associated with the development of systemic lupus erythematous?

- A. C4
- B. C5
- C. C6
- D. C7
- E. C8

SLE: C3 & C4 low

Low levels of C4a and C4b have been shown to be associated with an increased risk of developing systemic lupus erythematous

SLE: investigations

Immunology
- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

Monitoring
- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Question 5 of 97

Reactive arthritis is associated with which one of the following HLA antigens?

- A. HLA-B27
- B. HLA-A3
- C. HLA-DR4
- D. HLA-B5
- E. HLA-DR3

Question 5 of 97

Reactive arthritis is associated with which one of the following HLA antigens?

- A. HLA-B27
- B. HLA-A3
- C. HLA-DR4
- D. HLA-B5
- E. HLA-DR3

Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA)

The American College of Rheumatology now define reactive arthritis as an episode of peripheral arthritis lasting for greater than 1 month associated with urethritis/cervicitis or diarrhoea

Epidemiology
- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

Organisms often responsible for post-dysenteric form
- *Shigella* flexneri
- *Salmonella typhi*murium
- *Salmonella* enteritidis
- *Yersinia enterocolitica*
- *Campylobacter*

Organisms often responsible for post-STI form
- *Chlamydia trachomatis*

Question 6 of 97

A 34-year-old woman with a history of antiphospholipid syndrome presents with a swollen and painful leg. Doppler ultrasound confirms a deep vein thrombosis (DVT). She had a previous DVT 4 months ago and was taking warfarin (with a target INR of 2-3) when the DVT occurred. How should her anticoagulation be managed?

- A. Life-long warfarin, increase target INR to 3 - 4
- B. Add in life-long low-dose aspirin
- C. A further 6 months warfarin, target INR 2 - 3
- D. A further 6 months warfarin, target INR 3 - 4
- E. Life-long warfarin, target INR 2 - 3

Question 6 of 97

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- B. Add in life-long low-dose aspirin
- C. A further 6 months warfarin, target INR 2 - 3
- D. A further 6 months warfarin, target INR 3 - 4
- E. Life-long warfarin, target INR 2 - 3

The evidence base is scanty here but most clinicians would increase the target INR to 3-4 if a patient has had a further thrombosis with an INR of 2-3. Please see the BCSH guidelines

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features
- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE
- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines
- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 7 of 97

A 41-year-old man with a past history of asthma presents with pain and weakness in his left hand. Examination findings are consistent with a left ulnar nerve palsy. Blood tests reveal an eosinophilia. Which one of the following antibodies is most likely to be present?

- A. ANA
- B. Anti-Scl70
- C. pANCA
- D. Antiphospholipid antibodies
- E. cANCA

Question 7 of 97

A 41-year-old man with a past history of asthma presents with pain and weakness in his left hand. Examination findings are consistent with a left ulnar nerve palsy. Blood tests reveal an eosinophilia. Which one of the following antibodies is most likely to be present?

- A. ANA
- B. Anti-Scl70
- C. pANCA
- D. Antiphospholipid antibodies
- E. cANCA

This patient has Churg-Strauss syndrome as evidenced by the asthma, mononeuritis and eosinophilia

Churg-Strauss syndrome

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis

Features
- asthma
- blood eosinophilia (e.g. > 10%)
- paranasal sinusitis
- mononeuritis multiplex
- pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

Question 8 of 97

Which one of the following is not a risk factor for developing osteoporosis?

- A. Smoking
- B. Obesity
- C. Sedentary lifestyle
- D. Premature menopause
- E. Female sex

Question 8 of 97

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Low body mass, rather than obesity is associated with an increased risk of developing osteoporosis

Osteoporosis: causes

Risk factors
- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Asians and Orientals

Diseases which predispose
- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- GI problems: malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Question 9 of 97

A 31-year-old female intolerant of methotrexate is started on azathioprine for rheumatoid arthritis. Routine blood monitoring shows:

Hb 7.9 g/dl

Plt 97 * 10^9/l

WBC 2.7 * 10^9/l

Which of the following factors will predispose her to azathioprine toxicity?

- A. Cimetidine
- B. Rifampicin
- C. Fast acetylator status
- D. Thiopurine methyltransferase deficiency
- E. Alcohol excess

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- E. Alcohol excess

Thiopurine methyltransferase (TPMT) deficiency is present in about 1 in 200 people and predisposes to azathioprine related pancytopaenia

Azathioprine

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and lower doses of azathioprine should be used

Question 10 of 97

A 34-year-old intravenous drug user is admitted with a purpuric rash affecting her legs. Blood tests reveal the following:

Hb	11.4g/dl
Platelets	489 * 10^9/l
WCC	12.3 * 10^9/l
HCV PCR	positive
HBsAg	negative
Rheumatoid factor	positive
C3/C4	reduced

What is the most likely diagnosis?

- A. Polyarteritis nodosa
- B. Henoch-Schonlein purpura
- C. Wegener's granulomatosis
- D. Cryoglobulinaemia
- E. Systemic lupus erythematous

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- D. Cryoglobulinaemia
- E. Systemic lupus erythematous

Hepatitis C infection is associated with type II (mixed) cryoglobulinaemia, suggested by the purpuric rash, positive rheumatoid factor and reduced complement levels

Cryoglobulinaemia

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One third of cases are idiopathic

Three types

- type I (25%): monoclonal
- type II (25%): mixed monoclonal and polyclonal: usually with RF
- type III (50%): polyclonal: usually with RF

Type I

- monoclonal - IgG or IgM
- associations: multiple myeloma, Waldenström macroglobulinaemia

Type II

- mixed monoclonal and polyclonal: usually with RF
- associations: hepatitis C, RA, Sjogren's, lymphoma

Type III

- polyclonal: usually with RF
- associations: RA, Sjogren's

Symptoms (if present in high concentrations)

- Raynaud's only seen in type I
- cutaneous: vascular purpura, distal ulceration, ulceration
- arthralgia
- renal involvement (diffuse glomerulonephritis)

Tests

- low complement (esp. C4)
- high ESR

Treatment

- immunosuppression
- plasmapheresis

Question 11 of 97

A 34-year-old is diagnosed with chronic fatigue syndrome. Which one of the following interventions is most useful?

- A. Graded exercise therapy
- B. Psychodynamic psychotherapy
- C. Graded physiotherapy
- D. Advice to avoid alcohol and caffeine
- E. Low-dose fluoxetine

Question 11 of 97

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- B. Psychodynamic psychotherapy
- C. Graded physiotherapy
- D. Advice to avoid alcohol and caffeine
- E. Low-dose fluoxetine

Chronic fatigue syndrome

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

Epidemiology
- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include
– sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep–wake cycle
– muscle and/or joint pains
– headaches
– painful lymph nodes without enlargement
– sore throat
– cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
– physical or mental exertion makes symptoms worse
– general malaise or 'flu-like' symptoms
– dizziness
- nausea

– palpitations

Investigation
- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin*, coeliac screening and also urinalysis

Management
- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

*children and young people only

Question 12 of 97

Which of the following features are not typically seen in a patient with adult onset Still's disease?

- A. Maculopapular rash
- B. Rheumatoid factor
- C. Pyrexia
- D. High ferritin level
- E. Lymphadenopathy

Question 12 of 97

Which of the following features are not typically seen in a patient with adult onset Still's disease?

- A. Maculopapular rash
- B. Rheumatoid factor
- C. Pyrexia
- D. High ferritin level
- E. Lymphadenopathy

Adult onset Still's disease is typically rheumatoid factor negative

Still's disease in adults

Adult Still's disease
- typically affects 16-35 year olds

Features
- arthralgia
- elevated serum ferritin
- rash: salmon-pink, maculopapular
- pyrexia
- lymphadenopathy
- rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative

Question 13 of 97

A health trust in the United Kingdom which serves a population of 100,000 is planning services for patients with rheumatoid arthritis. How many of the population would be expected to have the disease?

- A. 100
- B. 300
- C. 1,000
- D. 2,000
- E. 10,000

Question 13 of 97

A health trust in the United Kingdom which serves a population of 100,000 is planning services for patients with rheumatoid arthritis. How many of the population would be expected to have the disease?

- A. 100
- B. 300
- C. 1,000
- D. 2,000
- E. 10,000

The prevalence of rheumatoid arthritis in the UK population is approximately 1%

Rheumatoid arthritis: epidemiology

Epidemiology

- peak onset = 30-50 years, although occurs in all age groups
- F:M ratio = 3:1
- prevalence = 1%
- some ethnic differences e.g. high in Native Americans
- associated with HLA-DR4 (especially Felty's syndrome)

Question 14 of 97

A 59-year-old man with a history of gout presents with a swollen and painful first metatarsophalangeal joint. He currently takes allopurinol 400mg od as gout prophylaxis. What should happen to his allopurinol therapy?

- A. Stop and recommence 4 weeks after acute inflammation has settled
- B. Reduce allopurinol to 100mg od until acute attack has settled
- C. Stop and switch to colchicine prophylaxis
- D. Stop and recommence 2 weeks after acute inflammation has settled
- E. Continue allopurinol in current dose

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Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 15 of 97

A 79-year-old man presents with a history of lower back pain and right hip pain. Blood tests reveal the following:

Calcium	2.20 mmol/l
Phosphate	0.8 mmol/l
ALP	890 u/L

What is the most likely diagnosis?

