

Which of the following drugs is most likely to cause drug-induced lupus erythematosus (DILE) syndrome?

(Please select 1 option)



Baclofen



Isoniazid



Methotrexate



Procainamide



Sulphasalazine

<input type="radio"/>	Baclofen	
<input type="radio"/>	Isoniazid	
<input type="radio"/>	Methotrexate	
<input type="radio"/>	Procainamide	This is the correct answer
<input checked="" type="radio"/>	Sulphasalazine	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- At least 38 drugs currently in use can cause DILE. However, most cases have been associated with procainamide (15-20%), hydralazine (7-13%), or quinidine.

Explanation

A recessive gene is responsible for the activity of hepatic N-acetyl transferase resulting in slow or fast (intermediate and fast groups get lumped together) acetylation.

45% of the United Kingdom population are slow acetylators.

Drugs affected include:

- isoniazid
- hydralazine
- dapsone
- procainamide, and
- sulphasalazine.

Slow acetylators have increased risk of isoniazid-induced peripheral neuropathy, and hydralazine or procainamide-induced systemic lupus erythematosus (SLE).

At least 38 drugs currently in use can cause DILE. However, most cases have been associated with these three:

- procainamide
- hydralazine, and
- quinidine.

The risk for developing lupus-like disease from any of the other 35 drugs is low or very low; with some drugs only one or two cases have been reported.

- Isoniazid (INH) - low risk
- Sulfasalazine - low risk.

A 70-year-old man presents with an episode of syncope.

On subsequent investigation he is found to have marked postural hypotension. He has been taking felodipine for hypertension for a number of years and he also takes aspirin. On further questioning he appears to have taken up a new healthier lifestyle on his seventieth birthday.

Which of the following health supplements is he most likely to have taken that would have contributed to the calcium-channel blocker induced hypotension?

(Please select 1 option)

<input type="radio"/>	Cod liver oil capsules
<input type="radio"/>	Cranberry juice
<input type="radio"/>	Ginseng
<input type="radio"/>	Grapefruit juice
<input type="radio"/>	Vitamin C

Please select 1 option



Cod liver oil capsules



Cranberry juice



Ginseng



Grapefruit juice

This is the correct answer



Vitamin C

Incorrect answer selected

Key Learning Points

Pharmacology

- Grapefruit juice contains bergamottin which INHIBITS CYP3A4, thereby increasing the bioavailability of felodipine and the risk of toxicity.

Explanation

Multiple studies have demonstrated this interaction between grapefruit juice and felodipine. Felodipine is normally metabolised in the GI tract and liver by CYP3A4. Grapefruit juice contains bergamottin which INHIBITS CYP3A4, thereby increasing the bioavailability of felodipine and the risk of toxicity.

Dr Assem

A 52-year-old man has been started on regular diclofenac for back pain. He is concerned as over the past few days he has been suffering from deteriorating vision.

On examination his BP is 142/82 mmHg, pulse is 72 and regular. There is bilateral decreased visual acuity and loss of colour vision. The rest of the neurological examination is unremarkable.

Which of the following is most likely to have occurred?

(Please select 1 option)

<input type="radio"/>	Cataract formation
<input type="radio"/>	Closed angle glaucoma
<input type="radio"/>	Open angle glaucoma
<input type="radio"/>	Optic neuritis
<input type="radio"/>	Retinal detachment

<input type="radio"/>	Cataract formation	
<input type="radio"/>	Closed angle glaucoma	
<input type="radio"/>	Open angle glaucoma	
<input type="radio"/>	Optic neuritis	This is the correct answer
<input checked="" type="radio"/>	Retinal detachment	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- Optic neuritis is described as being associated with diclofenac therapy but rarely.

Explanation

Optic neuritis is described as being rarely associated with diclofenac therapy. A range of other CNS side effects has also been noted on the summary of product characteristics, these include headache, dizziness, vertigo and in rare circumstances drowsiness.

Cataract formation would not lead to loss of colour vision or to a sudden deterioration in sight over the course of a few days.

Glaucoma and retinal detachment are not thought to be associated with diclofenac treatment.

A 42-year-old man presents with gingival hypertrophy.

Which of his cardiac medications is likely to be responsible?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Atenolol
<input type="radio"/>	Digoxin
<input type="radio"/>	GTN
<input type="radio"/>	Simvastatin

Please select 1 option/

<input type="radio"/>	Amlodipine	This is the correct answer
<input type="radio"/>	Atenolol	
<input type="radio"/>	Digoxin	
<input type="radio"/>	GTN	
<input checked="" type="radio"/>	Simvastatin	Incorrect answer selected

Key Learning Points

Pharmacology

- Drugs associated with gingival hypertrophy include calcium channel blockers, phenytoin and cyclosporin

Explanation

Calcium channel blockers and drugs like phenytoin and cyclosporin are associated with gingival hypertrophy.

You are asked to see a 27-year-old woman on the oncology ward. She has been admitted for a course of chemotherapy and has been taking high dose steroids for a few days. The nurses report that she is very agitated and talks about trying to open the window of her room and jump out from the fourth floor.

You review her notes and see that she admits to drinking a few glasses of wine per week and has smoked cannabis on a few occasions.

On examination her BP is 145/88 mmHg, her pulse is 80 and regular and she looks agitated and upset.

Investigations show:

Haemoglobin	121 g/L	(115-165)
White cell count	$16.2 \times 10^9/L$	(4-11)
Platelets	$200 \times 10^9/L$	(150-400)
C-reactive protein	9 nmol/L	(<10)
Sodium	140 mmol/L	(135-146)
Potassium	3.9 mmol/L	(3.5-5)
Creatinine	92 μ mol/L	(79-118)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Alcohol withdrawal
<input type="radio"/>	Cannabis-related psychosis
<input type="radio"/>	Corticosteroid-related psychosis
<input type="radio"/>	Manic depressive psychosis
<input type="radio"/>	Personality disorder

<input type="radio"/>	Alcohol withdrawal
<input type="radio"/>	Cannabis-related psychosis
<input type="radio"/>	Corticosteroid-related psychosis This is the correct answer
<input type="radio"/>	Manic depressive psychosis
<input checked="" type="radio"/>	Personality disorder Incorrect answer selected

Key Learning Points

Pharmacology

- Corticosteroid-related psychosis is seen within a few days of starting high dose oral or intravenous corticosteroids, although some patients have been diagnosed with the condition up to 12 weeks or more after commencing therapy.

Explanation

Corticosteroid-related psychosis is seen within a few days of starting high dose oral or intravenous corticosteroids, although some patients have been diagnosed with the condition up to 12 weeks or more after commencing therapy.

Symptoms which are seen include:

- agitation
- hypomania, and
- suicidal intent.

Given the close proximity of her symptoms to the onset of steroid therapy this is much more likely to be the diagnosis than cannabis or alcohol related psychiatric disorder.

In severe cases, typical or atypical antipsychotics or benzodiazepines to manage agitation may be required.

A 56-year-old man with septic shock is fully ventilated, on continuous veno-venous haemofiltration receiving noradrenaline, vancomycin and ciprofloxacin.

He has a mean arterial pressure (MAP) of 60 mmHg which is then not improved after changing from noradrenaline to adrenaline. There is no evidence of myocardial dysfunction.

Which of the following would be the most appropriate next step in managing this patient?

(Please select 1 option)

☐ ACTH stimulation test

☐ Activated protein C

☐ Change of inotropes

☐ Hydrocortisone

☐ Nitric oxide

Please select a option

<input type="radio"/>	ACTH stimulation test
<input type="radio"/>	Activated protein C
<input type="radio"/>	Change of inotropes
<input checked="" type="radio"/>	Hydrocortisone This is the correct answer
<input type="radio"/>	Nitric oxide Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- Steroids have been shown to improve prognosis in severe sepsis, and should be administered within 24 hours.

Explanation

The Surviving Sepsis Campaign (a partnership of the Society of Critical Care Medicine, the European Society of Intensive Care Medicine, and the International Sepsis Forum) has teamed up with the Institute for Healthcare Improvement to develop severe sepsis bundles. A 'bundle' is a group of interventions related to a disease process that, when executed together, result in better outcomes than when implemented individually.

Sepsis Resuscitation Bundle:

Should begin immediately, but must be accomplished within the first six hours of presentation.

- Serum lactate measured.
- Blood cultures obtained prior to antibiotic administration.
- From the time of presentation, broad-spectrum antibiotics administered within three hours for ED admissions and one hour for non-ED ICU admissions.
- In the event of hypotension and/or lactate > 4 mmol/l (36 mg/dl):
 - Deliver an initial minimum of 30 ml/kg of crystalloid (or colloid equivalent).
 - Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65 mm Hg.
- In the event of persistent hypotension despite fluid resuscitation (septic **shock**) and/or lactate > 4 mmol/l (36 mg/dl):
 - Achieve central venous pressure (CVP) of > 8 mm Hg.
 - Achieve central venous oxygen saturation (ScvO₂) of $> 70\%$.

Sepsis Management Bundle:

To be accomplished as soon as possible may be completed within twenty-four hours of presentation.

- Steroids administered for septic **shock** in accordance with a standardised ICU policy. ACTH stimulation test not required prior to this.
- Glucose control maintained $>$ lower limit of normal, but < 150 mg/dl (8.3 mmol/l).
- Inspiratory plateau pressures maintained < 30 cm H₂O for mechanically ventilated patients.

Drotrecogin alpha (activated protein C) used to be recommended by NICE for the treatment of severe sepsis. However, in October 2011 the company withdrew this from the market following the results of the PROWESS-SHOCK study, which showed there was no statistically significant reduction in 28-day all-cause mortality in patients with septic shock.

Nitric oxide is a non-proven therapy in adult respiratory distress syndrome (ARDS), but is less likely to be effective in this situation.

A 28-year-old car mechanic is admitted to the hospital having taken an overdose of methanol after splitting up from his wife.

On admission to the Emergency department he is drowsy and intoxicated. His BP is 134/82 mmHg, and he has a tachycardia with a pulse of 95.

Investigations show:

Haemoglobin	140 g/L	(135-177)
White cell count	$8.1 \times 10^9/L$	(4-11)
Platelets	$190 \times 10^9/L$	(150-400)
Serum sodium	137 mmol/L	(135-146)
Serum potassium	4.2 mmol/L	(3.5-5)
Bicarbonate	17 mmol/L	(22-30)
Creatinine	130 $\mu\text{mol/L}$	(79-118)

Which of the following is the most appropriate antidote for methanol poisoning?

(Please select 1 option)

<input type="radio"/>	Atenolol
<input type="radio"/>	Ethanol
<input type="radio"/>	Glucagon
<input type="radio"/>	Insulin
<input type="radio"/>	Polyethylene glycol

<input type="radio"/>	Atenolol
<input type="radio"/>	Ethanol This is the correct answer
<input type="radio"/>	Glucagon
<input type="radio"/>	Insulin
<input checked="" type="radio"/>	Polyethylene glycol Incorrect answer selected

Key Learning Points

Pharmacology

- Inhibition of metabolism of methanol by alcohol dehydrogenase with either ethanol or fomepizole is the treatment of choice for methanol poisoning.

Explanation

Methanol, like ethanol, is metabolised by alcohol dehydrogenase to form formaldehyde. Formaldehyde is then further metabolised by aldehyde dehydrogenase to formic acid.

Formate formation leads to a severe metabolic acidosis, and crystals forming within the eye can lead to so called 'snow field' cataract formation.

Inhibition of metabolism of methanol by alcohol dehydrogenase with either ethanol or fomepizole is the treatment of choice.

Which of the following pharmacological agents acts through the opening of potassium channels?

(Please select 1 option)

<input type="radio"/>	Amiloride
<input type="radio"/>	Glibenclamide
<input type="radio"/>	Lidocaine
<input type="radio"/>	Nicorandil
<input type="radio"/>	Phenytoin

<input type="radio"/>	Amiloride	
<input type="radio"/>	Glibenclamide	
<input type="radio"/>	Lidocaine	
<input type="radio"/>	Nicorandil	This is the correct answer
<input checked="" type="radio"/>	Phenytoin	Incorrect answer selected

Key Learning Points

Pharmacology

- Nicorandil is a potent potassium channel activator.

Explanation

Nicorandil is a potent potassium channel activator. It relaxes vascular smooth muscle through membrane hyperpolarisation via increased transmembrane potassium conductance and, like nitrates, through an increase in intracellular cyclic guanosine monophosphate (GMP).

Glibenclamide blocks potassium channels.

Amiloride inhibits the action of aldosterone on the distal convoluted tubule producing potassium reabsorption.

An 18-year-old woman is brought to the Emergency department with shortness of breath, stridor, and an urticarial rash.

On examination her BP is 90/50 mmHg and she has a tachycardia of 95 beats per minute. You give her hydrocortisone and an IV fluid challenge but her BP fails to improve. You decide to administer adrenalin.

Which of the following is the most appropriate method of administration and dosage?

(Please select 1 option)

- | | |
|-----------------------|---------------------------------|
| <input type="radio"/> | 0.5 ml of 1:1000 adrenalin IM |
| <input type="radio"/> | 0.5 ml of 1:10000 adrenalin IV |
| <input type="radio"/> | 1 mcg/min IV adrenalin infusion |
| <input type="radio"/> | 1 ml of 1:10000 adrenalin IM |
| <input type="radio"/> | 4 mcg/min IV adrenalin infusion |

Please select 1 option)

<input type="radio"/>	0.5 ml of 1:1000 adrenalin IM	This is the correct answer
<input type="radio"/>	0.5 ml of 1:10000 adrenalin IV	
<input type="radio"/>	1 mcg/min IV adrenalin infusion	
<input type="radio"/>	1 ml of 1:10000 adrenalin IM	
<input checked="" type="radio"/>	4 mcg/min IV adrenalin infusion	Incorrect answer selected

Key Learning Points

Pharmacology

- Adrenalin is used for its alpha-agonist effects. IM administration is preferred because of a superior safety profile with respect to cardiac adverse events compared with the IV route.

Explanation

Multimodal therapy involving use of an IV corticosteroid, IV antihistamine and fluid loading is usually employed in the treatment of anaphylaxis.

IV corticosteroids are designed to modulate downstream release of cytokines from inflammatory cells, they reduce the duration and severity of anaphylaxis.

IV antihistamine is designed to block the effects of histamine on the vascular tree, which ameliorates hypotension, and on the airways, reducing shortness of breath and stridor. Fluid loading is designed to raise blood pressure.

Adrenalin is used for its alpha-agonist effects that include increased peripheral vascular resistance and reversed peripheral vasodilatation, systemic hypotension, and vascular permeability.

Beta-agonist effects include bronchodilatation, chronotropic cardiac activity, and positive inotropic effects.

IM administration is preferred because of a superior safety profile with respect to cardiac adverse events compared with the IV route, although 1:10000 adrenalin IV may be used in a life-threatening situation.

Reference:

A 64-year-old gentleman consults you in clinic because he is having trouble putting his shoes on due to swelling.

He has COPD, hypertension and angina.

Which medication is likely to be causing this problem?

(Please select 1 option)

<input type="radio"/>	Diltiazem
<input type="radio"/>	Eplerenone
<input type="radio"/>	Isosorbide mononitrate
<input type="radio"/>	Nicorandil
<input type="radio"/>	Propranolol

<input type="radio"/>	Diltiazem	This is the correct answer
<input type="radio"/>	Eplerenone	
<input type="radio"/>	Isosorbide mononitrate	
<input type="radio"/>	Nicorandil	
<input checked="" type="radio"/>	Propranolol	Incorrect answer selected

Key Learning Points

Pharmacology

- Diltiazem, as with nearly all the calcium channel blockers, causes gravitational/ankle oedema.

Explanation

Diltiazem, as with nearly all the calcium channel blockers, causes gravitational/ankle oedema.

Eplerenone is an aldosterone antagonist and therefore is used to treat ankle oedema.

Isosorbide mononitrate commonly causes headaches and hypotension.

Nicorandil rarely causes angioedema, but not ankle swelling.

Propranolol does not cause ankle oedema although it may worsen decompensated heart failure, so is usually avoided until the patient has been diuresed appropriately.

A 75-year-old patient being treated for heart failure presents with hyperkalaemia, the potassium being 6.9 mmol/L (3.5-5.0). He was recently commenced on amiloride.

The interaction of amiloride with which of his drugs listed below is likely to have caused the hyperkalaemia?