- A. Primary hyperparathyroidism
- B. Chronic renal failure
- C. Osteomalacia
- D. Osteoporosis
- E. Paget's disease

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- D. Osteoporosis
- E. Paget's disease

The normal calcium and phosphate combined with a raised alkaline phosphate points to a diagnosis of Paget's

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors
- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic
- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's
- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications
- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 16 of 97

An autoantibody screen reveals that a patient is positive for anti-Jo 1 antibodies. What is the most likely underlying diagnosis?

- A. Limited cutaneous systemic sclerosis
- B. Mixed connective tissue disease
- C. Dermatomyositis
- D. Polymyositis
- E. Diffuse cutaneous systemic sclerosis

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- D. Polymyositis
- E. Diffuse cutaneous systemic sclerosis

Anti-Jo 1 antibodies are more commonly seen in polymyositis than dermatomyositis

Extractable nuclear antigens

Overview
- specific nuclear antigens
- usually associated with being ANA positive

Examples
- anti-Ro: Sjogren's syndrome, SLE, congenital heart block
- anti-La: Sjogren's syndrome
- anti-Jo 1: polymyositis
- anti-scl-70: diffuse cutaneous systemic sclerosis
- anti-centromere: limited cutaneous systemic sclerosis

Question 17 of 97

A 54-year-old female is reviewed in the rheumatology clinic due to dry eyes and arthralgia. A diagnosis of primary Sjogren's syndrome is suspected. Which one of the following features is least associated with this condition?

- A. Renal tubular acidosis
- B. Xerostomia
- C. Sensory polyneuropathy
- D. Dilated cardiomyopathy
- E. Raynaud's phenomenon

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- C. Sensory polyneuropathy
- D. Dilated cardiomyopathy
- E. Raynaud's phenomenon

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features
- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation
- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management
- artificial saliva and tears
- pilocarpine may stimulate saliva production

Question 18 of 97

Which one of the following statements regarding systemic lupus erythematous is true?

- A. It is linked with HLA A5
- B. Onset is typically between 20-40 years old
- C. It is more common in Caucasians
- D. The female:male ratio is 3:1
- E. The incidence has decreased in the past 30 years

Question 18 of 97

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Systemic lupus erythematosus

Epidemiology
- much more common in females (F:M = 9:1)
- more common in Afro-Caribbeans* and Asian communities
- onset is usually 20-40 years
- incidence has risen substantially during the past 50 years (3 fold using American College of Rheumatology criteria)

Pathophysiology
- autoimmune disease
- associated with HLA B8, DR2, DR3
- thought to be caused by immune system dysregulation leading to immune complex formation
- immune complex deposition can affect any organ including the skin, joints, kidneys and brain

*It is said the incidence in black Africans is much lower than in black Americans - the reasons for this are unclear

Question 19 of 97

A 57-year-old man presents with pain in his right knee. An x-ray shows osteoarthritis. He has no past medical history of note. What is the most suitable treatment option for the management of his pain?

- A. Diclofenac with omeprazole
- B. Glucosamine
- C. Diclofenac
- D. Ibuprofen
- E. Paracetamol

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- D. Ibuprofen
- E. Paracetamol

Osteoarthritis - paracetamol + topical NSAIDs (if knee/hand) first-line

Oral NSAIDs should be used second line in osteoarthritis due to their adverse effect profile

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with either drug. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Question 20 of 97

A 45-year-old female with a history of rheumatoid arthritis presents to the Emergency Department with a two day history of a hot, painful, swollen right elbow joint. What is the most appropriate management?

- A. Joint aspiration
- B. Start infliximab
- C. Oral high-dose prednisolone
- D. Short course of methotrexate
- E. Depomederone injection

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Joint aspiration is mandatory in all patients with a hot, swollen joint to rule out septic arthritis. If this was excluded in the above patient then intra-articular or system steroid therapy may be considered.

Septic arthritis

Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin + fusidic acid or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

Question 21 of 97

A 68-year-old female presents with a two week history of intermittent headaches and lethargy. Blood tests reveal the following:

ESR 67 mm/hr

What is the most likely diagnosis?

- A. Polymyalgia rheumatica
- B. Cluster headaches
- C. Polyarteritis nodosa
- D. Migraine
- E. Temporal arteritis

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- D. Migraine
- E. Temporal arteritis

This is a classic history of temporal arteritis. Treatment should be started immediately with high dose steroids (e.g. prednisolone 1mg/kg/day) to reduce the chance of visual loss

Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

Question 22 of 97

Which one of the following cytokines is the most important in the pathophysiology of rheumatoid arthritis?

- A. IFN-beta
- B. IFN-alpha
- C. IL-4
- D. Tumour necrosis factor
- E. IL-2

Question 22 of 97

Which one of the following cytokines is the most important in the pathophysiology of rheumatoid arthritis?

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- B. IFN-alpha
- C. IL-4
- D. Tumour necrosis factor
- E. IL-2

Rheumatoid arthritis - TNF is key in pathophysiology

Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of bodies response to Gram negative septicaemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF-alpha binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also cause activation of NFkB

Endothelial effects include increase expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

TNF blockers

- infliximab: monoclonal antibody, IV administration
- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

Question 23 of 97

Which one of the following features is least commonly seen in drug-induced lupus?

- A. Glomerulonephritis
- B. Arthralgia
- C. Myalgia
- D. Malar rash
- E. Pleurisy

Question 23 of 97

Which one of the following features is least commonly seen in drug-induced lupus?

- A. Glomerulonephritis
- B. Arthralgia
- C. Myalgia
- D. Malar rash
- E. Pleurisy

Glomerulonephritis is unusual in drug-induced lupus

Drug-induced lupus

In drug-induced lupus not all the typical features of systemic lupus erythematosus are seen, with renal and nervous system involvement being unusual. It usually resolves on stopping the drug

Features

- arthralgia
- myalgia
- skin (e.g. malar rash) and pulmonary involvement (e.g. pleurisy) are common
- ANA positive in 100%, dsDNA negative
- anti-Ro, anti-Smith positive in around 5%

Causes

- procainamide
- isoniazid
- minocycline
- hydralazine
- chlorpromazine
- anti-epileptics: phenytoin

Question 24 of 97

Which one of the following is least recognised as a risk factor for developing osteoporosis?

- A. Cushing's syndrome
- B. Turner's syndrome
- C. Hyperparathyroidism
- D. Hypothyroidism
- E. Diabetes mellitus

Question 24 of 97

Which one of the following is least recognised as a risk factor for developing osteoporosis?

- A. Cushing's syndrome
- B. Turner's syndrome
- C. Hyperparathyroidism
- D. Hypothyroidism
- E. Diabetes mellitus

Hyperthyroidism is associated with an increased risk of osteoporosis. Patients with hypothyroidism who take excessive amounts of levothyroxine may also be at risk of osteoporosis

Osteoporosis: causes

Risk factors
- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Asians and Orientals

Diseases which predispose
- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- GI problems: malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Question 25 of 97

Which of the following is associated with a good prognosis in rheumatoid arthritis?

- A. Rheumatoid factor negative
- B. HLA DR4
- C. Anti-CCP antibodies
- D. Rheumatoid nodules
- E. Insidious onset

Question 25 of 97

Which of the following is associated with a good prognosis in rheumatoid arthritis?

- A. Rheumatoid factor negative
- B. HLA DR4
- C. Anti-CCP antibodies
- D. Rheumatoid nodules
- E. Insidious onset

Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

Question 26 of 97

A 64-year-old man with chronic kidney disease stage 3 secondary to type 2 diabetes mellitus presents with pain and swelling at the right first metatarsophalangeal joint. On examination the joint is hot, erythematous and tender to touch, although he can still flex the big toe. What is the most appropriate initial management?

- A. Colchicine
- B. Prednisolone
- C. Co-codamol 30/500
- D. Allopurinol
- E. Indomethacin

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- D. Allopurinol
- E. Indomethacin

Colchicine is useful in patients with renal impairment who develop gout as NSAIDs are relatively contraindicated. The BNF advises to reduce the dose by up to 50% if creatinine clearance is less than 50 ml/min and to avoid if creatinine clearance is less than 10 ml/min.

Co-codamol 30/500 may be used as an adjunct but would not provide relief as monotherapy.

Prednisolone is an option but would adversely affect his diabetic control.

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
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- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 27 of 97

A 43-year-old woman presents with right-sided elbow pain. This has been present for the past month and she reports no obvious trigger. On examination she reports pain when the wrist is extended whilst the elbow is extended. What is the most likely diagnosis?

- A. Cubital tunnel syndrome
- B. Lateral epicondylitis
- C. Carpal tunnel syndrome
- D. Medial epicondylitis
- E. Pronator syndrome

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Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

Features
- pain and tenderness localised to the lateral epicondyle
- pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

Management options
- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy

Question 28 of 97

Perinuclear antineutrophil cytoplasmic antibodies (pANCA) are most strongly associated with which condition?

- A. Goodpasture's syndrome
- B. Churg-Strauss syndrome
- C. Polyarteritis nodosa
- D. Wegener's granulomatosis
- E. Autoimmune hepatitis

Question 28 of 97

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- D. Wegener's granulomatosis
- E. Autoimmune hepatitis

cANCA = Wegener's; pANCA = Churg-Strauss + others

ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:
- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

cANCA
- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

pANCA
- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)
- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

Question 29 of 97

A 25-year-old woman presents with a three day history of dysuria and a painful left knee. During the review of symptoms she mentions a bout of diarrhoea and crampy abdominal pain three weeks ago. She is normally fit and well and takes no regular medication. Her father died of colorectal cancer in his sixth decade. On examination the left knee is red, swollen and hot to touch. What is the most likely diagnosis?

- A. Reactive arthritis secondary to *Salmonella* spp.
- B. Reactive arthritis secondary to *Chlamydia trachomatis*
- C. Rheumatoid arthritis
- D. Ulcerative colitis
- E. Gonococcal arthritis

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Urethritis + arthritis + conjunctivitis = reactive arthritis

Two of the classic three features of reactive arthritis (urethritis, arthritis and conjunctivitis) are present in this patient. The family history of colorectal cancer is of no particular significance

Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA)

The American College of Rheumatology now define reactive arthritis as an episode of peripheral arthritis lasting for greater than 1 month associated with urethritis/cervicitis or diarrhoea

Epidemiology
- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

Organisms often responsible for post-dysenteric form
- *Shigella* flexneri
- *Salmonella typhi*murium
- *Salmonella* enteritidis
- *Yersinia enterocolitica*
- *Campylobacter*

Organisms often responsible for post-STI form
- *Chlamydia trachomatis*

Question 30 of 97

A 45-year-old woman with a history of primary Sjogren's syndrome is reviewed in clinic. Her main problem is a dry mouth, which unfortunately has not responded to artificial saliva. Which one of the following medications is most likely to be beneficial?

- A. Rivastigmine
- B. Neostigmine
- C. Clonidine
- D. Atropine
- E. Pilocarpine

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Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features
- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation
- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management
- artificial saliva and tears
- pilocarpine may stimulate saliva production

Question 31 of 97

A 51-year-old male presents with an acute onset of swelling and pain in his right knee. Aspiration shows negatively birefringent crystals with no organisms seen. His pain fails to settle with NSAIDs. What is the most appropriate next step in his management?

- A. Repeat joint aspiration and intra-articular depomederone
- B. Allopurinol
- C. IV flucloxacillin
- D. Diuretics
- E. Low dose methotrexate

Question 31 of 97

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Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 32 of 97

A 45-year-old woman is referred to rheumatology outpatients with a 4 month history of joint pains, myalgia and generalised lethargy. An autoantibody screen reveals she is ANA positive and ribonuclear protein positive. The creatine kinase is elevated at 525. What is the most likely diagnosis?

- A. Systemic lupus erythematous
- B. Mixed connective tissue disease
- C. Polymyositis
- D. Dermatomyositis
- E. CREST syndrome

Question 32 of 97

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- A. Systemic lupus erythematous
- B. Mixed connective tissue disease
- C. Polymyositis
- D. Dermatomyositis
- E. CREST syndrome

Anti-ribonuclear protein (anti-RNP) = mixed connective tissue disease

Mixed connective tissue disease

Features of SLE, systemic sclerosis and polymyositis

Anti-RNP positive

Question 33 of 97

Which one of the following is not part of the American College of Rheumatology criteria for diagnosing rheumatoid arthritis?

- A. Raised ESR or CRP
- B. Morning stiffness > 1 hr
- C. Subcutaneous nodules
- D. Symmetrical arthritis
- E. Rheumatoid factor positive

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- C. Subcutaneous nodules
- D. Symmetrical arthritis
- E. Rheumatoid factor positive

Rheumatoid arthritis: diagnosis

NICE have stated that clinical diagnosis is more important than criteria such as those defined by the American College of Rheumatology.

American College of Rheumatology criteria:

- sensitivity = 92%, specificity = 89%
- requires 4 of the following 7 criteria
- morning stiffness > 1 hr (for at least 6 weeks)
- soft-tissue swelling of 3 or more joints (for at least 6 weeks)
- swelling of PIP, MCP or wrist joints (for at least 6 weeks)
- symmetrical arthritis
- subcutaneous nodules
- rheumatoid factor positive
- radiographic evidence of erosions or periarticular osteopenia

Question 34 of 97

A 41-year-old female presents with lethargy and pain all over her body. This has been present for the past six months and is often worse when she is stressed or cold. Clinical examination is unremarkable other than a large number of tender points throughout her body. A series of blood tests including an autoimmune screen, inflammatory markers and thyroid function are normal. Given the likely diagnosis, which one of the following is not helpful in management?

- A. Amitriptyline
- B. Trigger point injections
- C. Cognitive behavioural therapy
- D. Exercise programme
- E. Paracetamol

Question 34 of 97

A 41-year-old female presents with lethargy and pain all over her body. This has been present for the past six months and is often worse when she is stressed or cold. Clinical examination is unremarkable other than a large number of tender points throughout her body. A series of blood tests including an autoimmune screen, inflammatory markers and thyroid function are normal. Given the likely diagnosis, which one of the following is not helpful in management?

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- B. Trigger point injections
- C. Cognitive behavioural therapy
- D. Exercise programme
- E. Paracetamol

A recent JAMA paper supported the use of anti-depressants in fibromyalgia

Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis; 2009 Jan 14;301(2):198-209

Fibromyalgia

Fibromyalgia is a syndrome characterised by widespread pain throughout the body with tender points at specific anatomical sites. The cause of fibromyalgia is unknown.

Epidemiology
- women are 10 times more likely to be affected
- typically presents between 30-50 years old

Features
- pain: at multiple site, sometimes 'pain all over'
- lethargy
- sleep disturbance, headaches, dizziness are common

Diagnosis is clinical and sometimes refers to the American College of Rheumatology classification criteria which lists 9 pairs of tender points on the body. If a patient is tender in at least 11 of these 18 points it makes a diagnosis of fibromyalgia more likely

The management of fibromyalgia is often difficult and needs to be tailored to the individual patient. A psychosocial and multidisciplinary approach is helpful. Unfortunately there is currently a paucity of evidence and guidelines to guide practice. The following is partly based on consensus guidelines from the European League against Rheumatism (EULAR) published in 2007.
- explanation
- exercise programme
- cognitive behavioural therapy
- anti-depressants: amitriptyline

Question 35 of 97

A 31-year-old female with a history of SLE gives birth following a 39 week pregnancy. The newborn is noted to be bradycardic. Which one of the following autoantibodies are associated with congenital heart block?

- A. Anti-Ro
- B. Anti-scl-70
- C. Anti-RNP
- D. AMA
- E. Anti-Jo 1

Question 35 of 97

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- C. Anti-RNP
- D. AMA
- E. Anti-Jo 1

SLE - antibodies associated with congenital heart block = anti-Ro

SLE: pregnancy

Overview

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematous
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

Question 36 of 97

Which one of the following statements concerning discoid lupus is correct?

- A. Commonly progresses to SLE
- B. Causes non-scarring alopecia
- C. Characterised by follicular keratin plugs
- D. Is rarely photosensitive
- E. Typically presents in older males

Question 36 of 97

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- A. Commonly progresses to SLE
- B. Causes non-scarring alopecia
- C. Characterised by follicular keratin plugs
- D. Is rarely photosensitive
- E. Typically presents in older males

Discoid lupus erythematosus is characterised by follicular keratin plugs

Discoid lupus erythematous

Discoid lupus erythematous is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematous is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

Features

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Management

- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure

Question 37 of 97

A 54-year-old man presents to the Emergency Department with a 2 day history of an swollen, painful left knee. Aspirated joint fluid shows calcium pyrophosphate crystals. Which of the following blood tests is most useful in revealing an underlying cause?

- A. Transferrin saturation
- B. ACTH
- C. ANA
- D. Serum ferritin
- E. LDH

Question 37 of 97

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- B. ACTH
- C. ANA
- D. Serum ferritin
- E. LDH

This is a typical presentation of pseudogout. An elevated transferrin saturation may indicate haemochromatosis, a recognised cause of pseudogout

A high ferritin level is also seen in haemochromatosis but can be raised in a variety of infective and inflammatory processes, including pseudogout, as part of an acute phase response

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Features
- knee, wrist and shoulders most commonly affected
- x-ray: chondrocalcinosis

Risk factors
- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Management
- aspiration of joint fluid, to exclude septic arthritis and show weakly-positively birefringent brick shaped crystals
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Question 38 of 97

A 57-year-old man with a history of ischaemic heart disease presents with an hot, erythematous and painful left metatarsophalangeal joint. The attack settles following a course of non-steroidal anti-inflammatories. He currently takes aspirin 75 mg od for secondary prevention of ischaemic heart disease. What should happen regarding his medication?

- A. Switch aspirin to clopidogrel
- B. Continue aspirin at current dose
- C. Increase aspirin dose to 300mg od
- D. Switch aspirin to dipyridamole
- E. Stop aspirin

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- B. Continue aspirin at current dose
- C. Increase aspirin dose to 300mg od
- D. Switch aspirin to dipyridamole
- E. Stop aspirin

Aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - see below

Gout: drug causes

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Drug causes

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

Question 39 of 97

Which one of the following is true regarding the investigation of a patient with dermatomyositis?