(Please select 1 option)

<input type="radio"/>	Bisoprolol
<input type="radio"/>	Digoxin
<input type="radio"/>	Metolazone
<input type="radio"/>	Perindopril
<input type="radio"/>	Warfarin

<input type="radio"/>	Bisoprolol	
<input type="radio"/>	Digoxin	
<input type="radio"/>	Metolazone	
<input type="radio"/>	Perindopril	This is the correct answer
<input checked="" type="radio"/>	Warfarin	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- ACE inhibitors in combination with potassium sparing diuretics may result in profound hyperkalaemia.

Explanation

The co-administration of a potassium-sparing diuretic and an ACE inhibitor, in this case Perindopril, may result in profound hyperkalaemia, as has occurred in this patient. Thus patients on both these drugs should have their potassium monitored closely.

Metolazone may result in profound hypokalaemia.

A 17-year-old woman is admitted by emergency ambulance. She has apparently taken a large overdose of her father's anti-hypertensive medication after he refused to allow her to see her boyfriend who is 21.

On admission to the Emergency department she is hypotensive, with a BP of 80/55 mmHg, and a pulse of 28.

Investigations show

Hb	121 g/L	(135-180)
WCC	$7.8 \times 10^9/L$	(4-10)
PLT	$191 \times 10^9/L$	(150-400)
Na	139 mmol/L	(134-143)
K	4.6 mmol/L	(3.5-5)
Cr	85 μ mol/L	(60-120)
Gluc	2.8 g/dL	(7.0-11.0)

Her rate increases to 35 after 3 mg of atropine, but little improvement in BP is seen.

Which of the following is the next most appropriate step?

(Please select 1 option)

<input type="radio"/>	Further 1 mg atropine
<input type="radio"/>	IM adrenalin
<input type="radio"/>	IV adrenalin
<input type="radio"/>	IV glucagon
<input type="radio"/>	Temporary pacing

<input type="radio"/>	Further 1 mg atropine	
<input type="radio"/>	IM adrenalin	
<input type="radio"/>	IV adrenalin	
<input type="radio"/>	IV glucagon	This is the correct answer
<input checked="" type="radio"/>	Temporary pacing	Incorrect answer selected

Key Learning Points

Pharmacology

- Glucagon is the conventional antidote for beta-blocker overdose. It reverses hypoglycaemia, and improves myocardial contractility and heart rate by stimulating production of cyclic AMP.

Explanation

Glucagon is the conventional antidote for beta-blocker overdose, the most likely cause of this patient's presentation. It reverses hypoglycaemia, and improves myocardial contractility and heart rate by stimulating production of cyclic AMP.

Doses of glucagon used are much higher than those conventionally used for reversing hypoglycaemia in diabetes, with a bolus of 3-10 mg being required, then 2-5 mg/hr by infusion.

A 71-year-old man is treated for paroxysmal atrial fibrillation with 200 mg of amiodarone per day.

He is finding extreme problems with photosensitivity and wants to discontinue the medication.

Which of the following is true of amiodarone therapy?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | It has a half life of 36 hours so stopping the medication will be associated with an immediate improvement |
| <input type="radio"/> | Photosensitivity is a rare occurrence |
| <input type="radio"/> | Purple skin discoloration is seen independent of photosensitivity |
| <input type="radio"/> | Skin sensitivity can be prevented by using a sun block |
| <input type="radio"/> | Thyroid dysfunction is seen more commonly in patients who experience photosensitivity |

Please select 1 option

<input type="radio"/>	It has a half life of 36 hours so stopping the medication will be associated with an immediate improvement
<input type="radio"/>	Photosensitivity is a rare occurrence
<input type="radio"/>	Purple skin discoloration is seen independent of photosensitivity
<input checked="" type="radio"/>	Skin sensitivity can be prevented by using a sun block Correct
<input type="radio"/>	Thyroid dysfunction is seen more commonly in patients who experience photosensitivity

Key Learning Points

Pharmacology, Therapeutics

- Photosensitivity is seen very commonly in those patients who are prescribed amiodarone therapy. It is distinct from the slate grey skin discolouration which can occur with prolonged amiodarone use and can be prevented by using a total sun block preparation.

Explanation

Photosensitivity is seen very commonly in those patients who are prescribed amiodarone therapy. It is distinct from the slate grey skin discolouration which can occur with prolonged amiodarone use and can be prevented by using a total sun block preparation.

The half life of amiodarone has a mean of around 50 days, and may be as short as 20 days in some individuals and as long as 100 days in others. Slate grey or blue skin appearance is the commonest pigmentation change seen in association with treatment.

The incidence of amiodarone induced thyroid dysfunction has no relationship at all to photosensitivity.

A 77-year-old woman comes to the clinic for review. She has suffered a previous Colles' fracture, and has a history of a previous left leg DVT.

She takes a range of medication including omeprazole for severe reflux oesophagitis. A T score was measured at -4.2, and she was unable to tolerate weekly alendronate due to symptoms of indigestion.

Which of the following is the most appropriate alternative for her?

(Please select 1 option)

<input type="radio"/>	Daily calcium and vitamin D
<input type="radio"/>	Daily strontium ranelate
<input type="radio"/>	Monthly ibandronate
<input type="radio"/>	Monthly risedronate
<input type="radio"/>	Six monthly denosumab

<input type="radio"/>	Daily calcium and vitamin D	
<input type="radio"/>	Daily strontium ranelate	
<input type="radio"/>	Monthly ibandronate	
<input checked="" type="radio"/>	Monthly risedronate	Incorrect answer selected
<input type="radio"/>	Six monthly denosumab	This is the correct answer

Key Learning Points

Pharmacology, Rheumatology

- Six monthly denosumab is effective in managing patients with severe osteoporosis intolerant or with contraindications to Alendronate or Zoledronic acid.

Explanation

Six monthly denosumab is correct because it is effective in managing osteoporosis in this patient type. This patient falls into the severe osteoporosis range and definitely requires therapy in excess of calcium and vitamin D.

Whilst bisphosphonates can be given monthly, they still cause oesophagitis and are not appropriate here.

Denosumab is a rank ligand inhibitor leading to inhibition of osteoclast activity. It is given by six monthly subcutaneous injection and is associated with a 40% reduction in the risk of hip fracture over three years. It is recommended in NICE guidance on Osteoporotic fractures - denosumab (TA204) for this patient type.

Daily calcium and vitamin D are incorrect because they are less effective than bisphosphonates in the treatment of osteoporosis.

Strontium ranelate is incorrect because it is associated with increased risk of deep vein thrombosis.

Monthly ibandronate is incorrect because it is still associated with symptoms of oesophagitis.

Monthly risedronate is incorrect because it is still associated symptoms of oesophagitis.

A 40-year-old ex-footballer presents requesting treatment for alcoholism and is prescribed disulfiram.

What is the mode of action of disulfiram?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Decreases severity of alcohol withdrawal |
| <input type="radio"/> | Helps alcoholics to drink safely |
| <input type="radio"/> | Inhibits acetaldehyde dehydrogenase activity |
| <input type="radio"/> | Inhibits alcohol dehydrogenase activity |
| <input type="radio"/> | Reduces the desire for alcohol |

<input type="radio"/>	Decreases severity of alcohol withdrawal	
<input type="radio"/>	Helps alcoholics to drink safely	
<input type="radio"/>	Inhibits acetaldehyde dehydrogenase activity	This is the correct answer
<input type="radio"/>	Inhibits alcohol dehydrogenase activity	
<input checked="" type="radio"/>	Reduces the desire for alcohol	Incorrect answer selected

Key Learning Points

Pharmacology, Psychiatry

- Disulfiram irreversibly inhibits the oxidation of acetaldehyde, the subsequent increased levels of which are thought to produce the typically unpleasant side effects

Explanation

Alcohol is mainly metabolised in the liver to acetaldehyde by alcohol dehydrogenase.

Acetaldehyde is then oxidised to acetate by acetaldehyde dehydrogenase (AcDH).

Disulfiram irreversibly inhibits the oxidation of acetaldehyde by competing with the cofactor nicotinamide adenine dinucleotide (NAD) for binding sites on (AcDH).

The increased acetaldehyde levels are thought to produce the unpleasant side effects associated with acetaldehyde syndrome such as headaches, nausea, flushing etcetera.

A 32-year-old female smoker presents with acute severe asthma.

The SaO_2 are 91% on 15 L of oxygen and the pO_2 is 8.2 kPa (10.5-13). There is widespread expiratory wheeze throughout the chest.

She is given IV hydrocortisone, 100% oxygen and 5 mg of nebulised salbutamol and 500 micrograms of nebulised ipratropium with little response. Nebulisers are repeated 'back-to-back' but she remains tachypnoeic with wheeze but good air entry.

What is the next step in your management?

(Please select 1 option)

<input type="radio"/>	IV Augmentin
<input type="radio"/>	IV Magnesium
<input type="radio"/>	IV Potassium
<input type="radio"/>	Non-invasive ventilation
<input type="radio"/>	Oral prednisolone

<input type="radio"/>	IV Augmentin	
<input checked="" type="radio"/>	IV Magnesium	This is the correct answer
<input type="radio"/>	IV Potassium	
<input checked="" type="radio"/>	Non-invasive ventilation	Incorrect answer selected
<input type="radio"/>	Oral prednisolone	

Key Learning Points

Pharmacology, Respiratory Medicine

- The mechanism by which it has its effect is not fully understood, but it is thought that low magnesium levels in bronchial smooth muscle favour bronchoconstriction.

Explanation

This question focuses on acute treatment of asthma.

Your initial approach should be SOS:

- Salbutamol
- Oxygen, and
- Steroids (IV).

In the meantime a CXR should be organised to rule out pneumothorax.

You should then consider further efforts to treat bronchoconstriction - a silent chest, or a tiring patient should suggest ITU review.

The recommended dose of magnesium is 2 g over 30 minutes. The mechanism by which it has its effect is not fully understood, but it is thought that low magnesium levels in bronchial smooth muscle favour bronchoconstriction.

IV theophylline may be considered, but magnesium would be higher on the list.

IV antibiotic may be indicated, but your initial focus should be promoting bronchodilation.

IV potassium may be required as the beta agonists push down the potassium.

Oral prednisolone can wait, as you have already given IV hydrocortisone as part of your SOS approach.

Non-invasive ventilation has no role in the acute management of asthma.

A 44-year-old woman is taking lithium for bipolar disorder. She also suffers from hypertension and angina and recently underwent a medication review at her GP. She also suffers from osteoarthritis of her knees and has suffered a recent respiratory tract infection.

Over the past few days she has become increasingly drowsy, with ataxia, dizziness and slurred speech. A lithium level is measured at 4 mmol/l.

Which of the following is most likely to have resulted in her presentation with lithium toxicity?

(Please select 1 option)

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Atenolol
<input type="radio"/>	Paracetamol
<input type="radio"/>	Ramipril
<input type="radio"/>	Verapamil

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Atenolol
<input type="radio"/>	Paracetamol
<input checked="" type="radio"/>	Ramipril Correct
<input type="radio"/>	Verapamil

Key Learning Points

Pharmacology

- ACE inhibitors and dihydropyridine calcium antagonists are known to increase serum lithium levels.

Explanation

ACE inhibitors are known to increase serum lithium levels, as are dihydropyridine calcium antagonists.

Atenolol, in contrast, is a relatively safer option for the treatment of hypertension in association with long term lithium use.

Verapamil in combination with lithium leads to neurotoxicity; this is independent of any increase in serum lithium levels.

If patients have poorly controlled hypertension and they are taking lithium, it may be better to discuss the case with the psychiatrist to see if they can be changed to another mood stabilising agent, such as sodium valproate.

A 76-year-old man is reviewed in clinic having recently been diagnosed with severe heart failure (HF) associated with very limiting breathlessness. He was formerly a heavy smoker with a medical history of COPD. His lung function test demonstrates mild to moderate obstructive airways disease and he has 5% airways reversibility.

On clinical examination his heart rate is 95 bpm and BP 156/90 mmHg. No wheeze is present. He has an elevated JVP +5 cms but no clinical signs of fluid congestion. He is already taking aspirin 75 mg od, ramipril 10 mg od, furosemide 40 mg od and simvastatin 40 mg nocte.

You decide to add in a beta blocker as the next step.

Which would be the most appropriate choice?

(Please select 1 option)

<input type="radio"/>	Atenolol 25 mg od
<input type="radio"/>	Bisoprolol 5 mg od
<input type="radio"/>	Bisoprolol 1.25 mg od
<input type="radio"/>	Carvedilol 6.25 mg bd
<input type="radio"/>	Carvedilol 12.5 mg bd

Dr Assem

Please select 1 option

<input type="radio"/>	Atenolol 25 mg od	
<input type="radio"/>	Bisoprolol 5 mg od	
<input type="radio"/>	Bisoprolol 1.25 mg od	This is the correct answer
<input type="radio"/>	Carvedilol 6.25 mg bd	
<input checked="" type="radio"/>	Carvedilol 12.5 mg bd	Incorrect answer selected

Key Learning Points

Pharmacology

- In chronic obstructive pulmonary disease (COPD) patients with HF, cardioselective β blockers appear safer at lower doses than higher doses or non-selective β blockers (refs in DTB article).

Explanation

NICE recommends β blockers in all HF patients.

In chronic obstructive pulmonary disease (COPD) patients with HF, cardioselective β blockers appear safer at lower doses than higher doses or non-selective β blockers (refs in DTB article).

Bisoprolol 5 mgs is too high an initial starting dose, a low dose can always be titrated up later, if tolerated.

Carvedilol though effective treatment for heart failure is not selective and therefore carries a greater risk of causing bronchospasm.

Atenolol though cardioselective has no clinical evidence for prognostic benefit in heart failure.

The patient should be closely monitored for deterioration in lung function post-administration.

A 65-year-old man is admitted from home with a community-acquired pneumonia (CAP).

He has a history of skin rash to penicillin documented in his medical notes. He has adverse prognostic features and a CURB score of 4.

What would be an appropriate empirical antibiotic choice?

(Please select 1 option)

- | | |
|-----------------------|----------------------------------|
| <input type="radio"/> | Augmentin |
| <input type="radio"/> | Augmentin and gentamycin |
| <input type="radio"/> | Cefotaxime and erythromycin |
| <input type="radio"/> | Cefuroxime and metronidazole |
| <input type="radio"/> | Ciprofloxacin and clarithromycin |

<input type="radio"/>	Augmentin	
<input type="radio"/>	Augmentin and gentamycin	
<input type="radio"/>	Cefotaxime and erythromycin	This is the correct answer
<input type="radio"/>	Cefuroxime and metronidazole	
<input checked="" type="radio"/>	Ciprofloxacin and clarithromycin	Incorrect answer selected

Key Learning Points

Pharmacology, Respiratory Medicine

- Consider the severity of the allergic reaction when selecting antibiotics in penicillin allergic patients. The chance of cross reactivity with beta-lactams is 10%.

Explanation

Community-acquired pneumonia is most commonly caused by *Strep. pneumoniae*, hence the use of a beta-lactam antibiotic. Because of the increased incidence of atypical organisms such as *Mycoplasma*, a macrolide such as erythromycin is also recommended.

Augmentin is contraindicated as it is penicillin-based.

Ciprofloxacin has poor cover against *Strep. pneumoniae* and metronidazole is used for anaerobic infections.

In this case a credible alternative for beta-lactam sensitivity is not mentioned and the best choice, because of clinical necessity since severe pneumonia can be fatal if treated with antibiotics that are not effective, is to go with the only cephalosporin and macrolide combination that is offered.

The chance of cross reactivity of penicillin allergy with beta-lactams is only 10%. A rash is not a contraindication for this.

If the patient has a documented anaphylactic reaction specifically to penicillin then this case would need to be discussed between the medical and microbiology consultants before the prescription was given. Different trusts have different policies regarding this and consequently it is highly unlikely you will be tested on this.

A 63-year-old female presents with dry mouth of three months duration.

She is taking medication for hypertension, stress incontinence and reflux oesophagitis.

Which of the following is most likely to be responsible for her dry mouth?

(Please select 1 option)

☐ Bendroflumethiazide

☐ Cimetidine

☐ Doxazosin

☐ Hydralazine

☐ Oxybutinin

Please select 1 option

<input type="radio"/>	Bendroflumethiazide
<input type="radio"/>	Cimetidine
<input type="radio"/>	Doxazosin
<input type="radio"/>	Hydralazine
<input checked="" type="radio"/>	Oxybutinin Correct

Key Learning Points

Therapeutics

- Oxybutinin is used for detrusor instability as a parasympathetic muscarinic antagonist hence dry mouth is seen in 70% of cases.