- A. Creatine kinase is characteristically normal
- B. Muscle biopsy is contraindicated
- C. Anti-Jo-1 antibodies are usually negative
- D. Antinuclear antibodies are always negative
- E. EMG is normal

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- D. Antinuclear antibodies are always negative
- E. EMG is normal

Anti-Jo-1 antibodies are more common in polymyositis than dermatomyositis

Dermatomyositis: investigations and management

Investigations
- elevated creatine kinase
- EMG
- muscle biopsy
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever
- ANA positive in 60%

Management
- prednisolone

Question 40 of 97

Osteopetrosis is due to a defect in:

- A. Osteoclast function
- B. PTH receptors
- C. Osteoblast function
- D. Calcium resorption in proximal tubule
- E. Calcium absorption

Question 40 of 97

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- A. Osteoclast function
- B. PTH receptors
- C. Osteoblast function
- D. Calcium resorption in proximal tubule
- E. Calcium absorption

Osteopetrosis

Overview
- aka marble bone disease
- rare disorder of defective osteoclast function resulting in failure of normal bone resorption
- stem cell transplant and interferon-gamma have been used for treatment

Question 41 of 97

Which of the following is not a recognised cause of Raynaud's phenomenon?

- A. Oral contraceptive pill
- B. Cervical rib
- C. Type I cryoglobulinaemia
- D. Pizotifen
- E. Scleroderma

Question 41 of 97

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- A. Oral contraceptive pill
- B. Cervical rib
- C. Type I cryoglobulinaemia
- D. Pizotifen
- E. Scleroderma

Ergotamine rather than pizotifen is associated with Raynaud's phenomenon

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease
- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthrits or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes
- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management
- calcium channel blockers
- IV prostacyclin infusions

Question 42 of 97

Which of the following is least likely to be associated with ankylosing spondylitis?

- A. Apical fibrosis
- B. Achilles tendonitis
- C. Amyloidosis
- D. Achalasia
- E. Heart block

Question 42 of 97

Which of the following is least likely to be associated with ankylosing spondylitis?

- A. Apical fibrosis
- B. Achilles tendonitis
- C. Amyloidosis
- D. Achalasia
- E. Heart block

Ankylosing spondylitis features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

Achalasia is not a recognised association of ankylosing spondylitis

Ankylosing spondylitis: features

Features
- typically a young man who presents with lower back pain and stiffness
- stiffness is usually worse in morning and improves with activity
- peripheral arthritis (25%, more common if female)

Other features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome

X-rays are often normal early in disease, later changes include:
- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)

- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints

Question 43 of 97

A 54-year-old male presents with weakness of his upper arms. On examination he is found to have a macular rash over his back and the extensor aspects of his upper arms. He is a heavy smoker and his sodium is 121 mmol/l. What is the most likely underlying diagnosis?

- A. Addison's disease
- B. Polymyositis
- C. Overlap syndrome
- D. Dermatomyositis
- E. Hypothyroidism

Question 43 of 97

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- C. Overlap syndrome
- D. Dermatomyositis
- E. Hypothyroidism

This man may have an underlying small cell lung cancer causing SIADH

Dermatomyositis

Overview
- inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions
- may be idiopathic or associated with connective tissue disorders or underlying malignancy (found in 20-25% - more if patient older)
- polymyositis is a variant of the disease where skin manifestations are not prominent

Skin features
- photosensitive
- macular rash over back and shoulder
- heliotrope rash over cheek
- Gottron's papules - roughened red papules over extensor surfaces of fingers
- nail fold capillary dilatation

Other features
- proximal muscle weakness +/- tenderness
- Raynaud's
- respiratory muscle weakness
- interstitial lung disease: e.g. fibrosing alveolitis or organising pneumonia
- dysphagia, dysphonia

Question 44 of 97

Which one of the following drugs is least likely to cause gout?

- A. Lithium
- B. Bendrofluazide
- C. Alcohol
- D. Pyrazinamide
- E. Frusemide

Question 44 of 97

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- A. Lithium
- B. Bendrofluazide
- C. Alcohol
- D. Pyrazinamide
- E. Frusemide

Lithium was actually used to treat gout in the 19th century

Gout: drug causes

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Drug causes

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

Question 45 of 97

Which one of the following conditions is least associated with HLA-B27?

- A. Reiter's syndrome
- B. Psoriatic arthritis
- C. Ankylosing spondylitis
- D. Crohn's disease
- E. Sacroilitis

Question 45 of 97

Which one of the following conditions is least associated with HLA-B27?

- A. Reiter's syndrome
- B. Psoriatic arthritis
- C. Ankylosing spondylitis
- D. Crohn's disease
- E. Sacroilitis

There is an indirect association between HLA-B27 and Crohn's as some patients may develop enteropathic arthritis, but this is the least common association of the above

Seronegative spondyloarthropathies

Common features
- associated with HLA-B27
- rheumatoid factor negative - hence 'seronegative'
- peripheral arthritis, usually asymmetrical
- sacroilitis
- enthesopathy: e.g. Achilles tendonitis, plantar fasciitis
- extra-articular manifestations: uveitis, pulmonary fibrosis (upper zone), amyloidosis, aortic regurgitation

Spondyloarthropathies
- ankylosing spondylitis
- psoriatic arthritis
- Reiter's syndrome (including reactive arthritis)
- enteropathic arthritis (associated with IBD)

Question 46 of 97

Which of the following findings is not typical in a patient with antiphospholipid syndrome?

- A. Prolonged APTT
- B. Thrombocytosis
- C. Recurrent venous thrombosis
- D. Recurrent arterial thrombosis
- E. Livedo reticularis

Question 46 of 97

Which of the following findings is not typical in a patient with antiphospholipid syndrome?

- A. Prolonged APTT
- B. Thrombocytosis
- C. Recurrent venous thrombosis
- D. Recurrent arterial thrombosis
- E. Livedo reticularis

Antiphospholipid syndrome: arterial/venous thrombosis, miscarriage, livedo reticularis

Thrombocytopenia is associated with antiphospholipid syndrome

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features
- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE
- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines
- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 47 of 97

Each one of the following is seen in reactive arthritis, except:

- A. Urethritis
- B. Keratoderma blenorrhagica
- C. Conjunctivitis
- D. Aseptic meningoencephalitis
- E. Circinate balanitis

Question 47 of 97

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- C. Conjunctivitis
- D. Aseptic meningoencephalitis
- E. Circinate balanitis

Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. Hans Reiter described a classic triad is of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection. The American College of Rheumatology now define reactive arthritis as an episode of peripheral arthritis lasting for greater than 1 month associated with urethritis/cervicitis or diarrhoea

Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- may present as monoarthritis e.g. knee
- symptoms of urethritis
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blenorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease

Question 48 of 97

Which one of the following antibodies is most specific for limited cutaneous systemic sclerosis?

- A. Anti-Jo 1antiobodies
- B. Rheumatoid factor
- C. Anti-Scl-70 antibodies
- D. Anti-centromere antibodies
- E. Anti-nuclear factor

Question 48 of 97

Which one of the following antibodies is most specific for limited cutaneous systemic sclerosis?

- A. Anti-Jo 1antiobodies
- B. Rheumatoid factor
- C. Anti-Scl-70 antibodies
- D. Anti-centromere antibodies
- E. Anti-nuclear factor

Limited (**central**) systemic sclerosis = anti-**centro**mere antibodies

Although ANA is positive in 90% of patients with systemic sclerosis, anti-centromere antibodies are the most specific test for limited cutaneous systemic sclerosis

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis
- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis
- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)
- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

Antibodies
- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

Question 49 of 97

An 28-year-old man is investigated for recurrent lower back pain. A diagnosis of ankylosing spondylitis is suspected. Which one of the following investigations is most useful?

- A. ESR
- B. X-ray of the sacro-iliac joints
- C. HLA-B27 testing
- D. X-ray of the thoracic spine
- E. CT of the lumber spine

Question 49 of 97

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- C. HLA-B27 testing
- D. X-ray of the thoracic spine
- E. CT of the lumber spine

X-ray of the sacro-iliac joints is the most useful investigation for diagnosis and monitoring, but changes may not be seen for many years after the onset of symptoms

Ankylosing spondylitis

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathies. It typically presents in males (sex ratio 5:1) aged 20-30 years old

HLA-B27 is of little use in making the diagnosis as it is positive in:
- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis

Management
- NSAIDs
- physiotherapy
- sulphasalazine may be useful if there is peripheral joint involvement - doesn't improve spinal mobility
- TNF-alpha blockers such as etanercept and adalimumab are increasingly used. This approach for severe ankylosing spondylitis was supported by NICE in 2008

Question 50 of 97

Which one of the following is least recognised in polyarteritis nodosa?

- A. Cytoplasmic-antineutrophil cytoplasmic antibodies
- B. Hypertension
- C. Mononeuritis multiplex
- D. Pyrexia
- E. Renal failure

Question 50 of 97

Which one of the following is least recognised in polyarteritis nodosa?

- A. Cytoplasmic-antineutrophil cytoplasmic antibodies
- B. Hypertension
- C. Mononeuritis multiplex
- D. Pyrexia
- E. Renal failure

Perinuclear-antineutrophil cytoplasmic antibodies are found in around 20% of patients

Polyarteritis nodosa

Polyarteritis nodosa (PAN) is a vasculitis affecting medium-sized arteries with necrotizing inflammation leading to aneurysm formation. PAN is more common in middle-aged men and is associated with hepatitis B infection

Features

- fever, malaise, arthralgia
- hypertension
- mononeuritis multiplex, sensorimotor polyneuropathy
- haematuria, renal failure
- testicular pain
- abdominal pain (e.g. from mesenteric ischaemia)
- perinuclear-antineutrophil cytoplasmic antibodies (ANCA) are found in around 20% of patients with 'classic' PAN

Question 51 of 97

Which one of the following is the most common ocular manifestation of rheumatoid arthritis?

- A. Scleritis
- B. Episcleritis
- C. Keratoconjunctivitis sicca
- D. Corneal ulceration
- E. Keratitis

Question 51 of 97

Which one of the following is the most common ocular manifestation of rheumatoid arthritis?

- A. Scleritis
- B. Episcleritis
- C. Keratoconjunctivitis sicca
- D. Corneal ulceration
- E. Keratitis

Keratoconjunctivitis sicca is characterised by dry, burning and gritty eyes caused by decreased tear production

Rheumatoid arthritis: ocular manifestations

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

Ocular manifestations
- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

Iatrogenic
- steroid-induced cataracts
- chloroquine retinopathy

Question 52 of 97

Which one of the following is least recognised as a risk factor for developing osteoporosis?

- A. Multiple myeloma
- B. Rheumatoid arthritis
- C. Long-term phenytoin therapy
- D. Chronic renal failure
- E. Diabetes mellitus

Question 52 of 97

Which one of the following is least recognised as a risk factor for developing osteoporosis?

- A. Multiple myeloma
- B. Rheumatoid arthritis
- C. Long-term phenytoin therapy
- D. Chronic renal failure
- E. Diabetes mellitus

Long-term phenytoin therapy may cause enhanced vitamin D metabolism leading to osteomalacia, rather than osteoporosis

Osteoporosis: causes

Risk factors
- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Asians and Orientals

Diseases which predispose
- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- GI problems: malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Question 53 of 97

A 54-year-old man with a history of type 2 diabetes mellitus presents with a history of right shoulder pain. On examination there is limited movement of the right shoulder in all directions. What is the most likely diagnosis?

- A. Adhesive capsulitis
- B. Dermatomyositis
- C. Avascular necrosis
- D. Lhermitte's syndrome
- E. Diabetic amyotrophy

Question 53 of 97

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- B. Dermatomyositis
- C. Avascular necrosis
- D. Lhermitte's syndrome
- E. Diabetic amyotrophy

Diabetic amyotrophy affects the lower limbs

Adhesive capsulitis

Adhesive capsulitis has a known association with diabetes. Patients typically have a painful freezing phase, an adhesive phase and a recovery phase. The episode typically lasts 2-3 years.

Question 54 of 97

A 44-year-old female with a history of Raynaud's phenomenon is reviewed in the rheumatology clinic. She is currently being investigated for dysphagia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications is she most likely to develop?

- A. Early onset dementia
- B. Erythema nodosum
- C. Malabsorption
- D. Constrictive pericarditis
- E. Erosive joint disease

Question 54 of 97

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- A. Early onset dementia
- B. Erythema nodosum
- C. Malabsorption
- D. Constrictive pericarditis
- E. Erosive joint disease

This patient is likely to have CREST syndrome, a subtype of limited cutaneous systemic sclerosis. Malabsorption can develop in these patients secondary to bacterial overgrowth of the sclerosed small intestine

Whilst diffuse systemic sclerosis is associated with more severe and rapid internal organ involvement it is also seen in the limited form.

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis
- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis
- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)
- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

Antibodies
- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

Question 55 of 97

The presence of anti-cyclic citrullinated peptide antibody is suggestive of which one of the following conditions?

- A. Systemic lupus erythematous
- B. Rheumatoid arthritis
- C. Type 1 diabetes mellitus
- D. Addison's disease
- E. Dermatomyositis

Question 55 of 97

The presence of anti-cyclic citrullinated peptide antibody is suggestive of which one of the following conditions?

- A. Systemic lupus erythematous
- B. Rheumatoid arthritis
- C. Type 1 diabetes mellitus
- D. Addison's disease
- E. Dermatomyositis

Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis

Anti-cyclic citrullinated peptide antibody may be detectable up to 10 years before the development of rheumatoid arthritis. It may therefore play a key role in the future of rheumatoid arthritis, allowing early detection of patients suitable for aggressive anti-TNF therapy. It has a sensitivity similar to rheumatoid factor (70-80%, see below) with a much higher specificity of 90-95%.

NICE recommends that patients with suspected rheumatoid arthritis who are rheumatoid factor negative should be test for anti-CCP antibodies.

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either
- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:
- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

Question 56 of 97

A 31-year-old patient is diagnosed with rheumatoid arthritis. Which of the following is associated with a good prognosis?

- A. Being a non-smoker
- B. Erosions on x-ray first developing 18 months after diagnosis
- C. Sudden onset
- D. Being diagnosed aged 35 years
- E. Anti-CCP antibodies

Question 56 of 97

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- C. Sudden onset
- D. Being diagnosed aged 35 years
- E. Anti-CCP antibodies

Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

Question 57 of 97

Which one of the following is not associated with carpal tunnel syndrome?

- A. Tinel's sign
- B. Compression of the median nerve
- C. Wasting of the hypothenar eminence
- D. Flexion of the wrist reproduces symptoms
- E. Weakness of thumb abduction

Question 57 of 97

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- E. Weakness of thumb abduction

Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel

History
- pain/pins and needles in thumb, index, middle finger e.g. at night
- patient flicks hand to obtain relief

Examination
- weakness of thumb abduction
- wasting of thenar eminence (NOT hypothenar)
- Tinel's sign: tapping causes paraesthesia
- Phalen's sign: flexion of wrist causes symptoms

Causes: pregnancy, premenstrual, oedema (CCF), lunate fracture, RA

Electrophysiology
- motor + sensory: prolongation of the action potential

Treatment
- carpal injection
- wrist splints at night
- surgical decompression (flexor retinaculum division)

Question 58 of 97

A 50-year-old man with no past medical history is investigated for ongoing back pain. He is found to have a vertebral collapse secondary to osteoporosis. What is the most appropriate test to determine the cause of his osteoporosis?

- A. Thyroid function tests
- B. Prostate specific antigen
- C. Oestrogen level
- D. Prolactin level
- E. Testosterone level

Question 58 of 97

A 50-year-old man with no past medical history is investigated for ongoing back pain. He is found to have a vertebral collapse secondary to osteoporosis. What is the most appropriate test to determine the cause of his osteoporosis?

- A. Thyroid function tests
- B. Prostate specific antigen
- C. Oestrogen level
- D. Prolactin level
- E. Testosterone level

Whilst thyrotoxicosis is a known cause of osteoporosis, testosterone deficiency is much more likely in a middle-aged male

Osteoporosis: causes

Risk factors
- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Asians and Orientals

Diseases which predispose
- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- GI problems: malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Question 59 of 97

Which one of the following features is least typical of polymyalgia rheumatica?

- A. Elevated creatinine kinase
- B. Low-grade fever
- C. Morning stiffness in proximal limb muscles
- D. Polyarthralgia
- E. Anorexia

Question 59 of 97

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Polymyalgia rheumatica

Pathophysiology
- overlaps with temporal arteritis
- histology shows vasculitis with giant cells, characteristically 'skips' certain sections of affected artery whilst damaging others
- muscle bed arteries affected most in polymyalgia rheumatica

Features
- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- aching, morning stiffness in proximal limb muscles (not weakness)
- also mild polyarthralgia, lethargy, depression, low-grade fever, anorexia, night sweats

Investigations
- ESR > 40 mm/hr
- note CK and EMG normal
- reduced CD8+ T cells

Treatment
- prednisolone e.g. 15mg/od - dramatic response

Question 60 of 97

Which one of the following is most useful in the management of Familial Mediterranean Fever?

- A. Prednisolone
- B. Erythromycin
- C. Cyclophosphamide
- D. Colchicine
- E. Benzylpenicillin

Question 60 of 97

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- B. Erythromycin
- C. Cyclophosphamide
- D. Colchicine
- E. Benzylpenicillin

Familial Mediterranean Fever

Familial Mediterranean Fever (FMF, also known as recurrent polyserositis) is an autosomal recessive disorder which typically presents by the second decade. It is more common in people of Turkish, Armenian and Arabic descent

Features - attacks typically last 1-3 days

- pyrexia
- abdominal pain (due to peritonitis)
- pleurisy
- pericarditis
- arthritis
- erysipeloid rash on lower limbs

Management

- colchicine may help

Question 61 of 97

A 41-year-old man presents with persistent fatigue for the past 8 months. Which one of the following features is least consistent with a diagnosis of chronic fatigue syndrome?

- A. Dizziness
- B. Painful lymph nodes without enlargement
- C. Having a busy day improves the symptoms
- D. Palpitations
- E. Headaches

Question 61 of 97

A 41-year-old man presents with persistent fatigue for the past 8 months. Which one of the following features is least consistent with a diagnosis of chronic fatigue syndrome?

- A. Dizziness
- B. Painful lymph nodes without enlargement
- C. Having a busy day improves the symptoms
- D. Palpitations
- E. Headaches

Physical or mental exertion usually makes the symptoms worse

Chronic fatigue syndrome

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

Epidemiology
- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include
– sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep–wake cycle
– muscle and/or joint pains
– headaches
– painful lymph nodes without enlargement
– sore throat
– cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
– physical or mental exertion makes symptoms worse
– general malaise or 'flu-like' symptoms
– dizziness
- nausea

– palpitations

Investigation
- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin*, coeliac screening and also urinalysis

Management
- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

*children and young people only

Question 62 of 97

A 33-year-old man who is suspected of having ankylosing spondylitis has a lumbar spine x-ray. Which one of the following features is most likely to be present?