Explanation

Oxybutinin is an effective treatment for detrusor instability and is a parasympathetic muscarinic antagonist. Consequently dry mouth is a problem in up to 70% of cases.

Bendroflumethiazide, the thiazide diuretic, at a dose of 2.5 mg per day is not associated with dry mouth.

Cimetidine is an H₂ antagonist and is not associated with dry mouth.

Doxazosin is an alpha-blocker used as an antihypertensive and is associated with a dry mouth in less than 5% of patients.

Hydralazine is a vasodilator and is not commonly linked to a dry mouth.

Dr. Assem

A 61-year-old man presents to the emergency department complaining of lethargy and muscle weakness. He has begun therapy for hypertension with bendroflumethiazide a few weeks earlier. Blood testing reveals a potassium of 2.5 mmol/l.

Which of the following is the most likely cause of his hypokalaemia?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Increased sodium within the ascending loop of Henle |
| <input type="radio"/> | Increased sodium within the descending loop of Henle |
| <input type="radio"/> | Increased sodium within the distal collecting duct |
| <input type="radio"/> | Increased sodium within the distal convoluted tubule |
| <input type="radio"/> | Increased sodium within the proximal convoluted tubule |

- | | | |
|----------------------------------|--|----------------------------|
| <input type="radio"/> | Increased sodium within the ascending loop of Henle | |
| <input type="radio"/> | Increased sodium within the descending loop of Henle | |
| <input type="radio"/> | Increased sodium within the distal collecting duct | |
| <input checked="" type="radio"/> | Increased sodium within the distal convoluted tubule | This is the correct answer |
| <input type="radio"/> | Increased sodium within the proximal convoluted tubule | Incorrect answer selected |

Key Learning Points

Pharmacology

- Thiazides block sodium reabsorption in the proximal segment of the distal convoluted tubule.

Explanation

Thiazides block sodium reabsorption in the proximal segment of the distal convoluted tubule. This promotes increased delivery of sodium to the distal segment of the distal convoluted tubule. There the aldosterone sensitive sodium potassium exchange pump is presented with increased luminal sodium, which leads to increased excretion of potassium and hydrogen ions.

Often thiazide diuretics are combined in the treatment of hypertension with an ACE inhibitor or angiotensin receptor blocker (ARB), in which case hypokalaemia does not normally present itself as a problem.

A patient is suspected of having taken a substance with anticholinesterase effects.

Which of the following combinations of signs, if present, would be the most likely to confirm this effect?

(Please select 1 option)

- | | |
|-----------------------|-----------------------------------|
| <input type="radio"/> | Bradycardia and miosis |
| <input type="radio"/> | Bradycardia and mydriasis |
| <input type="radio"/> | Bradycardia and urinary retention |
| <input type="radio"/> | Tachycardia and diarrhoea |
| <input type="radio"/> | Tachycardia and lacrimation |

<input type="radio"/>	Bradycardia and miosis	This is the correct answer
<input type="radio"/>	Bradycardia and mydriasis	
<input type="radio"/>	Bradycardia and urinary retention	
<input type="radio"/>	Tachycardia and diarrhoea	
<input checked="" type="radio"/>	Tachycardia and lacrimation	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- ACh can stimulate postganglionic receptors to produce effects such as bradycardia and miosis.

Explanation

An acetylcholinesterase inhibitor or anticholinesterase is a chemical that inhibits the cholinesterase enzyme from breaking down acetylcholine (ACh), so increasing both the level and duration of action of the neurotransmitter acetylcholine.

ACh can stimulate postganglionic receptors to produce effects such as:

- Salivation
- Lacrimation
- Defecation
- Micturition
- Sweating
- Miosis
- Bradycardia, and
- Bronchospasm.

Muscarine produces these effects, and hence they are referred to as [muscarinic effects](#), and the postganglionic receptors are called muscarine receptors.

SLUD (Salivation, Lacrimation, Urination, Defecation - and emesis) is a syndrome of pathological effects indicative of massive discharge of the parasympathetic nervous system.

Unlikely to occur naturally, SLUD is usually encountered only in cases of drug overdose or exposure to nerve gases. Nerve gases irreversibly inhibit the enzyme acetylcholinesterase; this results in a chronically high level of acetylcholine at cholinergic synapses throughout the body, thus chronically stimulating acetylcholine receptors throughout the body.

The nurse bleeped you because an obese patient is feeling nauseated and is vomiting. He is also complaining of seeing green and yellow halos.

He has recently been treated with a standard intravenous bolus of digoxin for fast atrial fibrillation. His creatinine clearance is normal. Digoxin toxicity is suspected.

What do you think is the cause of his symptoms?

(Please select 1 option)

<input type="radio"/>	Decreased hepatic excretion
<input type="radio"/>	Decreased protein binding
<input type="radio"/>	Decreased renal clearance
<input type="radio"/>	Decreased volume of distribution
<input type="radio"/>	Increased half life

- | | | |
|----------------------------------|----------------------------------|----------------------------|
| <input type="radio"/> | Decreased hepatic excretion | |
| <input type="radio"/> | Decreased protein binding | |
| <input type="radio"/> | Decreased renal clearance | |
| <input type="radio"/> | Decreased volume of distribution | This is the correct answer |
| <input checked="" type="radio"/> | Increased half life | Incorrect answer selected |

Key Learning Points

Pharmacology

- Ideal body weight should be used, rather than total body weight, when calculating doses of digoxin.

Explanation

Digoxin is concentrated in tissues and therefore has a large apparent volume of distribution. Serum digoxin concentrations are not significantly altered by large changes in fat tissue weight so that its distribution space correlates best with lean (that is, ideal) body weight, not total body weight.

In this case a higher dose than necessary was given due to calculation on the patient total body weight, resulting in digoxin toxicity. In other words his distribution space had been overestimated. Ideal body weight should be used, rather than total body weight, when calculating doses.

Approximately 25% of digoxin in the plasma is bound to protein.

A 54-year-old electrician is reviewed in the rheumatology clinic. He has been managed for psoriasis and severe psoriatic arthritis on methotrexate for the past nine months, but his symptoms are failing to improve despite this, NSAIDs and intermittent courses of oral corticosteroids. A decision is made to commence adalimumab therapy.

Which of the following correctly reflects the MoA of this treatment?

(Please select 1 option)

<input type="radio"/>	Costimulation blockade
<input type="radio"/>	IL-1 inhibition
<input type="radio"/>	IL-6 inhibition
<input type="radio"/>	IL-21 inhibition
<input type="radio"/>	TNF alpha inhibitor

<input type="radio"/>	Costimulation blockade
<input type="radio"/>	IL-1 inhibition
<input type="radio"/>	IL-6 inhibition
<input type="radio"/>	IL-21 inhibition
<input checked="" type="radio"/>	TNF alpha inhibitor Correct

Key Learning Points

Pharmacology

- Adalimumab is a human monoclonal antibody that forms complexes with TNF- α , preventing the binding of TNF- α to its receptors.

Explanation

The answer is TNF alpha inhibitor. Adalimumab is a human monoclonal antibody that forms high affinity, stable complexes with both the soluble and transmembrane bioactive forms of human TNF- α , which prevents the binding of TNF- α to its receptors. It is used in the treatment of conditions such as rheumatoid arthritis and psoriasis / psoriatic arthritis, where TNF-alpha driven inflammation is known to play a major role. As with other agents acting via this pathway, screening for latent TB should be undertaken before therapy is initiated.

Costimulation blockade is the target for abatacept, a fusion protein consisting of CTLA-4 and the Fc portion of IgG, which binds to CD80 and CD86 and prevents T-cell activation. IL-1 and IL-6 inhibitors are both used the treatment of arthritis, examples include canakinumab and siltuximab. IL-21 is an inflammatory cytokine which is elevated in acute viral infection. The application of IL-21 antagonists in new onset Type 1 diabetes is currently being evaluated.

A 60-year-old man who has been prescribed lisinopril for hypertension presents with an irritating cough.

What is the mechanism responsible for ACE-induced cough?

(Please select 1 option)

☐ Angiotensin I accumulation

☐ Asthma

☐ Bradykinin accumulation

☐ Laryngeal irritation

☐ Renin accumulation

- | | | |
|----------------------------------|----------------------------|----------------------------|
| <input type="radio"/> | Angiotensin I accumulation | |
| <input type="radio"/> | Asthma | |
| <input type="radio"/> | Bradykinin accumulation | This is the correct answer |
| <input type="radio"/> | Laryngeal irritation | |
| <input checked="" type="radio"/> | Renin accumulation | Incorrect answer selected |

Key Learning Points

Pharmacology

- The enzyme ACE is also responsible for the metabolism of bradykinin in mast cells.

Explanation

The enzyme ACE is also responsible for the metabolism of bradykinin in mast cells.

The accumulation of this substance is responsible for the cough found in up to 30% of subjects taking ACE-inhibitors.

This phenomenon is not seen in subjects taking angiotensin receptor blockers such as losartan.

A young woman has acne and is taking oral medication. She develops polyarthritis and has raised liver enzyme tests.

Investigations show:

AST	95 U/L	(1-31)
ALT	170 U/L	(5-35)
Bilirubin	16 µmol/L	(1-22)
Antinuclear antibodies	Strongly positive at 1/20	
	Negative at 1/640	

Which of the following drugs is she most likely to have been prescribed?

(Please select 1 option)

<input type="radio"/>	Erythromycin
<input type="radio"/>	Isotretinoin
<input type="radio"/>	Minocycline
<input type="radio"/>	Oxytetracycline
<input type="radio"/>	Trimethoprim

Dr Assen

<input type="radio"/> Erythromycin	
<input type="radio"/> Isotretinoin	
<input checked="" type="radio"/> Minocycline	This is the correct answer
<input type="radio"/> Oxytetracycline	
<input checked="" type="radio"/> Trimethoprim	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Minocycline can account for polyarthritides and antinuclear antibody (ANA), due to its ability to cause drug-induced lupus erythematosus.

Explanation

All other drugs listed above can be used in the treatment of acne. All of these can cause hepatotoxicity, and therefore raised alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Minocycline is the only drug listed which can account for the polyarthritides and antinuclear antibody (ANA), due to its ability to cause drug-induced lupus erythematosus.

Classically, drug-induced lupus erythematosus is characterised by:

- Systemic disease with a lower incidence of nephritis
- Lack of cutaneous involvement and
- The presence of antihistone antibodies¹.

The most commonly associated drugs have historically been procainamide and hydralazine², although their use is now decreasing. Medications associated more recently include the anti-TNF alpha agents, statins and minocycline.

Minocycline is unusual in that it seems to be associated with the development of long term immunological memory, and therefore exacerbation of symptoms within 12-24 hours of rechallenge².

Minocycline has been well documented as a cause of drug-induced **systemic lupus erythematosus** (SLE). Characteristically, the erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) are both markedly elevated, the ANA is strongly positive and there is a hypergammaglobulinaemia.

Anti-dsDNA antibodies are usually negative; antihistone antibodies are positive in 95% of drug-induced lupus (but also 50-80% of idiopathic SLE).

A strongly positive ANA is a risk factor for developing drug-induced lupus, but a negative ANA would not exclude the diagnosis².

Drug-induced lupus is defined as a lupus-like syndrome temporally related to continuous drug exposure which resolves after discontinuation of the offending drug⁶.

There are several features which distinguish drug-induced lupus from idiopathic SLE:

- Males and females are equally affected in drug-induced lupus, whereas idiopathic SLE affects females nine times more frequently³.
- Caucasians are affected by drug-induced lupus more commonly than Afro-Caribbeans, whereas the inverse is true of idiopathic SLE.
- In addition, the age of onset is typically older in drug-induced lupus, but this depends on the age at drug exposure.
- Fever, arthralgia, serositis and ANA occur at least as frequently in drug-induced lupus as idiopathic SLE.
- Haematological, renal and central nervous system (CNS) involvement, and double-stranded DNA autoantibodies are rare³.

The pathogenesis of drug-induced lupus is unclear. Factors that influence drug metabolism, such as acetylator status, have been implicated. In addition, lupus-inducing drugs have been shown to generate a variety of cytotoxic products on exposure to MPO released from activated neutrophils².

The time taken for symptoms to resolve after stopping minocycline is highly variable, from a few days to two years³. Typically, no further treatment is required but there are situations where corticosteroids or disease modifying antirheumatic drugs (DMARDs) are required to aid resolution³.

A patient is prescribed warfarin for prophylaxis of DVT.

Which vitamin does warfarin antagonise?

(Please select 1 option)

<input type="radio"/>	A
<input type="radio"/>	B6
<input type="radio"/>	C
<input type="radio"/>	D
<input type="radio"/>	K

Please select 1 option

<input type="radio"/>	A
<input type="radio"/>	B6
<input type="radio"/>	C
<input type="radio"/>	D
<input checked="" type="radio"/>	K Correct

Key Learning Points

Pharmacology

- Warfarin antagonises vitamin K.

Explanation

Warfarin inhibits hepatic vitamin K epoxide reductase, which is an enzyme that converts vitamin K to its active form (hydroquinone).

This results in the impairment of the hepatic synthesis of vitamin K dependent clotting factors (II [prothrombin], VII, IX, and X).

A 25-year-old male presents after being bitten on the hand by a terrier. The wound appears deep and is associated with swelling.

After the wound is cleaned and he has received tetanus immunisation.

Which of the following antibiotic regimes would be most appropriate for this patient?

(Please select 1 option)

☐ Co-amoxiclav oral

☐ Doxycycline oral

☐ Flucloxacillin oral

☐ Penicillin G IM

☐ Trimethoprim oral

<input type="radio"/>	Co-amoxiclav oral	This is the correct answer
<input type="radio"/>	Doxycycline oral	
<input type="radio"/>	Flucloxacillin oral	
<input type="radio"/>	Penicillin G IM	
<input checked="" type="radio"/>	Trimethoprim oral	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- Co-amoxiclav is recommended as first-line treatment for all cat or human bites and other complicated animal bites.

Explanation

The use of prophylactic antibiotics in dog bites is controversial although evidence supports their use in deep wounds, bites to the hands, and signs of infection. Additionally, immune compromise should be considered as an indication together with involvement of deep structures such as joints or tendons or in the presence of prosthetic joints.

Co-amoxiclav is recommended as first-line treatment for all cat or human bites and other complicated animal bites. You should also note that the treatment of animal bites, particularly of the hand, may not be limited to antibiotics alone and you may need to seek the advice of a plastic surgeon about debridement or tendon repair.

A middle-aged lady presents with cervical and inguinal lymphadenopathy. She is also experiencing pins and needles in a glove and stocking distribution, and has gum hypertrophy. She has a previous history of epilepsy and is on regular medication.

Which of the following drugs is most likely to cause her symptoms?

(Please select 1 option)

- | | |
|-----------------------|------------------|
| <input type="radio"/> | Carbamazepine |
| <input type="radio"/> | Phenobarbitone |
| <input type="radio"/> | Phenytoin |
| <input type="radio"/> | Sodium valproate |
| <input type="radio"/> | Vigabatrin |

<input type="radio"/>	Carbamazepine
<input type="radio"/>	Phenobarbitone
<input type="radio"/>	Phenytoin This is the correct answer
<input checked="" type="radio"/>	Sodium valproate Incorrect answer selected
<input type="radio"/>	Vigabatrin

Key Learning Points

Pharmacology

- Recognised side effects of phenytoin include lymphadenopathy.

Explanation

Recognised side effects of phenytoin include

- Drowsiness
- Ataxia
- Confusion
- Blurred vision
- Dizziness
- Nystagmus
- Permanent cerebellar ataxia
- Peripheral neuropathy
- Rashes
- Gum hypertrophy
- Thickening of the facial features
- Lymphadenopathy
- Chorea
- Sleep disturbance.

Remarkable side effects of other anti-epileptic drugs are:

- Drowsiness
- Blurred vision
- Dizziness
- Leukopenia
- SIADH and rash (carbamazepine)
- Liver toxicity (sodium valproate)
- Severe rash (lamotrigine)
- Retinal damage (vigabatrin)
- Aplastic anaemia (felbamate)

You have a 23-year-old female patient who suffers from complex partial epilepsy.

When she comes to her clinic appointment she tells you she is worried because her fit frequency has increased and wants more medication. On examination you also notice that she has a significant fungal infection. Medication includes the oral contraceptive pill.

Which of the following agents is likely significantly to increase her risk of getting pregnant?

(Please select 1 option)

<input type="radio"/>	Fluconazole
<input type="radio"/>	Ketoconazole
<input type="radio"/>	Lamotrigine
<input type="radio"/>	Levetiracetam
<input type="radio"/>	Phenytoin

<input type="radio"/>	Fluconazole	
<input type="radio"/>	Ketoconazole	
<input type="radio"/>	Lamotrigine	
<input checked="" type="radio"/>	Levetiracetam	Incorrect answer selected
<input type="radio"/>	Phenytoin	This is the correct answer

Key Learning Points

Pharmacology

- Phenytoin is a potent enzyme inducer of the cytochrome P450 system; as such it reduces plasma levels of agents which undergo hepatic metabolism, including sex steroids given in the oral contraceptive pill.

Explanation

Phenytoin is a potent enzyme inducer of the cytochrome P450 system; as such it reduces plasma levels of agents which undergo hepatic metabolism, including sex steroids given in the oral contraceptive pill.

Fluconazole and ketoconazole are all inhibitors of the CYP450 system and would lead to increased levels of other agents.

Studies have shown a modest decrease in the plasma concentration of levonorgestrel when taking lamotrigine, but less effect on ovulation.

Levetiracetam does not alter the pharmacokinetics of the oral contraceptive.

A new drug is being studied to find the most appropriate dose in a dose response study.

Small doses of the drug lead to a linear increase in serum drug concentration.

At higher doses there is an exponential rise in serum drug concentration.

Which of the following best describes the pharmacokinetic properties of this new drug?

(Please select 1 option)

<input type="radio"/>	First order kinetics
<input type="radio"/>	First pass effect
<input type="radio"/>	Long plasma half life
<input type="radio"/>	Saturation kinetics
<input type="radio"/>	Zero order kinetics

<input type="radio"/>	First order kinetics	
<input type="radio"/>	First pass effect	
<input type="radio"/>	Long plasma half life	
<input checked="" type="radio"/>	Saturation kinetics	This is the correct answer
<input type="radio"/>	Zero order kinetics	Incorrect answer selected

Key Learning Points

Therapeutics

- Saturation kinetics describes drugs that initially have a linear response to small doses (first order kinetics) but then the serum concentration of the drug rises sharply (zero order kinetics) due to saturation.

Explanation

The description of the kinetics of this new drug show that with small doses there is a linear response (first order kinetics) to dosing but this becomes saturated and the serum concentration of the drug rises sharply (zero order kinetics).

Drugs following zero order kinetics continue to be metabolised at a steady rate, independent of the concentration of the substrate. The plot of metabolism against time is linear.

Drugs which have saturation kinetics initially follow a linear line, but then their metabolism slows down leading to a plateau of the line, for example due to enzyme depletion. Small doses in the drug then lead to large increases in plasma concentration.

This response is typical of drugs such as phenytoin (saturates liver metabolism).

Which of the following drugs interacts with cranberry juice?

(Please select 1 option)

<input type="radio"/>	Amiodarone
<input type="radio"/>	Digoxin
<input type="radio"/>	Propranolol
<input type="radio"/>	Simvastatin
<input type="radio"/>	Warfarin

Dr. Assen

Please select 1 option/

<input type="radio"/>	Amiodarone
<input type="radio"/>	Digoxin
<input type="radio"/>	Propranolol
<input type="radio"/>	Simvastatin
<input checked="" type="radio"/>	Warfarin Correct

Key Learning Points

Pharmacology

- Warfarin interacts with cranberry juice. Simvastatin interacts with grapefruit juice.

Explanation

Questions on this theme have appeared on previous examinations.

Warfarin interacts with cranberry juice. Simvastatin interacts with grapefruit juice.

Dr Assem

A 70-year-old man presented with increasing dyspnoea.

In his history he had suffered a myocardial infarction two years previously which had been complicated by ventricular arrhythmias.

At admission his oxygen saturations were 85% on air and a chest x ray revealed bilateral patchy infiltration of both lung fields with a cardiothoracic ratio of 20/30 cm.

Which of the following drugs that he has been prescribed is most likely to explain these findings?

(Please select 1 option)

<input type="radio"/>	Amiodarone
<input type="radio"/>	Aspirin
<input type="radio"/>	Atorvastatin
<input type="radio"/>	Furosemide
<input type="radio"/>	Ramipril

<input type="radio"/>	Amiodarone	This is the correct answer
<input type="radio"/>	Aspirin	
<input type="radio"/>	Atorvastatin	
<input type="radio"/>	Furosemide	
<input checked="" type="radio"/>	Ramipril	Incorrect answer selected

Key Learning Points

Pharmacology, Respiratory Medicine, Toxicology

- Desaturation with patchy infiltration on CXR suggests a diagnosis of amiodarone-induced lung disease.

Explanation

This patient has desaturation with patchy infiltration on CXR suggesting a diagnosis of amiodarone-induced lung disease.

Usually the presentation is insidious and the disorder associated with the cumulative dose.

Treatment depends on withdrawing amiodarone and initiation of steroid therapy.

Differential diagnosis is any lymphangitis/pneumonitis but high resolution CT can help by demonstration of radio-dense plaques, etc.

Which of the following statements regarding Antabuse (disulfiram) is/are correct?

(Please select 1 option)

<input type="radio"/>	Antabuse acts by promoting the metabolism of acetaldehyde	
<input type="radio"/>	Can be used in patients with a history of psychosis in order to limit alcohol excess	
<input type="radio"/>	Can be used to assist abstinence from alcohol in patients with heart disease	
<input type="radio"/>	Patients using alcohol based perfumes may develop serious reactions	This is the correct answer
<input checked="" type="radio"/>	Requires regular dose titration once initiated	Incorrect answer selected

Dr. Assen

- | | |
|----------------------------------|--|
| <input type="radio"/> | Antabuse acts by promoting the metabolism of acetaldehyde |
| <input type="radio"/> | Can be used in patients with a history of psychosis in order to limit alcohol excess |
| <input type="radio"/> | Can be used to assist abstinence from alcohol in patients with heart disease |
| <input checked="" type="radio"/> | Patients using alcohol based perfumes may develop serious reactions |
| <input type="radio"/> | Requires regular dose titration once initiated |

This is the correct answer

Incorrect answer selected

Key Learning Points

Pharmacology

- Patients prescribed Antabuse (disulfiram) should be warned of serious reactions if using alcohol based perfumes.

Explanation

Antabuse inhibits the breakdown of acetaldehyde, which is a major metabolite of alcohol.

It is the accumulation of acetaldehyde which causes the flushing, sweating, palpitations, nausea, and vomiting seen in patients taking Antabuse who imbibe alcohol.

These reactions may also occur with alcohol based products, for example, perfume.

Antabuse is contraindicated in cirrhosis and heart disease, and psychosis is a relative contraindication for its use.

A 27-year-old patient presented to his GP with persistent cough and weight loss. He had night sweats.

He was diagnosed with TB and referred to the respiratory clinic. He was started on treatment. His urine became orange in colour.

Which one of the following drugs causes this?

(Please select 1 option)

<input type="radio"/>	Ciprofloxacin
<input type="radio"/>	Ethambutol
<input type="radio"/>	Isoniazide
<input type="radio"/>	Pyrazinamide
<input type="radio"/>	Rifampicin

☐ Ciprofloxacin

☐ Ethambutol

☐ Isoniazide

☐ Pyrazinamide

☒ Rifampicin

Correct

Key Learning Points

Pharmacology

- Side effects of drugs for TB

Explanation

It is very important to be aware of side effects of drugs especially those for TB.

Patients should be warned about this. It can also be used to confirm compliance.

Orange staining occurs to contact lenses.

A 72-year-old man presents with painful lumps in his feet and is diagnosed with gout.

Following initial treatment with non-steroidal anti-inflammatory agents he is started on allopurinol.

How does allopurinol work?

(Please select 1 option)

- | | |
|-----------------------|---------------------------------------|
| <input type="radio"/> | Increases urinary uric acid excretion |
| <input type="radio"/> | Inhibits cyclooxygenase II |
| <input type="radio"/> | Inhibits macrophage tubular formation |
| <input type="radio"/> | Inhibits nitric oxide synthase |
| <input type="radio"/> | Inhibits xanthine oxidase |

- ☐ Increases urinary uric acid excretion
- ☐ Inhibits cyclooxygenase II
- ☐ Inhibits macrophage tubular formation
- ☐ Inhibits nitric oxide synthase
- ☒ Inhibits xanthine oxidase **Correct**

Key Learning Points

Pharmacology

- Allopurinol inhibits xanthine oxidase, the enzyme involved in the conversion of purines into uric acid.

Explanation

Allopurinol inhibits xanthine oxidase, the enzyme involved in the conversion of purines into uric acid.

Which term best describes the affinity of a drug for its receptor?

(Please select 1 option)

<input type="radio"/>	Efficacy
<input type="radio"/>	Intrinsic activity
<input type="radio"/>	Potency
<input type="radio"/>	Selectivity
<input type="radio"/>	Therapeutic effect

<input type="radio"/>	Efficacy	
<input type="radio"/>	Intrinsic activity	
<input type="radio"/>	Potency	This is the correct answer
<input type="radio"/>	Selectivity	
<input checked="" type="radio"/>	Therapeutic effect	Incorrect answer selected

Key Learning Points

Pharmacology

- Affinity and intrinsic activity are determinants of potency.

Explanation

Affinity is the measure of the net molecular attraction between a drug (or neurotransmitter or hormone) and its receptor.

The receptor's affinity for binding a drug determines the concentration of drug required to form a significant number of drug-receptor complexes.

Affinity and intrinsic activity are determinants of potency.

Efficacy contributes both to potency and to the maximum effect of the agonist. Efficacy is a measure of the efficiency of the drug-receptor complex in initiating the signal transduction process.

A 55-year-old lady has recently commenced on 20 mg of leflunomide daily for sero-negative rheumatoid arthritis.

At baseline, prior to commencing the drug, her AST was 22 U/L (1-31) and her ALT was 30U/L (5-35).

She attends for routine blood monitoring. Her FBC is normal but her liver function tests (LFTs) reveal:

AST	58 U/L	(1-31)
ALT	71 U/L	(5-35)
Alkaline phosphatase	100 U/L	(45-105)
Bilirubin	12 μ mol/L	(1-22)

What is the most appropriate management option for this patient?

(Please select 1 option)

<input type="radio"/>	Continue leflunomide and monitor LFTs in one month
<input type="radio"/>	Continue leflunomide and monitor LFTs in two weeks
<input type="radio"/>	Reduce the dose and recheck LFTs in one week
<input type="radio"/>	Stop leflunomide and commence washout procedure
<input type="radio"/>	Stop the leflunomide and repeat tests in two weeks

<input type="radio"/>	Continue leflunomide and monitor LFTs in one month	
<input checked="" type="radio"/>	Continue leflunomide and monitor LFTs in two weeks	
<input type="radio"/>	Reduce the dose and recheck LFTs in one week	This is the correct answer
<input type="radio"/>	Stop leflunomide and commence washout procedure	
<input type="radio"/>	Stop the leflunomide and repeat tests in two weeks	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- If aspartate aminotransferase (AST) or alanine aminotransferase (ALT) is between two and three times the upper limit of normal, and the leflunomide dose is more than 10 mg daily, the dose should be reduced to 10 mg and LFTs rechecked weekly until normalised.

Explanation

Leflunomide is associated with serious hepatotoxicity.

Increased aminotransferases are commonly seen in association with therapy occurring in 15-20% of cases (less than a twofold rise).

However, more serious elevation (greater than threefold) is seen in less than 5%.

Generally, most hepatic events occur within the first six months of use. It is recommended liver function tests (LFTs) be checked monthly for six months and, if stable, two monthly thereafter.

If aspartate aminotransferase (AST) or alanine aminotransferase (ALT) is between two and three times the upper limit of normal, and the leflunomide dose is more than 10 mg daily, the dose should be reduced to 10 mg and LFTs rechecked weekly until normalised. If the ALT and AST are returning to normal, the patient should be left on 10 mg per day. If the LFTs remain elevated, leflunomide should be stopped and discussed with the specialist team.

If the AST or ALT is more than three times the upper limit of normal, the LFTs should be rechecked within 72 hours. If they remain more than three times the reference range, leflunomide should be stopped and washout considered (cholestyramine and activated charcoal). It is important to note that the half life of leflunomide is usually two weeks (mean 1-4) therefore if a rapid response is required, washout should be considered.

Current UK guidance also recommends frequent monitoring for patients on leflunomide. Full blood count (FBC) should be checked monthly for six months and, if stable, two monthly thereafter.

White cell count less than 3.5, neutrophils less than 2 or platelets less than 150 should be discussed with the specialist team, and leflunomide withheld until this has taken place.

Monitoring should be continued at least monthly in the long term if leflunomide is co-prescribed with any other immunosuppressant or potentially hepatotoxic agent.

In addition, signs of leflunomide toxicity should be monitored. If the patient develops a rash or itch dose reduction should be considered, with or without the addition of antihistamines. If severe, leflunomide should be stopped and washout considered.

Hair loss, headaches and gastrointestinal upset may also warrant dose reduction or washout.

A blood pressure of greater than 140/90 mmHg should be treated as per NICE guidelines. If it remains elevated, stop leflunomide and consider washout.

Weight should be monitored, and a weight loss of greater than 10% should be identified. If no other cause can be found, consider dose reduction or washout.

If there is increasing shortness of breath, pneumonitis should be considered and leflunomide should be stopped.

Which of the following is not a cause of drug-induced hepatitis?

(Please select 1 option)

<input type="radio"/>	Amiodarone
<input type="radio"/>	Ethambutol
<input type="radio"/>	Isoniazid
<input type="radio"/>	Methyldopa
<input type="radio"/>	Pyrazinamide

Please select 1 option)

<input type="radio"/>	Amiodarone
<input checked="" type="radio"/>	Ethambutol This is the correct answer
<input type="radio"/>	Isoniazid
<input type="radio"/>	Methyldopa
<input checked="" type="radio"/>	Pyrazinamide Incorrect answer selected

Key Learning Points

Therapeutics

- Ethambutol can result in loss of visual acuity, colour blindness and restriction of visual fields.

Explanation

Side effects of ethambutol are largely confined to visual disturbances in the form of:

- Loss of acuity
- Colour blindness, and
- Restriction of visual fields.

It does not cause hepatitis and is renally excreted.

Some causes of drug-induced hepatitis include:

- Isoniazid
- Amiodarone
- Pyrazinamide, and
- Methyldopa.

Which of the following is true regarding poisoning/overdose?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Aspirin causes acidosis due to hypoventilation |
| <input type="radio"/> | Chlormethiazole causes hyperthermia and hypertension |
| <input type="radio"/> | Ethylene glycol causes a metabolic alkalosis and renal failure |
| <input type="radio"/> | Methanol causes a metabolic acidosis with an increased anion gap |
| <input type="radio"/> | Phenobarbitone causes a metabolic acidosis |

(Please select 1 option)

<input type="radio"/>	Aspirin causes acidosis due to hypoventilation	
<input type="radio"/>	Chlormethiazole causes hyperthermia and hypertension	
<input type="radio"/>	Ethylene glycol causes a metabolic alkalosis and renal failure	
<input type="radio"/>	Methanol causes a metabolic acidosis with an increased anion gap	This is the correct answer
<input checked="" type="radio"/>	Phenobarbitone causes a metabolic acidosis	Incorrect answer selected

Key Learning Points

Therapeutics, Toxicology

- Methanol ingestion causes a metabolic acidosis with an increased anion gap, secondary to formic acid production.

Explanation

Aspirin causes hyperventilation, which may result in a respiratory alkalosis; a massive overdose may cause a metabolic acidosis.

Phenobarbitone and chlormethiazole both suppress the central nervous system causing:

- Hypoventilation (and therefore a respiratory acidosis)
- Hypotension, and
- Hypothermia.

Ethylene glycol causes a metabolic acidosis.

Methanol is metabolised to formaldehyde and formic acid, resulting in a metabolic acidosis.

An 85-year-old woman presented with bilateral osteoarthritis of the knees. She had no history of previous gastrointestinal disease.