- A. Wedge shaped discs
- B. Sclerosis
- C. 'Rugger-Jersey' spine
- D. Osteophytes
- E. Subchondral cysts

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Ankylosing spondylitis: features

Features
- typically a young man who presents with lower back pain and stiffness
- stiffness is usually worse in morning and improves with activity
- peripheral arthritis (25%, more common if female)

Other features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome

X-rays are often normal early in disease, later changes include:
- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)

- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints

Question 63 of 97

A 24-year-old female is investigated for intermittent pain and swelling of the metacarpal phalangeal joints for the past 3 months. An x-ray shows loss of joint space and soft-tissue swelling. Rheumatoid factor is positive and a diagnosis of rheumatoid arthritis is made. What is the most appropriate management to slow disease progression?

- A. Infliximab
- B. Methotrexate
- C. Sulfasalazine
- D. Methotrexate + sulfasalazine + short-course of prednisolone
- E. Diclofenac

Question 63 of 97

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E. Diclofenac

The 2009 NICE guidelines recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids). Women of child-bearing age should be given effective contraception for the duration of treatment and for 3 months after methotrexate has been stopped.

Rheumatoid arthritis: management

The management of rheumatoid arthritis (RA) has been revolutionised by the introduction of disease-modifying therapies in the past decade. NICE has issued a number of technology appraisals on the newer agents and released general guidelines in 2009.

Patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. Other important treatment options include analgesia, physiotherapy and surgery.

Initial therapy

- in the 2009 NICE guidelines it is recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids)

DMARDs

- methotrexate is the most widely used DMARD. Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. Other important side-effects include pneumonitis
- sulfasalazine
- leflunomide
- hydroxychloroquine

TNF-inhibitors

- the current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate
- etanercept: subcutaneous administration, can cause demyelination
- infliximab: intravenous administration, risks include reactivation of tuberculosis
- adalimumab: subcutaneous administration

Rituximab

- anti-CD20 monoclonal antibody, results in B-cell depletion
- two 1g intravenous infusions are given two weeks apart
- infusion reactions are common

Abatacept

- fusion protein that modulates a key signal required for activation of T lymphocytes
- leads to decreased T-cell proliferation and cytokine production
- given as an infusion
- not currently recommend by NICE

Question 64 of 97

A 64-year-old female is referred to rheumatology out-patients by her GP with a history of arthritis in both hands. Which one of the following x-ray findings would most favour a diagnosis of rheumatoid arthritis over other possible causes?

- A. Loss of joint space
- B. Periarticular osteopenia
- C. Subchondral sclerosis
- D. Osteophytes
- E. Subchondral cysts

Question 64 of 97

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- B. Periarticular osteopenia
- C. Subchondral sclerosis
- D. Osteophytes
- E. Subchondral cysts

Periarticular osteopenia and osteoporosis would point towards a diagnosis of rheumatoid arthritis (RA). Loss of joint space is common in both RA and osteoarthritis

Rheumatoid arthritis: x-ray changes

Early x-ray findings
- loss of joint space
- juxta-articular osteoporosis
- soft-tissue swelling

Late x-ray findings
- periarticular erosions
- subluxation

Question 65 of 97

A 54-year-old farm worker presents for review. She has recently been diagnosed with osteoarthritis of the hand but has no other past medical history of note. Despite regular paracetamol she is still experiencing considerable pain, especially around the base of both thumbs. What is the most suitable next management step?

- A. Add oral diclofenac + lansoprazole
- B. Switch paracetamol for co-codamol 8/500
- C. Add topical ibuprofen
- D. Add oral ibuprofen
- E. Add oral glucosamine

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- D. Add oral ibuprofen
- E. Add oral glucosamine

Osteoarthritis - paracetamol + topical NSAIDs (if knee/hand) first-line

The 2008 NICE guidelines suggest the use of paracetamol and topical NSAIDs first-line

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with either drug. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Question 66 of 97

Which one of the following conditions has polygenic inheritance?

- A. Bartter's syndrome
- B. Huntington disease
- C. Ankylosing spondylitis
- D. Fragile X syndrome
- E. Von Willebrand's disease

Question 66 of 97

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- C. Ankylosing spondylitis
- D. Fragile X syndrome
- E. Von Willebrand's disease

Ankylosing spondylitis

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathies. It typically presents in males (sex ratio 5:1) aged 20-30 years old

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis

Management

- NSAIDs
- physiotherapy
- sulphasalazine may be useful if there is peripheral joint involvement - doesn't improve spinal mobility
- TNF-alpha blockers such as etanercept and adalimumab are increasingly used. This approach for severe ankylosing spondylitis was supported by NICE in 2008

Question 67 of 97

A 68-year-old presents with left knee pain. A plain radiograph is report as follows:
Some loss of joint space
Linear calcification of the articular cartilage

What is the most likely diagnosis?

- A. Pseudogout
- B. Rheumatoid arthritis
- C. Sarcoidosis
- D. Gout
- E. Osteoarthritis

Question 67 of 97

A 68-year-old presents with left knee pain. A plain radiograph is report as follows:
Some loss of joint space
Linear calcification of the articular cartilage

What is the most likely diagnosis?

- A. Pseudogout
- B. Rheumatoid arthritis
- C. Sarcoidosis
- D. Gout
- E. Osteoarthritis

This x-ray describes chondrocalcinosis. Non-specific changes such as loss of joint space are common in this age group and pseudogout itself may cause osteoarthritic-like changes.

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Features
- knee, wrist and shoulders most commonly affected
- x-ray: chondrocalcinosis

Risk factors
- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Management
- aspiration of joint fluid, to exclude septic arthritis and show weakly-positively birefringent brick shaped crystals
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Question 68 of 97

A 54-year-old man is recovering following his first episode of gout. The pain and inflammation settled 4 days ago. He has no risk factors for the development of gout and there is no evidence of gouty tophi on examination. What is the most suitable point to start uric acid lowering therapy?

- A. Immediately
- B. If more than 6 episodes of gout in a 1 year period
- C. If one further attack of gout in the next 12 months
- D. 4 weeks after the initial attack of gout has settled
- E. If more than 4 episodes of gout in a 1 year period

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- D. 4 weeks after the initial attack of gout has settled
- E. If more than 4 episodes of gout in a 1 year period

Gout: start allopurinol if >= 2 attacks in 12 month period

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 69 of 97

Approximately what percentage of patients with psoriasis develop an associated arthropathy?

- A. 0.5%
- B. 12-15%
- C. 4-5%
- D. 1%
- E. 10%

Question 69 of 97

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Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% percent of patients with skin lesions develop an arthropathy with males and females being equally affected

Types*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis

*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

Question 70 of 97

A 47-year-old female presents with elbow pain. She has just spent the weekend painting the house. On examination there is localised pain around the lateral epicondyle and a diagnosis of lateral epicondylitis is suspected. Which one of the following movements would characteristically worsen the pain?

- A. Resisted thumb flexion
- B. Thumb extension
- C. Flexion of the elbow
- D. Pronation of the forearm with the elbow flexed
- E. Resisted wrist extension with the elbow extended

Question 70 of 97

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- D. Pronation of the forearm with the elbow flexed
- E. Resisted wrist extension with the elbow extended

Lateral epicondylitis: worse on resisted wrist extension/suppination whilst elbow extended

Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

Features

- pain and tenderness localised to the lateral epicondyle
- pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

Management options

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy

Question 71 of 97

A 39-year-old woman with a history of rheumatoid arthritis presents with a two day history of a red right eye. There is no itch or pain. Pupils are 3mm, equal and reactive to light. Visual acuity is 6/5 in both eyes. What is the most likely diagnosis?

- A. Keratoconjunctivitis sicca
- B. Scleritis
- C. Glaucoma
- D. Episcleritis
- E. Anterior uveitis

Question 71 of 97

A 39-year-old woman with a history of rheumatoid arthritis presents with a two day history of a red right eye. There is no itch or pain. Pupils are 3mm, equal and reactive to light. Visual acuity is 6/5 in both eyes. What is the most likely diagnosis?

- A. Keratoconjunctivitis sicca
- B. Scleritis
- C. Glaucoma
- D. Episcleritis
- E. Anterior uveitis

Scleritis is painful, episcleritis is not painful

Rheumatoid arthritis: ocular manifestations

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

Ocular manifestations
- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

Iatrogenic
- steroid-induced cataracts
- chloroquine retinopathy

Question 72 of 97

A 69-year-old man presents with an acute episode of gout on his left first metatarsal-phalangeal joint. What is the most likely underlying mechanism?

- A. Sedentary lifestyle
- B. Decreased renal excretion of uric acid
- C. Increased endogenous production of uric acid
- D. Starvation
- E. Too much protein in diet

Question 72 of 97

A 69-year-old man presents with an acute episode of gout on his left first metatarsal-phalangeal joint. What is the most likely underlying mechanism?

- A. Sedentary lifestyle
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- C. Increased endogenous production of uric acid
- D. Starvation
- E. Too much protein in diet

The vast majority of gout is due to decreased renal excretion of uric acid

Decreased renal excretion of uric acid is thought to account for 90% of cases of primary gout. Secondary risk factors such as alcohol intake and medications should also be investigated

Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid
- drugs*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid
- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome
- hypoxanthine-guanine phosphoribosyl transferase deficiency
- inheritance = x-linked recessive
- features: gout, renal failure, learning difficulties, head-banging

*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

Question 73 of 97

A 40-year-old woman who is known to have systemic lupus erythematosus is reviewed with an exacerbation of wrist pain. Which one of the following is the most useful marker for monitoring disease activity?