Which of the following is the most appropriate initial treatment for her?

(Please select 1 option)

<input type="radio"/>	Celecoxib
<input type="radio"/>	Dihydrocodeine
<input type="radio"/>	Naproxen
<input type="radio"/>	Paracetamol
<input type="radio"/>	Glucosamine

<input type="radio"/>	Celecoxib	
<input type="radio"/>	Dihydrocodeine	
<input type="radio"/>	Naproxen	
<input checked="" type="radio"/>	Paracetamol	This is the correct answer
<input type="radio"/>	Glucosamine	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Paracetamol and/or topical NSAIDs (for knee or hand OA) should be offered before considering oral NSAIDs. Rubefacients, intra-articular hyaluronan, electro-acupuncture and chondroitin and glucosamine products are not recommended.

Explanation

NICE guidelines recommend formulating individualised management plans for patients with osteoarthritis. Behavioural change, such as exercise, weight loss and suitable footwear should be encouraged. Comorbidities which compound the effect of **osteoarthritis** symptoms should be identified and their treatment optimised.

Paracetamol and/or topical NSAIDs (for knee or hand OA) should be offered before considering oral NSAIDs.

If symptoms are not controlled with the above strategies, oral NSAIDs or COX-2 inhibitors (but not etoricoxib) can be used. A proton pump inhibitor should be co-prescribed. The lowest effective dose should be prescribed for the shortest period possible. If the patient is already taking low-dose aspirin, an alternative analgesic should be considered.

Treatments which are not recommended include rubefacients, intra-articular hyaluronan, electro-acupuncture and chondroitin or glucosamine products.

Adjuvants which can be used include opioid analgesics, topical capsaicin and intra-articular corticosteroids. Application of heat or cold packs, or TENS, can be considered if other strategies are ineffective. Manipulation and stretching can be helpful, particularly for hip osteoarthritis. Bracing/joint supports can be used for patients with biomechanical joint pain or instability.

Patients should be referred for joint surgery if they have already been offered all of the core treatments or if they have refractory joint symptoms which have a substantial impact on their quality of life. If there is a clear history of mechanical locking, referral for arthroscopic lavage and debridement should be considered.

A 33-year-old woman with a history of alcoholism and self-neglect, presents with an episode of blood streaked vomiting. This is attributed to minor Mallory-Weiss tear.

She is admitted to hospital and given an intravenous infusion of 5% dextrose. Her serum potassium concentration is noted the following day to have fallen to 1.9 mmol/L (normal range 3.5-4.9, 3.9 on admission).

What is the likely mechanism for the fall in potassium concentration?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Cortisol release in response to stress increasing renal potassium loss |
| <input type="radio"/> | Decompensated liver failure causing aldosterone secretion |
| <input type="radio"/> | Intracellular re-uptake in response to re-feeding with glucose |
| <input type="radio"/> | Metabolic acidosis increasing renal potassium excretion |
| <input type="radio"/> | Potassium levels falling following gastric loss in vomiting |

Please select 1 option)

<input type="radio"/>	Cortisol release in response to stress increasing renal potassium loss	
<input type="radio"/>	Decompensated liver failure causing aldosterone secretion	
<input type="radio"/>	Intracellular re-uptake in response to re-feeding with glucose	This is the correct answer
<input type="radio"/>	Metabolic acidosis increasing renal potassium excretion	
<input checked="" type="radio"/>	Potassium levels falling following gastric loss in vomiting	Incorrect answer selected

Key Learning Points

Pharmacology

- Refeeding syndrome is a potentially fatal consequence of a glucose load in patients who have previously been malnourished. It results in fluid retention, hypokalaemia, hypomagnesaemia and hypophosphataemia.

Explanation

Refeeding syndrome is potentially fatal, and occurs when previously malnourished patients are given a carbohydrate load. When malnourished, the body uses endogenous fuel stores for energy and maintains serum electrolytes by redistribution from intracellular spaces. Exogenously administered glucose results in insulin release, and subsequent difficulty for the body in trying to convert to exogenous fuel sources. This results in rapid uptake of glucose, potassium, phosphate and magnesium into cells, with dramatic falls in the extracellular concentrations. Additionally, for reasons which are not well understood, the body begins to retain fluid resulting in expansion of the extracellular space.

As a result of these fluid and electrolyte changes, there is an increase in cardiac work which can precipitate acute heart failure. There is also an increase in the respiratory quotient, which can cause dyspnoea and tachypnoea and in extreme cases respiratory failure. Nausea and diarrhoea is also common due to gut intolerance.

None of the other options are causes of hypokalaemia in this setting.

Whilst hospitalised after a hip replacement, a patient with acute intermittent porphyria has a tonic clonic seizure. The seizure was thought to have been due to alcohol withdrawal. The patient required large amounts of analgesia.

Six days post-operatively she suffers a porphyric attack.

Which of the following drugs on her prescription is likely to have been responsible?

(Please select 1 option)

<input type="radio"/>	Aspirin
<input type="radio"/>	Augmentin
<input type="radio"/>	Oramorph
<input type="radio"/>	Paracetamol
<input type="radio"/>	Sodium valproate

(Please select 1 option)

<input type="radio"/>	Aspirin
<input type="radio"/>	Augmentin
<input type="radio"/>	Oramorph
<input checked="" type="radio"/>	Paracetamol Incorrect answer selected
<input type="radio"/>	Sodium valproate This is the correct answer

Key Learning Points

Pharmacology, Toxicology

- Porphyric attacks may be precipitated by drugs including phenobarbitone, sulphonylureas, and oestrogens.

Explanation

AIP is an autosomal dominant disease resulting from defects in production or activity of the enzyme porphobilinogen (PBG) deaminase. Attacks may be precipitated by fasting, and by many drugs, such as:

- phenobarbitone
- alcohol
- sulphonylureas, and
- oestrogens.

Amoxicillin and opiates are thought to be safe in porphyria.

A 16-year-old female is admitted with a severe paracetamol overdose. She is treated with IV N-acetylcysteine (NAC).

By replenishing which of the following compounds does N-acetylcysteine function as an antidote in paracetamol overdose?

(Please select 1 option)

<input type="radio"/>	Arginine
<input type="radio"/>	Cysteine
<input type="radio"/>	Cystine
<input type="radio"/>	Glutathione
<input type="radio"/>	Methionine

<input type="radio"/>	Arginine
<input type="radio"/>	Cysteine
<input type="radio"/>	Cystine
<input checked="" type="radio"/>	Glutathione Correct
<input type="radio"/>	Methionine

Key Learning Points

Pharmacology, Toxicology

- In therapeutic doses N-acetyl-p-benzoquinoneimine is detoxified by conjugation with glutathione in the liver, but once the protective intracellular glutathione stores are depleted hepatic and renal damage may ensue.

Explanation

Paracetamol is predominantly metabolised to glucuronide and sulphate conjugates, which are excreted in the urine.

Hepatotoxicity is related to the conversion of a small proportion of the ingested dose to N-acetyl-p-benzoquinoneimine.

In therapeutic doses N-acetyl-p-benzoquinoneimine is detoxified by conjugation with glutathione in the liver, but once the protective intracellular glutathione stores are depleted hepatic and renal damage may ensue.

NAC and methionine replenishes glutathione stores in the liver and may also act through its sulphhydryl (-SH) group as a direct reducing agent.

A 56-year-old female who is taking warfarin for atrial fibrillation and has had a stable INR of between 2.0-2.5 over the last one year is noted to have an INR on the last visit of 7.8 (<1.4).

Consumption of which of the following may be responsible for this?

(Please select 1 option)

<input type="radio"/>	Carrot juice
<input type="radio"/>	Cranberry juice
<input type="radio"/>	Oil of evening primrose
<input type="radio"/>	Orange juice
<input type="radio"/>	St John's wort

<input type="radio"/>	Carrot juice	
<input type="radio"/>	Cranberry juice	This is the correct answer
<input type="radio"/>	Oil of evening primrose	
<input type="radio"/>	Orange juice	
<input checked="" type="radio"/>	St John's wort	Incorrect answer selected

Key Learning Points

Pharmacology

- Cranberry juice has been recognised to be responsible for a deranged INR, it being postulated that it inhibits cytochrome p450.

Explanation

Cranberry juice has been recognised to be responsible for a deranged INR, it being postulated that it inhibits cytochrome p450.

St John's wort induces cytoP450 and therefore reduces INR.

A 17-year-old boy is diagnosed with asthma and comes to the clinic for review. He is currently managed with 100 mcg BD of inhaled beclomethasone and salbutamol PRN.

His mother wants to enrol him in a class teaching the Buteyko technique.

What would you advise about its success?

(Please select 1 option)

<input type="radio"/>	It is associated with improved FEV1
<input type="radio"/>	It is associated with improved FVC
<input type="radio"/>	It is associated with improved symptoms
<input type="radio"/>	It should not be recommended to adults who require inhaled steroids
<input type="radio"/>	Patients enrolled tend to use more short acting beta agonists

<input type="radio"/>	It is associated with improved FEV1	
<input type="radio"/>	It is associated with improved FVC	
<input type="radio"/>	It is associated with improved symptoms	This is the correct answer
<input type="radio"/>	It should not be recommended to adults who require inhaled steroids	
<input checked="" type="radio"/>	Patients enrolled tend to use more short acting beta agonists	Incorrect answer selected

Key Learning Points

Pharmacology

- The Buteyko technique controls chronic hyperventilation, as such patients perceive less symptoms of shortness of breath, and their use of short acting bronchodilators is reduced.

Explanation

The Buteyko technique controls chronic hyperventilation, as such patients perceive less symptoms of shortness of breath, and their use of short acting bronchodilators is reduced.

This does not however have any impact on lung function including FEV1 and FVC.

It may be particularly valuable in patients who complain of symptoms of shortness of breath significantly in excess of those expected when you review their lung function.

A 50-year-old man returns to your clinic three weeks after Botox treatment for horizontal forehead furrows. He now complains that his eyebrows are drooping (eyebrow ptosis).

What is the cause of his complaint?

(Please select 1 option)

- | | |
|-----------------------|--------------------------------|
| <input type="radio"/> | Increased forehead skin laxity |
| <input type="radio"/> | Paralysis of corrugators |
| <input type="radio"/> | Paralysis of frontalis |
| <input type="radio"/> | Paralysis of procerus |
| <input type="radio"/> | Paralysis of zygomaticus major |

Please select 1 option)

<input type="radio"/>	Increased forehead skin laxity	
<input type="radio"/>	Paralysis of corrugators	
<input type="radio"/>	Paralysis of frontalis	This is the correct answer
<input type="radio"/>	Paralysis of procerus	
<input checked="" type="radio"/>	Paralysis of zygomaticus major	Incorrect answer selected

Key Learning Points

Pharmacology

- Anatomy of muscle of facial expression. Pharmacology of Botox.

Explanation

Botox is a neurotoxin derived from the bacteria, *Clostridium botulinum*. It blocks neuromuscular transmission inhibition of acetylcholine release at the presynaptic membrane. The end result is that the muscle contraction is inhibited.

The action of Botox is not permanent because collateral axonal sprouting establishes new neuromuscular junctions, restoring muscle function.

Botox does not affect skin laxity, hence this answer option is wrong.

Corrugator and procerus are both muscles that depress the eyebrow, therefore paralysis of these muscles would cause the opposite to eyebrow ptosis, hence paralysis of corrugators and paralysis of procerus are wrong.

Zygomaticus major elevates and retracts the angle of mouth and does not affect the eyebrows, hence paralysis of zygomaticus major is wrong.

Frontalis is a quadrilateral muscle found on the forehead that elevates the eyebrows; hence paralysis of this muscle can lead to eyebrow ptosis.

A 42-year-old woman was taking an antibiotic for a urinary tract infection when she suffered a left Achilles tendon rupture whilst playing badminton. She is very fit, exercising and doing stretching work up to four times per week, and feels the antibiotic may have been responsible.

Which of the following antibiotics is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Cephalexin
<input type="radio"/>	Co-amoxiclav
<input type="radio"/>	Ofloxacin
<input type="radio"/>	Trimethoprim

<input type="radio"/>	Amoxicillin	
<input type="radio"/>	Cephalexin	
<input type="radio"/>	Co-amoxiclav	
<input type="radio"/>	Ofloxacin	This is the correct answer
<input checked="" type="radio"/>	Trimethoprim	Incorrect answer selected

Key Learning Points

Pharmacology

- The whole class of quinolone antibiotics is associated with case reports of tendon rupture.

Explanation

The whole class of quinolone antibiotics is associated with case reports of tendon rupture. This may in part be related to decreased cellular proliferation and tendon fibroblast turnover.

In animal models where quinolones are continued post tendon rupture, it is associated with delayed healing.

Juvenile toxicity models also show increased rates of tendon abnormalities, and for this reason use of quinolones is not recommended in children or in pregnancy.

A 21-year-old nurse comes to the clinic requesting contraception. She works shifts including nights, and so often wakes up at odd times of the day. She has recently married and may want to start a family during the next two years.

Her mother suffered a DVT three years ago, aged 50.

On further questioning she has some problems with libido and has heard that progesterone only based preparations may impact on this. On examination she looks well, her BMI is 21 kg/m^2 , and her BP is 100/70 mmHg.

Which of the following is likely to be the most appropriate medication for her?

(Please select 1 option)

<input type="radio"/>	Combined oral contraceptive pill
<input type="radio"/>	Diaphragm
<input type="radio"/>	Mirena coil
<input type="radio"/>	Progesterone implant
<input type="radio"/>	Progesterone only pill

<input type="radio"/>	Combined oral contraceptive pill	This is the correct answer
<input type="radio"/>	Diaphragm	
<input type="radio"/>	Mirena coil	
<input checked="" type="radio"/>	Progesterone implant	Incorrect answer selected
<input type="radio"/>	Progesterone only pill	

Key Learning Points

Pharmacology

- The combined oral contraceptive pill is a safe contraceptive choice, but embolic risks have to be considered.

Explanation

The fact that her mother was older than 45 when she had her DVT means this is less relevant when assessing this lady's VTE risk with the combined pill.

For the progesterone only pill, it must be taken within three hours of the time the pill was taken on the previous day; given she works shifts this is likely to have a significant impact and increase the chances of a missed pill.

The time window for a missed pill with respect to the combined pill is 12 hours.

Given that she may decide to start a family at any time, the progesterone implant or Mirena coil do not seem to be ideal options, and progesterone only preparations may be associated with a reduced libido.

The diaphragm has a higher failure rate and should definitely not be the first choice in this patient.

The primary action of the combined oral contraceptive pill is inhibition of ovulation, although there are also alterations to the cervical mucus and endometrium which may contribute to effectiveness.

In contrast the progesterone only pill does not necessarily affect ovulation and its primary mode of action is on cervical mucus and implantation.

Long acting progesterone preparations prevent proliferation of the endometrium, thicken cervical mucus and suppress ovulation in some women.

The major risk of the combined oral contraceptive pill is thromboembolic disease; with respect to long acting progesterone, the major concerns are around irregular menstrual bleeding and changes in libido.

A patient is prescribed ciprofloxacin 500 mg twice daily for the treatment of cystitis.

In which of the following conditions should ciprofloxacin be used with caution?

(Please select 1 option)

☐ Asthma

☐ Diabetes

☐ Epilepsy

☐ Glaucoma

☐ Heart failure

Dr. Assem

Please select 1 option

<input type="radio"/>	Asthma	
<input type="radio"/>	Diabetes	
<input type="radio"/>	Epilepsy	This is the correct answer
<input type="radio"/>	Glaucoma	
<input checked="" type="radio"/>	Heart failure	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- Quinolones should be used with caution in patients with a history of epilepsy or conditions that predispose to seizures.

Explanation

Quinolones should be used with caution in patients with a history of epilepsy or conditions that predispose to seizures, in glucose-6-phosphate dehydrogenase (G6PD) deficiency, myasthenia gravis (risk of exacerbation), and in children or adolescents.

The CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking non-steroidal anti-inflammatory drugs (NSAIDs) at the same time may also induce them.

It should also be noted that ciprofloxacin is contraindicated in pregnancy.

Dr. Assem

A 20-year-old man presented after ingesting a drug at a party. Investigations revealed a serum creatine kinase of 10,000 IU/L (NR 24-195).

Which one of the following drugs is most likely to have been responsible?

(Please select 1 option)

<input type="radio"/>	Cannabis
<input type="radio"/>	Diazepam
<input type="radio"/>	Ecstasy (MDMA)
<input type="radio"/>	Gamma hydroxybutyrate (GHB)
<input type="radio"/>	Ketamine

(Please select 1 option)

<input type="radio"/>	Cannabis
<input type="radio"/>	Diazepam
<input type="radio"/>	Ecstasy (MDMA) This is the correct answer
<input type="radio"/>	Gamma hydroxybutyrate (GHB)
<input checked="" type="radio"/>	Ketamine Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- An ecstasy toxic reaction includes agitation, tachycardia, hypertension, dilated pupils and sweating.

Explanation

Symptoms of an acute MDMA toxic reaction include:

- Agitation
- Tachycardia
- Hypertension
- Dilated pupils
- Trismus, and
- Sweating.

More severe cases may be characterised by:

- Hyperthermia
- Disseminated intravascular coagulation (DIC)
- Rhabdomyolysis, and
- Acute renal failure.

In more severe cases, elevated creatine kinase levels are often present, with levels as high as 555,000 IU/L being reported.

Neither GHB nor ketamine are associated with elevated CK levels.

Phencyclidine (PVP) is another drug which may cause an elevated CK in overdose.

A 32-year-old woman who has a history of Crohn's disease which is managed with a stable dose of azathioprine as her only medication comes to the clinic for review. She has not had a flare of her disease for more than 2 years, and is wishing to try for a baby. Her Crohn's is quiescent, with no significant abdominal pain, and bowel opening 2-3 times per day with normal motion. Clinical examination is unremarkable with a BMI of 23, and routine bloods including FBC and LFTs are normal.

Which of the following is the most appropriate course of action with respect to her medication?

(Please select 1 option)

<input type="radio"/>	Continue azathioprine
<input type="radio"/>	Stop azathioprine
<input type="radio"/>	Switch to infliximab
<input type="radio"/>	Switch to mesalazine
<input type="radio"/>	Switch to prednisolone

Please select 1 option

<input type="radio"/>	Continue azathioprine	This is the correct answer
<input type="radio"/>	Stop azathioprine	
<input type="radio"/>	Switch to infliximab	
<input type="radio"/>	Switch to mesalazine	
<input checked="" type="radio"/>	Switch to prednisolone	Incorrect answer selected

Key Learning Points

Pharmacology

- In women with stable inflammatory bowel disease on azathioprine, there is no reason to discontinue therapy.

Explanation

The answer is Continue azathioprine. Due to the difficulties of running trials which include pregnant women, there is no high-quality evidence that azathioprine is linked with congenital malformations when used in pregnancy. A small increase in atrial defects was seen in women who took the drug in pregnancy for inflammatory bowel disease versus controls with IBD alone in a retrospective case control study, but there were possible confounding factors. Low birth weight, miscarriage and premature delivery have been noted, but may be due to active disease rather than azathioprine. Current UK guidelines therefore state that azathioprine is considered to be low risk in pregnancy, and it is felt the benefit outweighs the risk as having active disease during pregnancy is likely to have a greater detrimental impact on foetal development. There is less evidence to support use of infliximab in pregnancy, but it is also considered to be low-risk, however as this lady has stable disease it is not indicated. Corticosteroids are considered safe in pregnancy, as the amounts crossing the placenta are low, but the effects on the mother should be considered and again it is not indicated here as the disease is stable. Mesalazine is thought to be a relatively safe option in pregnancy, although it may be associated with low birth weight and increased risk of pre-term delivery. As this lady's disease is stable on azathioprine, you would not risk a flare by changing her medication at this point.

A 72-year-old woman comes to the Emergency department complaining of nausea and vomiting. Apparently she saw the on-call GP a few days earlier and was prescribed clarithromycin for a respiratory tract infection.

Past medical history of note includes COPD for which she takes high dose Seretide, tiotropium and oral theophylline, ischaemic heart disease for which she takes ramipril, amlodipine and indapamide and chronic renal failure.

On examination her BP is 132/70 mmHg, and her pulse is 105 (atrial fibrillation). She has bibasal crackles consistent with mild LVF.

Investigations show:

Haemoglobin	114 g/L	(115-165)
White cell count	$7.0 \times 10^9/L$	(4-11)
Platelets	$197 \times 10^9/L$	(150-400)
Serum sodium	139 mmol/L	(135-146)
Serum potassium	4.0 mmol/L	(3.5-5)
Creatinine	145 $\mu\text{mol/L}$	(79-118)

Which of the following medications is likely to have resulted in her presentation?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Indapamide
<input type="radio"/>	Ramipril
<input type="radio"/>	Theophylline
<input type="radio"/>	Tiotropium

Please select 1 option

<input type="radio"/>	Amlodipine	
<input type="radio"/>	Indapamide	
<input type="radio"/>	Ramipril	
<input type="radio"/>	Theophylline	This is the correct answer
<input checked="" type="radio"/>	Tiotropium	Incorrect answer selected

Key Learning Points

Pharmacology

- Clarithromycin leads to a significant increase in the theophylline AUC, precipitating toxicity with atrial fibrillation, nausea and vomiting.

Explanation

This question illustrates the potential dangers of polypharmacy. She has been prescribed clarithromycin which leads to a significant increase in the theophylline AUC, precipitating toxicity with atrial fibrillation, nausea and vomiting.

In reality theophylline is a reasonably ineffective option in the treatment of COPD and in a patient with a history of ischaemic heart disease, risk of arrhythmias is increased.

Clarithromycin is a potent inhibitor of CYP3A4, and as such may interfere significantly with metabolism of a number of medications, including theophylline, simvastatin, and cyclosporine as the most important drug interactions.

The effect of warfarin and digoxin may also be potentiated by clarithromycin.

Reference:

Dr Assem

With respect to symptoms of withdrawal related to chronic alcohol use, which of the following statements is correct?

(Please select 1 option)

- ☐ Benzodiazepines are ineffective in the treatment of seizures secondary to alcohol withdrawal, due to cross tolerance with ethanol a type A gamma-aminobutyric acid receptor
- ☐ Carbamazepine is as effective as benzodiazepines in the acute treatment of the symptoms of alcohol withdrawal
- ☐ Phenytoin is an effective treatment for seizures related to alcohol withdrawal
- ☐ Withdrawal reflects enhanced neurotransmission in type A gamma-aminobutyric acid pathways
- ☐ Withdrawal reflects reduced neurotransmission in N-methyl-D-aspartate pathways

<input type="radio"/>	Benzodiazepines are ineffective in the treatment of seizures secondary to alcohol withdrawal, due to cross tolerance with ethanol a type A gamma-aminobutyric acid receptor
<input type="radio"/>	Carbamazepine is as effective as benzodiazepines in the acute treatment of the symptoms of alcohol withdrawal This is the correct answer
<input type="radio"/>	Phenytoin is an effective treatment for seizures related to alcohol withdrawal
<input checked="" type="radio"/>	Withdrawal reflects enhanced neurotransmission in type A gamma-aminobutyric acid pathways Incorrect answer selected
<input type="radio"/>	Withdrawal reflects reduced neurotransmission in N-methyl-D-aspartate pathways

Key Learning Points

Pharmacology, Psychiatry

- Carbamazepine has been shown to be as effective as oxazepam in treating alcohol withdrawal

Explanation

Carbamazepine at a starting dose of 800 mg per 24 hours has been shown to be as effective as oxazepam in the treatment of acute alcohol withdrawal.

Phenytoin is not effective in the treatment of alcohol withdrawal-related seizures.

Alcohol withdrawal reflects the damping of neurotransmission through type A gamma-aminobutyric pathways, and enhanced neurotransmission through N-methyl-D-aspartate pathways.

Further Reading:

You are asked to see a 42-year-old man who complains of a cough at night. He also tells you that he has wheeze when he has a cold, and he smokes 20 cigarettes per day. He works as a landscaper on a housing development.

On examination his BP is 152/91 mmHg, his pulse is 70 and his BMI is 21. There is no significant wheeze.

You assess him at intermediate risk of having a diagnosis of asthma.

According to BTS guidelines, which FEV1/FVC ratio triggers asthma therapy?

(Please select 1 option)

<input type="radio"/>	0.5
<input type="radio"/>	0.6
<input type="radio"/>	0.7
<input type="radio"/>	0.8
<input type="radio"/>	0.9

Please select 1 option

<input type="radio"/>	0.5
<input type="radio"/>	0.6
<input type="radio"/>	0.7 This is the correct answer
<input checked="" type="radio"/>	0.8 Incorrect answer selected
<input type="radio"/>	0.9

Key Learning Points

Pharmacology

- Where the FEV1/FVC is greater than 0.7, referral for specialist advice is recommended if significant chest disease is suspected.

Explanation

Features described by the BTS guidelines as increasing the likelihood of asthma include:

- worse symptoms at night and in the early morning
- nocturnal cough or wheeze
- symptoms after exercise
- allergen exposure
- beta blockers or
- aspirin.

A history of asthma or atopy in the family and wheeze on examination also increase the likelihood of an asthma diagnosis.

Prominent dizziness or tingling of the hands and feet associated with shortness of breath may be a pointer towards hyperventilation, and chronic cough without wheeze is also a pointer against a diagnosis of asthma.

Where the FEV1/FVC is greater than 0.7, referral for specialist advice is recommended if significant chest disease is suspected.

A 15-year-old girl was admitted eight hours after taking an overdose of diazepam 30 mg and methotrexate 400 mg which her mother had been prescribed for rheumatoid arthritis.

On examination her Glasgow coma score (GCS) was 14, respiratory rate is 14 and saturations 96% on air.

Which one of the following is the most appropriate action?

(Please select 1 option)

<input type="radio"/>	Treat with flumazenil
<input type="radio"/>	Perform immediate gastric lavage
<input type="radio"/>	Treat with activated charcoal
<input type="radio"/>	Treat with folinic acid
<input type="radio"/>	Urgent liver function tests

<input type="radio"/>	Treat with flumazenil	
<input type="radio"/>	Perform immediate gastric lavage	
<input type="radio"/>	Treat with activated charcoal	
<input type="radio"/>	Treat with folinic acid	This is the correct answer
<input checked="" type="radio"/>	Urgent liver function tests	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Methotrexate is a folic acid antagonist which can result in multi-organ failure in overdose. Folinic acid is the antidote and should be given intravenously as soon as possible, regardless of the liver function tests.

Explanation

Methotrexate is a folic acid antagonist which can result in multi-organ failure in overdose. Folinic acid is the antidote and should be given intravenously as soon as possible, regardless of the liver function tests.

It is too late to consider gastric lavage or activated charcoal.

Flumazenil is a benzodiazepine receptor antagonist which is usually only given for patients with depressed respiratory function in the context of a benzodiazepine overdose.

A 24-year-old female who has previously suffered with severe depression presents with secondary amenorrhoea.

She is found to have a prolactin of 645 mU/L (normal 50-350).

Which of the drugs which she takes may cause this?

(Please select 1 option)

<input type="radio"/>	Becotide
<input type="radio"/>	Montelukast
<input type="radio"/>	Omeprazole
<input type="radio"/>	Risperidone
<input type="radio"/>	Sertraline

<input type="radio"/>	Becotide
<input type="radio"/>	Montelukast
<input type="radio"/>	Omeprazole
<input checked="" type="radio"/>	Risperidone Correct
<input type="radio"/>	Sertraline

Key Learning Points

Pharmacology, Therapeutics

- Antipsychotic medications, in particular the typical antipsychotics and risperidone, are known to elevate prolactin levels.

Explanation

Antipsychotic medications, in particular the typical antipsychotics and risperidone, are known to elevate prolactin levels. This is due to their ability to block dopamine D2 receptors. By doing so they block dopamine's action on the pituitary. This reduces inhibition of prolactin secretion, thereby causing hyperprolactinaemia.

Symptoms of this include:

- amenorrhoea
- galactorrhoea
- infertility
- loss of libido, and
- erectile dysfunction.

Sertraline is not thought to exert dopamine antagonist effects and thus does not commonly result in hyperprolactinaemia, but some cases have been reported in the literature.

The other medications on her list have not been commonly associated with hyperprolactinaemia.

A 71-year-old man with a history of hypertension, type 2 diabetes and erectile dysfunction comes to the clinic for review complaining of blue vision.

He takes amlodipine and ramipril for hypertension, digoxin for atrial fibrillation, sitagliptin and metformin for diabetes, and sildenafil for erectile dysfunction.

Which of the following is most likely to be responsible for his blue vision?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Digoxin
<input type="radio"/>	Metformin
<input type="radio"/>	Sildenafil
<input type="radio"/>	Sitagliptin

<input type="radio"/>	Amlodipine
<input type="radio"/>	Digoxin
<input type="radio"/>	Metformin
<input checked="" type="radio"/>	Sildenafil Correct
<input type="radio"/>	Sitagliptin

Key Learning Points

Pharmacology

- Sildenafil is a PDE-5 inhibitor, but at high dose it inhibits the activity of PDE-6, which is essential for the functioning of retinal rods cells. Inhibition of the enzyme leads to patients reporting blue tinged vision, particularly in low light conditions.

Explanation

Digoxin is associated with yellow/green visual disturbance.

Sildenafil is a PDE-5 inhibitor, but at high dose it inhibits the activity of PDE-6, which is essential for the functioning of retinal rods cells. Inhibition of the enzyme leads to patients reporting blue tinged vision, particularly in low light conditions.

The condition may be improved by reducing the dose of sildenafil, but of course this may limit efficacy with respect to improving erectile dysfunction.

A 67-year-old man presents to the Emergency department with uncontrolled nausea and vomiting.

He has a long history of COPD for which he takes high dose Seretide and theophylline tablets and has recently been prescribed some antibiotics by his GP for an exacerbation.

On examination his BP is 142/72 mmHg, his pulse is 92 and regular. Auscultation of the chest reveals wheeze and coarse crackles.

Investigations show:

Haemoglobin	134 g/L	(135-177)
White cell count	$7.1 \times 10^9/L$	(4-11)
Platelets	$172 \times 10^9/L$	(150-400)
Sodium	137 mmol/L	(135-146)
Potassium	3.0 mmol/L	(3.5-5)
Creatinine	115 $\mu\text{mol/L}$	(79-118)

Which of the following antibiotics is he most likely to have been prescribed?

(Please select 1 option)

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Azithromycin
<input type="radio"/>	Cefuroxime
<input type="radio"/>	Clarithromycin
<input type="radio"/>	Doxycycline

<input type="radio"/>	Amoxicillin	
<input type="radio"/>	Azithromycin	
<input type="radio"/>	Cefuroxime	
<input type="radio"/>	Clarithromycin	This is the correct answer
<input checked="" type="radio"/>	Doxycycline	Incorrect answer selected

Key Learning Points

Pharmacology, Respiratory Medicine, Toxicology

- Clarithromycin is a potent 3A4 inhibitor.

Explanation

This patient is showing symptoms of theophylline toxicity, and the most likely cause of toxicity is co-prescription of a CYP3A4 inhibitor. Of the options listed, only clarithromycin is a potent 3A4 inhibitor. Azole antibiotics, amiodarone, fluoxetine and cimetidine are other examples.

Azithromycin is a macrolide but is not a significant inhibitor of 3A4. Whilst case reports exist of azithromycin precipitating drug accumulation it is much less likely to do so than clarithromycin or erythromycin.

Amoxicillin, doxycycline and cephalosporins should not lead to theophylline accumulation.

Dr. Assef

A 35-year-old man carrying a medical emergency card indicating a history of acute intermittent porphyria is brought to the Emergency department by the police. He has been violent with acute psychosis.

Which of the following sedatives is recommended for use in this circumstance?

(Please select 1 option)

<input type="radio"/>	Chloral hydrate
<input type="radio"/>	Chlorpromazine
<input type="radio"/>	Diazepam
<input type="radio"/>	Haloperidol
<input type="radio"/>	Phenobarbitone

<input type="radio"/>	Chloral hydrate	
<input checked="" type="radio"/>	Chlorpromazine	This is the correct answer
<input type="radio"/>	Diazepam	
<input type="radio"/>	Haloperidol	
<input checked="" type="radio"/>	Phenobarbitone	Incorrect answer selected

Key Learning Points

Pharmacology, Psychiatry, Therapeutics

- Prochlorperazine is first line in management of psychotic symptoms during acute attacks of acute intermittent porphyria.