- A. C-reactive protein
- B. C2 levels
- C. Anti-nuclear antibody titres
- D. Anti-dsDNA titres
- E. Anti-Sm titres

Question 73 of 97

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- C. Anti-nuclear antibody titres
- D. Anti-dsDNA titres
- E. Anti-Sm titres

SLE: investigations

Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Question 74 of 97

Which one of the following is most likely to indicate an underlying connective tissue disorder in a patient with Raynaud's phenomenon?

- A. Chilblains
- B. Bilateral symptoms
- C. Female patient
- D. Onset at 18 years old
- E. Recurrent miscarriages

Question 74 of 97

Which one of the following is most likely to indicate an underlying connective tissue disorder in a patient with Raynaud's phenomenon?

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- B. Bilateral symptoms
- C. Female patient
- D. Onset at 18 years old
- E. Recurrent miscarriages

Raynaud's disease (i.e. primary) presents in young women with bilateral symptoms

A history of recurrent miscarriages could indicate systemic lupus erythematous or anti-phospholipid syndrome. Chilblains (pernio) are itchy, painful purple swellings which occur on the fingers and toes after exposure to the cold. They are occasionally associated with underlying connective tissue disease but this is rare

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease
- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthrits or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes
- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management
- calcium channel blockers
- IV prostacyclin infusions

Question 75 of 97

A 63-year-old man presents to the Emergency Department with a 2 day history of a painful and swollen left knee joint. Aspiration reveals positively birefringent crystals and no organisms are seen. Which of the following conditions are not recognised causes of the underlying condition?

- A. Haemochromatosis
- B. Low magnesium
- C. High phosphate
- D. Acromegaly
- E. Hyperparathyroidism

Question 75 of 97

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- B. Low magnesium
- C. High phosphate
- D. Acromegaly
- E. Hyperparathyroidism

A low phosphate predisposes to pseudogout

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Features
- knee, wrist and shoulders most commonly affected
- x-ray: chondrocalcinosis

Risk factors
- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Management
- aspiration of joint fluid, to exclude septic arthritis and show weakly-positively birefringent brick shaped crystals
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Question 76 of 97

A 24-year-old man is investigated for chronic back pain. Which one of the following would most suggest a diagnosis of ankylosing spondylitis?

- A. Reduced lateral flexion of the lumbar spine
- B. Pain gets worse during the day
- C. Accentuated lumbar lordosis
- D. Pain on straight leg raising
- E. Loss of thoracic kyphosis

Question 76 of 97

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- C. Accentuated lumbar lordosis
- D. Pain on straight leg raising
- E. Loss of thoracic kyphosis

Reduced lateral flexion of the lumbar spine is one of the earliest signs of ankylosing spondylitis. There tends to be a loss of lumbar lordosis and an accentuated thoracic kyphosis in patients with ankylosing spondylitis

Ankylosing spondylitis: features

Features
- typically a young man who presents with lower back pain and stiffness
- stiffness is usually worse in morning and improves with activity
- peripheral arthritis (25%, more common if female)

Other features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome

X-rays are often normal early in disease, later changes include:
- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)

- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints

Question 77 of 97

A 73-year-old man presents pain in his right thigh. This has been getting progressively worse for the past 9 months despite being otherwise well. An x-ray is reported as follows:

X-ray femur	right	Radiolucency of subarticular region suggestive of osteolysis. Some areas of patchy sclerosis

Bloods tests show:

Calcium	2.38 mmol/l
Phosphate	0.85 mmol/l
Alkaline phosphatase	544 u/L
Prostate specific antigen	4.4 ng/ml

What is the most appropriate action?

- A. Vitamin D supplementation
- B. Check serum testosterone
- C. Referral to an orthopaedic surgeon
- D. Referral to a urologist
- E. IV bisphosphonates

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- E. IV bisphosphonates

This patient has Paget's disease as evidenced by an isolated rise in ALP and characteristic x-ray changes. As he has bone pain he should be treated with bisphosphonates. A PSA of 4.4 ng/ml is probably normal in a 73-year-old man and is certainly not consistent with metastatic prostate cancer

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Question 78 of 97

Which one of the following is most recognised as a risk factor for developing osteoporosis?

- A. Osteogenesis imperfecta
- B. Marfan's syndrome
- C. Myotonic dystrophy
- D. Duchenne muscular dystrophy
- E. Ehler-Danlos syndrome

Question 78 of 97

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Osteoporosis: causes

Risk factors
- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Asians and Orientals

Diseases which predispose
- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- GI problems: malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Question 79 of 97

A 66-year-old female presents with pain at the base of her left thumb. She has no past medical history of note. On examination there is diffuse tenderness and swelling of her left first carpometacarpal joint. What is the most likely diagnosis?

- A. Osteoarthritis
- B. De Quervain's tenosynovitis
- C. Gout
- D. Rheumatoid arthritis
- E. Primary hyperparathyroidism

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- C. Gout
- D. Rheumatoid arthritis
- E. Primary hyperparathyroidism

The trapeziometacarpal joint (base of thumb) is the most common site of hand osteoarthritis

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with either drug. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Question 80 of 97

A 34-year-old kitchen worker presents with a two week history of pain in her right wrist. She has recently emigrated from Ghana and has no past medical history of note. On examination she is tender over the base of her right thumb and also over the radial styloid process. Ulnar deviation of the wrist recreates the pain. What is the most likely diagnosis?

- A. Rheumatoid arthritis
- B. Osteoarthritis of the carpometacarpal joint
- C. De Quervain's tenosynovitis
- D. Carpal tunnel syndrome
- E. Systemic lupus erythematosus

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De Quervain's tenosynovitis

De Quervain's tenosynovitis is a common condition in which the sheath containing the extensor pollicis brevis and abductor pollicis longus tendons is inflamed. It typically affects females aged 30 - 50 years old

Features

- pain on the radial side of the wrist
- tenderness over the radial styloid process
- abduction of the thumb against resistance is painful
- Finkelstein's test: with the thumb is flexed across the palm of the hand, pain is reproduced by movement of the wrist into flexion and ulnar deviation

Management

- analgesia
- steroid injection
- immobilisation with a thumb splint (spica) may be effective
- surgical treatment is sometimes required

Question 81 of 97

A 71-year-old man presents with an erythematous, swollen first metatarsophalangeal joint on the left foot. This is causing him considerable pain and he is having difficulty walking. He has never had any previous similar episodes. His past medical history includes atrial fibrillation and type 2 diabetes mellitus and his current medications are warfarin, metformin and simvastatin. What is the most appropriate treatment of this episode?

- A. Intra-articular corticosteroid
- B. Colchicine
- C. Ibuprofen
- D. Diclofenac
- E. Prednisolone

Question 81 of 97

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- B. Colchicine
- C. Ibuprofen
- D. Diclofenac
- E. Prednisolone

NSAIDs should be avoided in elderly patients taking warfarin due to the risk of a life-threatening gastrointestinal haemorrhage. Oral steroids are an option but would upset his diabetic control.

Whilst anticoagulation is not a contraindication to joint injection it would make this option less attractive

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 µmol/l)

Acute management
- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below
- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol*
- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications
- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*patients with Lesch-Nyhan syndrome often take allopurinol for life

Question 82 of 97

Which of the following statements is true regarding psoriatic arthropathy?

- A. Skin disease always precedes joint disease
- B. Approximately one-third of patients with psoriasis eventually develop arthropathy
- C. The mainstay of management is analgesia, physiotherapy and joint replacement
- D. Males and females are equally affected
- E. Arthritis mutilans is the most common subtype

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Males and females are affected equally by psoriatic arthritis

Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% percent of patients with skin lesions develop an arthropathy with males and females being equally affected

Types*
- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management
- treat as rheumatoid arthritis
- but better prognosis

*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

Question 83 of 97

A 66-year-old female is on long-term prednisolone therapy for polymyalgia rheumatica. What is the most appropriate protection against osteoporosis?

- A. Hormone replacement therapy
- B. Calcitonin
- C. Oral bisphosphonate
- D. Calcium and vitamin D
- E. Hip-protectors

Question 83 of 97

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Oral bisphosphonate therapy is recommended for patients older than 65 years who have taken, or who are likely to remain on oral corticosteroids for more than 3 months

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses
- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metatases

Adverse effects
- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- the MHRA has warned about an increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates
- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

Question 84 of 97

A 33-year-old female is admitted to the Emergency Department due to right-sided weakness. She has a past history of deep vein thrombosis following the birth of her daughter. The only other past history of note is two miscarriages. A CT head confirms an ischaemic stroke in the left middle cerebral artery territory. What is the likely finding on echocardiography?

- A. Normal
- B. Dilated cardiomyopathy
- C. Bicuspid aortic valve
- D. Atrial septal defect
- E. Ventricular septal defect

Question 84 of 97

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- D. Atrial septal defect
- E. Ventricular septal defect

This is a typical MRCP question. On first sight this question appears to be pointing towards a paradoxical embolus. However, given the history of miscarriages and DVT a diagnosis of antiphospholipid syndrome is more likely.

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features
- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE
- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines
- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 85 of 97

Which one of the following would not suggest an underlying connective tissue disorder in a patient with Raynaud's?