Explanation

Diazepam, haloperidol and chlorpromazine are safe for use in patients with AIP. However, chlorpromazine is the one which is recommended for the management of the psychiatric symptoms and can also reduce nausea. Diazepam is usually used for the management of seizures in these patients rather than as a sedative.

Haloperidol is not recommended as a first line.

Phenobarbitone can precipitate attacks of AIP and is therefore contraindicated in these patients.

A 55-year-old woman, who has a history of atrial fibrillation and is receiving warfarin and digoxin, informs you that she has been feeling down of late and has been self medicating with St John's wort which she obtained from a health shop.

Which of the following interactions may be expected between St John's Wort and her current medication?

(Please select 1 option)

<input type="radio"/>	Digoxin concentrations are unlikely to be affected
<input type="radio"/>	INR is likely to be increased
<input type="radio"/>	INR is likely to be reduced
<input type="radio"/>	INR is likely to be unaffected
<input type="radio"/>	There is an increased risk of digoxin toxicity

- | | | |
|----------------------------------|--|----------------------------|
| <input type="radio"/> | Digoxin concentrations are unlikely to be affected | |
| <input type="radio"/> | INR is likely to be increased | |
| <input type="radio"/> | INR is likely to be reduced | This is the correct answer |
| <input type="radio"/> | INR is likely to be unaffected | |
| <input checked="" type="radio"/> | There is an increased risk of digoxin toxicity | Incorrect answer selected |

Key Learning Points

Pharmacology

- St John's wort is a liver enzyme inducer that may reduce the efficacy of warfarin and digoxin

Explanation

St John's wort is now commonly taken for depressive symptoms, yet it is a liver enzyme inducer and therefore has interactions with medications typically reducing the efficacy.

In this regard, St John's wort may reduce the efficacy of warfarin, requiring increased dose to maintain the INR and it may also reduce the efficacy of digoxin.

Miss L is a 25-year-old woman attending the general medical clinic.

For the last six months she has felt generally fatigued and has noticed abdominal bloating and occasional diarrhoea. She has multiple symptoms that have been troubling her for the last few years and her GP would like some advice on diagnosis and management.

She has also been troubled by large, painful mouth ulcers that can be so severe that she is unable to eat. She says that she has had mouth ulcers since she was a teenager and gets them at least once per week.

She complains of joint pains affecting her hands and knees, and reports one brief episode of swelling of the right knee that resolved after a week or so of painkillers.

Last year, she was seen urgently by the ophthalmologists when she developed an acutely red and painful left eye associated with blurred vision and photophobia. She cannot remember what the diagnosis was, but was treated with steroid drops and this has not bothered her since.

On further questioning, you find out that she has also been seen in the GUM clinic complaining of painful vulval ulceration. Swabs and blood samples were taken, but no diagnosis was reached. The symptoms have recurred twice since the first episode two years ago.

You read the referral letter from her GP who describes an episode of erythema nodosum last year. He also mentions that she was treated for a DVT following a trip to Cyprus when she was 17.

What is the likely unifying diagnosis?

(Please select 1 option)

<input type="radio"/>	Behçet's disease
<input type="radio"/>	Brucellosis
<input type="radio"/>	Crohn's disease
<input type="radio"/>	Fibromyalgia
<input type="radio"/>	Systemic lupus erythematosus

<input checked="" type="radio"/>	Behçet's disease	This is the correct answer
<input type="radio"/>	Brucellosis	
<input type="radio"/>	Crohn's disease	
<input type="radio"/>	Fibromyalgia	
<input checked="" type="radio"/>	Systemic lupus erythematosus	Incorrect answer selected

Key Learning Points

Pharmacology

- The combination of venous ulceration, iritis, mouth ulceration and arthritis is typical of Behçet's disease.

Explanation

The combination of venous ulceration, iritis, mouth ulceration and arthritis is typical of Behçet's disease.

Behçet's syndrome is a **systemic vasculitis** with an unknown aetiology, which affects small and large vessels (venous and arterial). More than 60% of patients are HLA-B51, and there is a increased prevalence in the Mediterranean countries. It is commonly associated with mucocutaneous manifestations (oro-genital ulceration, **erythema nodosum**), ocular disease, gastrointestinal involvement and neurological features. Venous thrombosis is a common complication, but arterial occlusion can also occur.

The International Study Group criteria for classification of Behçet's disease requires the presence of recurrent oral ulceration (minor aphthous, major aphthous or herpetiform ulceration observed by physician or patient, which have recurred at least three times in a 12 month period), and two of the following:

- Recurrent genital ulceration - aphthous ulceration or scarring, observed by physician or patient
- Eye lesions - anterior **uveitis**, posterior **uveitis**, or cells in vitreous on slit lamp examination, or retinal vasculitis observed by ophthalmologist
- Skin lesions - **erythema nodosum** observed by physician or patient, pseudofolliculitis or papulopustular lesions; or acneiform nodules observed by the physician in post-adolescent patients not on corticosteroid treatment
- Positive pathergy test - read by physician at 24-48 hours

Pathergy is the non-specific hyper-reactivity of the skin following minor trauma, and is specific to Behçet's disease. It involves intradermal injection of skin with a 20-gauge needle under sterile conditions. It is considered positive if an erythematous sterile papule develops within 48 hours.

Brucellosis is an infective condition which presents most commonly with fever and malaise. It does not fit with the above scenario.

This presentation is not typical of Crohn's disease - one would expect a history of diarrhoea, abdominal pain and/or PR bleeding.

Fibromyalgia presents with pain and tenderness in a number of muscles. Extra-articular features such as genital ulceration are not seen.

Whilst a number of the features described in this scenario could fit with **systemic lupus erythematosus** (SLE) and/or antiphospholipid syndrome the history of oral and genital ulceration is much more typical of Behçet's disease.

A 57-year-old man with a history of stable coronary artery disease comes to the clinic for review.

He suffered an inferior myocardial infarction some seven years earlier, but has been troubled with only relatively minor chest pain since this time.

He takes a number of medications for control of blood pressure, cholesterol and his angina. On examination his BP is 145/72 mmHg, pulse is 70 and regular. His chest is clear and there is no ankle swelling.

He tells you that he has been buying sildenafil over the internet for erectile dysfunction.

Which of the following medications would concern you most with respect to possible drug interaction?

(Please select 1 option)

☐ Atorvastatin

☐ Bisoprolol

☐ Indapamide

☐ Nicorandil

☐ Ramipril

Dr Assem

(Please select 1 option)

<input type="radio"/>	Atorvastatin
<input type="radio"/>	Bisoprolol
<input type="radio"/>	Indapamide
<input type="radio"/>	Nicorandil This is the correct answer
<input checked="" type="radio"/>	Ramipril Incorrect answer selected

Key Learning Points

Pharmacology

- Sildenafil leads to significant hypotension with nitrates and drugs such as nicorandil which act as nitrate donors. As such it is contraindicated for use with these agents.

Explanation

Sildenafil leads to significant hypotension with nitrates and drugs such as nicorandil which act as nitrate donors. As such it is contraindicated for use with these agents.

Atorvastatin, bisoprolol, indapamide and ramipril are all commonly prescribed in patients with erectile dysfunction and no significant interaction with PDE-5 inhibitors is recognised.

Alpha blockers may lead to hypotension in patients prescribed sildenafil and caution is therefore advised where co-prescription is considered.

Sildenafil is metabolised via the CYP3A4 pathway, as such caution is also advised when co-prescribing agents such as erythromycin and increased consumption of grapefruit juice.

A 24-year-old woman comes to the dermatology clinic for review. She has a number of medical problems including arthritis, epilepsy and mild hypertension, and is concerned about a rash that she has developed on both shins. Her current medication includes lamotrigine, indapamide, methotrexate, amlodipine, and the combined oral contraceptive pill. On examination her BP is 138/82, pulse is 80 and regular. There is a rash with raised red/purple erythematous lesions on both shins. Her BMI is 24.

Which of the following is the most likely cause of the rash on her shins?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Combined oral contraceptive pill
<input type="radio"/>	Indapamide
<input type="radio"/>	Lamotrigine
<input type="radio"/>	Methotrexate

<input type="radio"/>	Amlodipine
<input type="radio"/>	Combined oral contraceptive pill This is the correct answer
<input type="radio"/>	Indapamide
<input checked="" type="radio"/>	Lamotrigine Incorrect answer selected
<input type="radio"/>	Methotrexate

Key Learning Points

Pharmacology

- EN is reported in up to 10% of patients prescribed the combined oral contraceptive pill, but is much more rarely described in patients prescribed the progesterone only pill.

Explanation

The answer is Combined oral contraceptive pill. This patient has erythema nodosum (EN), of which the contraceptive pill and pregnancy are very well recognised causes. Other drugs described as being associated with erythema nodosum include sulphonamides, salicylates, other nonsteroidal anti-inflammatory drugs, bromides and iodides. The rash usually resolves on cessation of therapy. With combined oral contraceptive pill use EN is reported in 3-10% of women, however it's much rarer in women who use the progesterone only pill.

The other options listed are not usually associated with erythema nodosum. The most common non-pharmacological causes of erythema nodosum are sarcoid and tuberculosis.

A 30-year-old patient with learning difficulties is admitted as a medical emergency.

The patient complains of headache, anorexia and vomiting.

On examination she is febrile with a temperature of 38°C, pulse 110 bpm and is clinically jaundiced.

Investigations reveal:

Bilirubin	60 µmol/L	(1-22)
Albumin	28 g/L	(37-49)
AST	400 IU/L	(5-40)
Alkaline phosphatase	400 IU/L	(45-105)
Prothrombin time	35 seconds	(<14)

She was commenced on a new medication within the last three months.

Which do you suspect may be contributing to the presentation?

(Please select 1 option)

<input type="radio"/>	Cabergoline
<input type="radio"/>	Carbamazepine
<input type="radio"/>	Lamotrigine
<input type="radio"/>	Metformin
<input type="radio"/>	Sodium valproate

(Please select 1 option)

<input type="radio"/>	Cabergoline
<input type="radio"/>	Carbamazepine
<input type="radio"/>	Lamotrigine
<input type="radio"/>	Metformin
<input checked="" type="radio"/>	Sodium valproate Correct

Key Learning Points

Pharmacology, Toxicology

- Sodium valproate can occasionally have an idiosyncratic response leading to severe or even fatal hepatic toxicity.

Explanation

Sodium valproate can occasionally have an idiosyncratic response leading to severe or even fatal hepatic toxicity.

This is more common if the patient has a metabolic or degenerative disorder, organic brain disease or severe seizures associated with mental retardation. Usually this reaction occurs within the first three months of therapy.

Carbamazepine can be associated with jaundice occasionally, however the history of mental retardation and short history of drug use point to sodium valproate as the cause.

Lamotrigine can disrupt liver function tests (LFTs).

Metformin and cabergoline do not affect liver function however caution is advised when using these drugs in patients with hepatic disease.

A 90-year-old man with chronic leukaemia presents with gout which his general practitioner treats with allopurinol.

How does allopurinol prevent the accumulation of uric acid?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | By competing for its transporter to the kidney |
| <input type="radio"/> | By enhancing its solubility |
| <input type="radio"/> | By inhibiting purine breakdown and synthesis |
| <input type="radio"/> | By inhibiting pyrimidine synthesis |
| <input type="radio"/> | By inhibiting the inflammatory response it causes |

- | | | |
|----------------------------------|---|----------------------------|
| <input type="radio"/> | By competing for its transporter to the kidney | |
| <input type="radio"/> | By enhancing its solubility | |
| <input type="radio"/> | By inhibiting purine breakdown and synthesis | This is the correct answer |
| <input type="radio"/> | By inhibiting pyrimidine synthesis | |
| <input checked="" type="radio"/> | By inhibiting the inflammatory response it causes | Incorrect answer selected |

Key Learning Points

Pharmacology

- Allopurinol works by inhibiting purine breakdown and synthesis

Explanation

Allopurinol is an isomer of hypoxanthine and as such is a purine analogue. It acts by inhibiting xanthine oxidase thereby blocking the oxidation of hypoxanthine and xanthine. This reduces the production of uric acid.

In addition, the build up of hypoxanthine and xanthine results in their conversion to adenosine and guanosine. This causes feedback inhibition of amidophosphoribosyl transferase, which is the rate-limiting enzyme of purine biosynthesis.

Allopurinol therefore reduces both purine breakdown and synthesis.

A 24-year-old promising athlete is diagnosed with chronic fatigue syndrome.

Which of the following treatments is indicated?

(Please select 1 option)

☐ Graded exercise therapy

☐ Group therapy

☐ Prednisolone

☐ Seroxat

☐ Thyroxine

Graded exercise therapy	Click to see related content
Sleep therapy	
Prednisolone	
Deslormetoprednisolone	Click to see related content
Thyroxine	

Key Learning Points

Pharmacology: Prednisolone

- The majority of research evidence is for cognitive behavioural therapy (CBT) and/or graded exercise therapy and these should be offered to all people with mild or moderate CFS.

Explanation

NICE have published guidance on the diagnosis and management of Chronic Fatigue Syndrome (CFS), also known as Myalgic Encephalomyelitis (ME/CFS). To confirm a diagnosis of fatigue the following main features need to be present:

- It must be new or recent, persistent or recurrent and unexplained by other conditions.
- It should be characterised by post-exertional malaise.
- It should result in a substantial reduction in activity level.

Associated symptoms include:

- Hyperaemia or [hypotonia](#)
- Muscle or joint pain without inflammation
- Painful lymph nodes without lymphadenopathy
- Headaches
- Cognitive dysfunction.

Red flag symptoms which suggest another diagnosis include:

- Significant weight loss
- Inflammatory aetiology or connective tissue disease
- Localising or focal neurological signs.

The diagnosis of CFS is one of exclusion, and features must have been present for at least four months in an adult.

Clinicians should check:

- Full blood count (FBC)
- Urea and electrolytes (U&Es)
- Urinalysis
- Liver function tests (LFTs)
- Thyroid function
- Erythrocyte sedimentation rate (ESR)
- C reactive protein (CRP)
- Blood glucose
- Creatinine
- Gluten sensitivity calcium
- Chestswab smear, and
- Faecitin.

Initial treatment should focus on management of symptoms, and minimising their impact on daily activities. Patients must be encouraged to continue work and studies. Any therapy should be person-centred and should aim to improve the patient's capacity to manage their symptoms.

The majority of research evidence is for cognitive behavioural therapy (CBT) and/or graded exercise therapy and these should be offered to all people with mild or moderate CFS.

In addition, patients should be given tailored sleep management advice including how to introduce rest periods into their daily routine. Relaxation techniques should be offered for the management of pain, sleep problems, stress and anxiety.

There is no research evidence to support the experience of some patients with CFS that they are more intolerant of drug treatment. In addition, there is insufficient evidence to recommend the use of complementary therapies or vitamin supplementation.

The following drugs should not be used:

- Microsomal oxidase inhibitors
- Gluco-corticoids
- Mixed anaesthetics
- Chemoparasites
- Thyroxine
- Anticidals

Referral to specialist CFS care should be offered within six months of presentation to people with mild CFS, within three to four months for moderate CFS and immediately for severe CFS.

If chronic pain is a predominant feature, referral to a pain management clinic should be considered. Analgesia should be considered for patients with poor sleep or pain.

Patients should be advised that relapses and setbacks are to be expected.

A 34-year-old man with a known history of Crohn's disease was admitted to hospital with abdominal pain and features of perforation.

He underwent laparotomy and a perforation of the terminal ileum was found with free faecal fluid in the abdominal cavity. He was transferred to the intensive care unit (ITU).

Together with traditional antimicrobial and supportive ITU therapy, which of the following therapeutic measures is most likely to improve this patient's outcome?

(Please select 1 option)

<input type="radio"/>	High-dose intravenous corticosteroids
<input type="radio"/>	Low-dose intravenous corticosteroids
<input type="radio"/>	Recombinant anti-endotoxin antibody
<input type="radio"/>	Recombinant human antithrombin III
<input type="radio"/>	Recombinant human tissue-factor pathway inhibitor

(Please select 1 option)

<input type="radio"/>	High-dose intravenous corticosteroids	
<input type="radio"/>	Low-dose intravenous corticosteroids	This is the correct answer
<input type="radio"/>	Recombinant anti-endotoxin antibody	
<input checked="" type="radio"/>	Recombinant human antithrombin III	Incorrect answer selected
<input type="radio"/>	Recombinant human tissue-factor pathway inhibitor	

Key Learning Points

Pharmacology, Therapeutics

- Low dose corticosteroids have a role in the management of sepsis

Explanation

The use of corticosteroids in sepsis remains controversial.