- A. Unilateral symptoms
- B. Digital ulcers
- C. Presence of autoantibodies
- D. Onset at 25 years old
- E. Calcinosis

Question 85 of 97

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Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease
- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthrits or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes
- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management
- calcium channel blockers
- IV prostacyclin infusions

Question 86 of 97

A 33-year-old female presents 6 weeks after the birth of her first child with a two-week history of polyarthralgia, fever and a skin rash. First-line investigations show:
ESR 45 mm/hour

What is the most likely diagnosis?

- A. Polymorphic eruption of pregnancy
- B. Systemic lupus erythematous
- C. Rheumatoid arthritis
- D. Reactive arthritis
- E. Pseudogout

Question 86 of 97

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- C. Rheumatoid arthritis
- D. Reactive arthritis
- E. Pseudogout

Unlike many autoimmune diseases systemic lupus erythematous (SLE) often becomes worse during pregnancy and the puerperium

SLE: pregnancy

Overview
- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematous
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

Question 87 of 97

A 57-year-old woman with a history of polymyalgia rheumatica has been taking prednisolone 10 mg for the past 5 months. A DEXA scan is reported as follows:

L2 T-score	-1.6 SD
Femoral neck T-score	-1.7 SD

What is the most suitable management?

- A. No treatment
- B. Vitamin D + calcium supplementation + repeat DEXA scan in 6 months
- C. Vitamin D + calcium supplementation
- D. Vitamin D + calcium supplementation + hormone replacement therapy
- E. Vitamin D + calcium supplementation + oral bisphosphonate

Question 87 of 97

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- C. Vitamin D + calcium supplementation
- D. Vitamin D + calcium supplementation + hormone replacement therapy
- E. Vitamin D + calcium supplementation + oral bisphosphonate

This patient has been taking 10mg of prednisolone for the past 5 months and hence should be assessed for bone protection. The T score of less than -1.5 SD is an indication for a bisphosphonate. This should be co-prescribed with calcium + vitamin D.

Osteoporosis: glucocorticoid-induced

Patients who take the equivalent of prednisolone 7.5 mg or more each day for 3 months or longer should be assessed and where necessary given prophylactic treatment

Assessment for treatment - patients taking the equivalent of prednisolone 7.5 mg or more each day for 3 months, and one of the following

- are over the age of 65 years
- have a history of a fragility fracture
- have a T-score less than - 1.5 SD

Treatment

- first-line: oral bisphosphonate
- second-line: alfacalcidol or calcitriol

Question 88 of 97

A 54-year-old woman is reviewed. She was discharged from the psychiatric ward around 5 weeks ago following an admission for an acute psychotic episode. Her psychotic symptoms have settled on risperidone but unfortunately she has now developed a dry mouth and arthralgia in both hands. A number of blood tests are requested:

Rheumatoid factor	Positive
Anti-Ro	Positive
Anti-Smith	Negative
ANA	Positive
C4	Low

What is the most likely diagnosis?

- A. Systemic lupus erythematous
- B. Sarcoidosis
- C. Drug-induced lupus erythematous
- D. Rheumatoid arthritis
- E. Sjogren's syndrome

Question 88 of 97

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- D. Rheumatoid arthritis
- E. Sjogren's syndrome

Risperidone (unlike chlorpromazine) is not a common trigger of lupus. Anti-Ro is positive in around 70% of patients with Sjogren's syndrome compared to around 10% of patients with rheumatoid arthritis

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

Question 89 of 97

A 23-year-old female presents with a painful ankle following an inversion injury whilst playing tennis. Which one of the following findings is least relevant when deciding whether an x-ray is needed?

- A. Swelling immediately after the injury and now
- B. Pain in the malleolar zone
- C. Tenderness at the medial malleolar zone
- D. Tenderness at the lateral malleolar zone
- E. Cannot walk 4 steps immediately after the injury and now

Question 89 of 97

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Ankle injury: Ottawa rules

The Ottawa Rules with for ankle x-rays have a sensitivity approaching 100%

An ankle x-ray is required only if there is any pain in the malleolar zone and any one of the following findings:

- bony tenderness at the lateral malleolar zone (from the tip of the lateral malleolus to include the lower 6 cm of posterior border of the fibular)
- bony tenderness at the medial malleolar zone (from the tip of the medial malleolus to the lower 6 cm of the posterior border of the tibia)
- inability to walk four weight bearing steps immediately after the injury and in the emergency department

There are also Ottawa rules available for both foot and knee injuries

Question 90 of 97

Which one of the following antibodies is most specific for systemic lupus erythematous?

- A. Anti-neutrophil cytoplasmic antibodies
- B. Anti-nuclear antibodies
- C. Anti-Sm antibodies
- D. Anti-RNP antibodies
- E. Anti-cardiolipin antibodies

Question 90 of 97

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- D. Anti-RNP antibodies
- E. Anti-cardiolipin antibodies

SLE: ANA is 99% sensitive - anti-Sm & anti-dsDNA are 99% specific

SLE: investigations

Immunology
- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

Monitoring
- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Question 91 of 97

A 30-year-old female who is known to have antiphospholipid syndrome is diagnosed as having a deep vein thrombosis. This is her first thrombotic event. How should her anticoagulation be managed?

- A. Life-long low-dose aspirin
- B. 6 months warfarin, target INR 2 - 3
- C. Life-long warfarin, target INR 3 - 4
- D. Life-long warfarin, target INR 2 - 3
- E. 6 months warfarin, target INR 2 - 3 followed by life-long low-dose aspirin and clopidogrel

Question 91 of 97

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- E. 6 months warfarin, target INR 2 - 3 followed by life-long low-dose aspirin and clopidogrel

This is a tough question and some textbooks may contradict this answer, suggesting either lifelong warfarin or a target INR of 3-4. Please see the link to the BCSH guidelines. There is also a recent review in JAMA 2006; 295(9): 1050-7

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features
- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE
- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines
- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 92 of 97

Which one of the following is least associated with the development of gout?

- A. Psoriasis
- B. Lesch-Nyhan syndrome
- C. Lymphoma
- D. Lithium toxicity
- E. Renal failure

Question 92 of 97

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Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid
- drugs*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid
- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome
- hypoxanthine-guanine phosphoribosyl transferase deficiency
- inheritance = x-linked recessive
- features: gout, renal failure, learning difficulties, head-banging

*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

Question 93 of 97

A 44-year-old woman is seen in the rheumatology clinic. She has been referred with Raynaud's phenomenon. During the review of systems she mentions that her GP is organising an endoscopy to investigate dyspepsia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications is she most likely to develop?

- A. Bronchiectasis
- B. Angiodysplasia
- C. Arterial hypertension
- D. Chronic kidney disease
- E. Pulmonary hypertension

Question 93 of 97

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- B. Angiodysplasia
- C. Arterial hypertension
- D. Chronic kidney disease
- E. Pulmonary hypertension

This patient is likely to have CREST syndrome. Unfortunately pulmonary hypertension is one of the more common late complications seen in such patients.

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis
- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis
- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)
- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

Antibodies
- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

Question 94 of 97

Which one of the following is most recognised as a potential complication in a patient with ankylosing spondylitis?

- A. Heart block
- B. Aortic stenosis
- C. Achalasia
- D. Diabetes mellitus
- E. Bronchiectasis

Question 94 of 97

Which one of the following is most recognised as a potential complication in a patient with ankylosing spondylitis?

- A. Heart block
- B. Aortic stenosis
- C. Achalasia
- D. Diabetes mellitus
- E. Bronchiectasis

Ankylosing spondylitis features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

Ankylosing spondylitis: features

Features
- typically a young man who presents with lower back pain and stiffness
- stiffness is usually worse in morning and improves with activity
- peripheral arthritis (25%, more common if female)

Other features - the 'A's
- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome

X-rays are often normal early in disease, later changes include:
- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)

- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints

Question 95 of 97

A 58-year-old woman with a history of left hip osteoarthritis presents for review. She is currently taking co-codamol 30/500 for pain on a regular basis but this is unfortunately not controlling her symptoms. There is no past medical history of note, in particular no asthma or gastrointestinal problems. What is the most suitable next step in management?

- A. Switch to regular oral tramadol
- B. Add topical ibuprofen
- C. Add oral diclofenac + proton pump inhibitor
- D. Add oral etoricoxib
- E. Add oral diclofenac

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NICE recommend co-prescribing a PPI with NSAIDs in all patients with osteoarthritis

Topical NSAIDs are only indicated for osteoarthritis of the knee or hand.

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with either drug. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Question 96 of 97

A 62-year-old man with lung cancer is suspected of having dermatomyositis. Which one of the following antibodies is most likely to be positive?

- A. Anti-nuclear antibodies
- B. Anti-centromere bodies
- C. Anti-scl-70 antibodies
- D. Anti-Jo-1 antibodies
- E. Anti-Mi-2 antibodies

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Dermatomyositis: investigations and management

Investigations
- elevated creatine kinase
- EMG
- muscle biopsy
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever
- ANA positive in 60%

Management
- prednisolone

Question 97 of 97

Which one of the following is most consistently associated with a poor prognosis in rheumatoid arthritis?

- A. Anti-CCP antibodies
- B. HLA DR2 allele
- C. Rapid onset
- D. Being a smoker
- E. Female sex

Question 97 of 97

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- D. Being a smoker
- E. Female sex

See below for further information on the effect of gender on prognosis.

Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.