Meta-analyses of all the trials of high-dose steroids (for example, methylprednisolone 1 g) have confirmed that there is either no benefit, or even that there is an adverse effect in septic patients. However, more recent randomised controlled trials have suggested that there is a benefit in sepsis when lower physiological doses of steroids are given.

The precise mechanism is not fully understood, although it is well known that septic patients have low levels of endogenous steroids.

The production of recombinant human anticoagulants has gathered pace in recent years and several products have been tested. There have been randomised clinical trials of recombinant human antithrombin III ([Kyber Sept trial](#)), activated protein C ([PROWESS trial](#)) and tissue-factor pathway inhibitor ([OPTIMIST trial](#)). Of these, only recombinant activated protein C has shown any significant survival benefit at 28 days. However, subsequent studies have failed to demonstrate a survival benefit, and have shown an increased bleeding risk. Activated protein C is therefore no longer recommended for the treatment of sepsis.

A 19-year-old Chinese man presents to the Emergency Department with a severe rash. He was reviewed in the neurology clinic seven days earlier where he was diagnosed with partial epilepsy and started on carbamazepine therapy. He has a fever and sore throat with severe mucocutaneous ulceration. There is a generalised skin rash affecting the torso, arms and legs which he says began as erythematous patches, but there are now many vesicles, a number of which appear to have been de-roofed to form ulcers.

Which of the following HLA types is he likely to have?

(Please select 1 option)

- | | |
|-----------------------|------------|
| <input type="radio"/> | HLA A 30 |
| <input type="radio"/> | HLA A 3101 |
| <input type="radio"/> | HLA B 1502 |
| <input type="radio"/> | HLA B 5701 |
| <input type="radio"/> | HLA B 5801 |

(Please select 1 option)

<input type="radio"/>	HLA A 30	
<input type="radio"/>	HLA A 3101	
<input checked="" type="radio"/>	HLA B 1502	This is the correct answer
<input type="radio"/>	HLA B 5701	
<input type="radio"/>	HLA B 5801	Incorrect answer selected

Key Learning Points

Pharmacology

- The HLA B 1502 subtype, most prevalent in Chinese and Thai individuals, is associated with the development of Stevens Johnson syndrome on commencement of carbamazepine.

Explanation

The answer is C, HLA B 1502. This man presents with Stevens Johnson syndrome (SJS), which is now well described in association with certain HLA types when carbamazepine is prescribed. HLA-B1502 has been shown to be a high-risk HLA type, and is present in about 10% of individuals of Han Chinese and Thai origin. Some guidelines therefore suggest HLA screening of this population prior to commencing carbamazepine treatment.

HLA A 3101 is the high risk HLA type for SJS in patients of Japanese and European origin. SJS in patients with A 3101 is generally less severe versus 1502, therefore screening isn't generally recommended. HLA A 30 is associated with a fixed drug eruption reaction in conjunction with co-trimoxazole prescribing, B5701 with hypersensitivity to abacavir and flucloxacillin liver hypersensitivity, and B 5801 is associated with hypersensitivity to allopurinol.

A 48-year-old female with rheumatoid arthritis has the following full blood count results:

Haemoglobin	114 g/L	(120-165)
Platelets	$470 \times 10^9/L$	(150-450)
White Cell Count	$9.0 \times 10^9/L$	(4-10)
MCV	102 fL	(83-95)

Which drug is she likely to be taking?

(Please select 1 option)

<input type="radio"/>	Ciclosporin
<input type="radio"/>	Hydroxychloroquine
<input type="radio"/>	Leflunomide
<input type="radio"/>	Methotrexate
<input type="radio"/>	Myocrisin

Dr Assem

<input type="radio"/>	Ciclosporin	
<input type="radio"/>	Hydroxychloroquine	
<input type="radio"/>	Leflunomide	
<input type="radio"/>	Methotrexate	This is the correct answer
<input checked="" type="radio"/>	Myocrisin	Incorrect answer selected

Key Learning Points

Rheumatology, Therapeutics

- Methotrexate may be associated with haematopoietic suppression

Explanation

Leflunomide is associated rarely with anaemia, thrombocytopaenia and eosinophilia. Ciclosporin may be associated with a mild anaemia. Methotrexate may be associated with haematopoietic suppression, leading to profound, and sometimes sudden leucopenia and thrombocytopaenia.

Myocrisin may also rarely lead to blood disorders, pancytopaenia and leucopenia. The elevated platelet count here probably relates to the rheumatoid arthritis itself as a late component of the acute phase response.

Macrocytosis is seen as a consequence of long term methotrexate therapy. Co-existent B12 or folate deficiency or thyroid disease should be excluded.

A 44-year-old immigrant from Romania presents to the emergency department with a headache, neck stiffness and gradually worsening confusion over the past few days.

You understand from his relative that he also has a chronic cough and has lost a significant amount of weight recently.

On examination he is pyrexial 37.8°C, his BP is 134/72 mmHg, pulse is 85 and regular. He has marked neck stiffness and photophobia.

Investigations show:

Haemoglobin	120 g/L	(135-177)
White cell count	$11.5 \times 10^9/L$	(4-11)
Platelets	$238 \times 10^9/L$	(150-400)
ESR	80 mm/hr	(<10)
Sodium	133 mmol/L	(135-146)
Potassium	4.2 mmol/L	(3.5-5)
Creatinine	94 $\mu\text{mol/L}$	(79-118)
CXR	fibrosis suspicious of tuberculosis	
Lumbar puncture	lymphocytic pleocytosis	
PCR	positive for tuberculosis	

Which of the following is the correct duration of four drug therapy?

(Please select 1 option)

<input type="radio"/>	1 month
<input type="radio"/>	2 months
<input type="radio"/>	6 months
<input type="radio"/>	10 months
<input type="radio"/>	18 months



1 month



2 months

This is the correct answer



6 months



10 months



18 months

Incorrect answer selected

Key Learning Points

Pharmacology

- TB meningitis requires 2 months of four-drug therapy and 10 months on two-drug therapy, to a total of 12 months.

Explanation

Whilst 12 months of therapy is recommended for the treatment of TB meningitis, it is still only an initial two months of four drug therapy which is needed. A glucocorticoid is usually added with a reducing dose schedule over two to three weeks.

All of the other options are incorrect because no matter what the location of infection, two months of four drug therapy is the standard, before reducing this to two drugs.

The exception is multi-drug resistant tuberculosis, where patients are commenced initially on five or more agents.

A 55-year-old man on treatment for hypertension, epilepsy and gastro-oesophageal reflux disease presented with an urticarial skin eruption. A drug reaction is suspected since he has recently started a new drug.

Which of the following medications is most likely to be responsible?

(Please select 1 option)

<input type="radio"/>	Aspirin
<input type="radio"/>	Atorvastatin
<input type="radio"/>	Omeprazole
<input type="radio"/>	Paracetamol
<input type="radio"/>	Sodium valproate

Dr. Assem



Aspirin

This is the correct answer



Atorvastatin



Omeprazole



Paracetamol



Sodium valproate

Incorrect answer selected

Key Learning Points

Pharmacology

- Patients with aspirin sensitivity can present with either mucosal reactions (the aspirin triad of nasal polyposis, sinusitis, and asthma) or cutaneous reactions (urticaria or anaphylaxis).

Explanation

Urticaria is one of the most common dermatologic problems seen by primary care physicians and often a source of frustration for patient and physician alike. Pinpointing the cause may be challenging--or impossible--because of the many and varied triggers.

Patients with aspirin sensitivity can present with either mucosal reactions (the aspirin triad of nasal polyposis, sinusitis, and asthma) or cutaneous reactions (urticaria or anaphylaxis).

A 60-year-old retired nurse with idiopathic Parkinson's disease presented with motor oscillations and on-off periods. She had received Co-Beneldopa for 5 years. Selegiline was added to her treatment.

Which one of the following enzymes does Selegiline act on to cause this adjuvant action?

(Please select 1 option)

<input type="radio"/>	Catechol-O-methyltransferase
<input type="radio"/>	Dopa decarboxylase
<input type="radio"/>	Dopamine hydroxylase
<input type="radio"/>	Monoamine oxidase
<input type="radio"/>	Tyrosine hydroxylase

<input type="radio"/>	Catechol-O-methyltransferase	
<input type="radio"/>	Dopa decarboxylase	
<input type="radio"/>	Dopamine hydroxylase	
<input type="radio"/>	Monoamine oxidase	This is the correct answer
<input checked="" type="radio"/>	Tyrosine hydroxylase	Incorrect answer selected

Key Learning Points

Pharmacology

- Selegiline is a MAO-B inhibitor.

Explanation

Selegiline is a MAO-B inhibitor.

A 21-year-old man who has a past history of IV drug abuse presents 12 hours after taking an overdose of 480 mg of codeine and 30 g of paracetamol.

His blood pressure is 100/60 mmHg and he has pin-point pupils.

What is the most appropriate management for this patient?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | 500ml 10% glucose IV over four hours |
| <input type="radio"/> | 1 litre normal saline IV over six hours |
| <input type="radio"/> | IV naloxone |
| <input type="radio"/> | IV flumazenil |
| <input type="radio"/> | Start N-acetylcysteine |

<input type="radio"/>	500ml 10% glucose IV over four hours
<input type="radio"/>	1 litre normal saline IV over six hours
<input type="radio"/>	IV naloxone
<input checked="" type="radio"/>	IV flumazenil Incorrect answer selected
<input type="radio"/>	Start N-acetylcysteine This is the correct answer

Key Learning Points

Pharmacology, Toxicology

- Trials of N-acetylcysteine suggest that the incidence of hepatotoxicity is 1% in those treated within eight hours as opposed to 46% in those treated after 16 hours.

Explanation

This patient presents 12 hours after taking a potentially fatally toxic dose of paracetamol.

In the circumstances provided in this question where there is an absence of data relating to pulse rate (as he is probably not in shock), respiratory rate (reflecting respiratory depression) or blood glucose, the most appropriate intervention at this 12 hour time-point would be N-acetylcysteine.

The urgency of treatment is underlined by the fact that the incidence of hepatotoxicity is worse if treatment is delayed.

Trials of N-acetylcysteine suggest that the incidence of hepatotoxicity is 1% in those treated within eight hours as opposed to 46% in those treated after 16 hours.

A 52-year-old accountant presents with a five hour history of confusion and agitation. He is known to have an alcohol problem but has avoided all alcohol for the last three days.

On examination, he is sweating, agitated, and disorientated. He claims to see things on the walls.

His temperature is 37.5°C, pulse 110 bpm regular and blood pressure is 152/74 mmHg. FBC and U&Es are both normal.

Investigations reveal:

Plasma glucose	4.6 mmol/L	(3.6-6)
----------------	------------	---------

Which of the following agents would be the most appropriate treatment for this man?

(Please select 1 option)

- | | |
|-----------------------|------------------|
| <input type="radio"/> | IV haloperidol |
| <input type="radio"/> | Oral lorazepam |
| <input type="radio"/> | IV phenobarbital |
| <input type="radio"/> | IV phenytoin |
| <input type="radio"/> | Oral diazepam |

<input type="radio"/>	IV haloperidol	
<input checked="" type="radio"/>	Oral lorazepam	This is the correct answer
<input type="radio"/>	IV phenobarbital	
<input type="radio"/>	IV phenytoin	
<input checked="" type="radio"/>	Oral diazepam	Incorrect answer selected

Key Learning Points

Pharmacology

- In people with delirium tremens, offer oral lorazepam as first-line treatment. If symptoms persist or oral medication is declined, offer parenteral lorazepam or haloperidol.

Explanation

This is a typical history of delirium tremens (DTs).

In the UK it is estimated 24% of adults drink in a hazardous way, which is highest in the North East, North West and Yorkshire and Humber. Approximately 20% of patients admitted to hospital for illnesses unrelated to alcohol are drinking at potentially hazardous levels, and it's therefore important to ask all patients about their alcohol use. An abrupt reduction in alcohol intake in a person who has been drinking excessively for a prolonged period of time, for example as occurs on admission to hospital, may result in the development of alcohol withdrawal.

Symptoms typically present about 8 hours after a significant fall in blood alcohol levels. The peak is on day two, and by day five the symptoms are significantly better. Minor withdrawal symptoms appear 6-12 hours after cessation of alcohol and include: insomnia, fatigue, tremor, anxiety, nausea, vomiting, headache, sweating, palpitations, anorexia, depression and craving. Alcoholic hallucinosis can appear 12-24 hours after stopping alcohol and includes visual, auditory and tactile hallucinations. Withdrawal seizures can appear 24-48 hours after cessation and are generalised tonic-clonic seizures. Alcohol withdrawal delirium (delirium tremens) can appear 48-72 hours after cessation.

This patient has delirium tremens, which should be treated as a medical emergency. The signs of altered mental status alert you to the fact that this is different from simple alcohol withdrawal. These signs can include hallucinations (auditory, visual, olfactory), confusion, delusions and severe agitation. Seizures can also occur. Delirium tremens is a hyperadrenergic state, and is often associated with tachycardia, hyperthermia, hypertension, tachypnoea, tremor and mydriasis. Patients at increased risk are those with a previous history of delirium tremens or alcohol withdrawal seizures, those with a co-existing infection or abnormal liver function, and older patients. It is a clinical diagnosis.

Delirium tremens should be treated with oral lorazepam as first-line treatment. If the symptoms persist, or the medication is refused, parenteral lorazepam, haloperidol or olanzapine should be given. Intensive care may be required.

If delirium tremens develops during treatment for acute withdrawal, the reducing regime should be reviewed.

The mortality rate can be up to 35% if untreated, which reduces to 5% with early recognition and treatment.

In patients with alcohol withdrawal seizures, a quick-acting benzodiazepine should be given (such as lorazepam). Phenytoin should not be given.

Patients who are at high-risk of alcohol withdrawal but have no or only mild symptoms are typically given a reducing dose of chlordiazepoxide (a long-acting benzodiazepine) over 5-7 days. Diazepam is an alternative. Chlormethiazole may also be offered as an alternative, but is rarely used as if used with alcohol there is a risk of fatal respiratory depression, especially in patients with liver cirrhosis.

In addition, you should not forget the importance of giving high-potency B vitamins, specifically thiamine (e.g. pabrinex) to all patients with a history of high alcohol intake to reduce the risk of Wernicke's encephalopathy.

A 60-year-old lady presented with heartburn. She is known to have osteoporosis and has been taking alendronate for a number of years.

Which of the following is the most likely cause of her symptoms?

(Please select 1 option)

<input type="radio"/>	Achalasia
<input type="radio"/>	Calcification of lower oesophageal sphincter
<input type="radio"/>	Crush fracture
<input type="radio"/>	Ischaemic heart disease
<input type="radio"/>	Oesophagitis

Dr. Assen

<input type="radio"/>	Achalasia	
<input type="radio"/>	Calcification of lower oesophageal sphincter	
<input type="radio"/>	Crush fracture	
<input checked="" type="radio"/>	Ischaemic heart disease	Incorrect answer selected
<input type="radio"/>	Oesophagitis	This is the correct answer

Key Learning Points

Pharmacology, Therapeutics

- GI side effects are common with bisphosphonates, with the most severe resulting in oesophagitis

Explanation

"Oral bisphosphonates seem to induce serious esophagitis in some patients, may result in gastritis and cause diarrhoea. When used as recommended, serious esophageal complications are few. Patients with known esophageal disease (e.g. achalasia, stricture, Barrett's esophagus, severe reflux and scleroderma) should avoid taking oral bisphosphonates."

Interestingly, when patients get GI side effects with bisphosphonates, treatment with PPIs is usually ineffective and the only way of alleviating is by stopping the bisphosphonate.

A 10-year-old child presents with a respiratory tract infection. You decide to treat him empirically with a broad spectrum antibiotic.

The child is taking no other medication, has no other co-morbidity factors and has no known detected allergies.

Which of the following antibiotics is contraindicated in this patient?

(Please select 1 option)

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Clarithromycin
<input type="radio"/>	Erythromycin
<input type="radio"/>	Flucloxacillin
<input type="radio"/>	Minocycline

Please select 1 option

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Clarithromycin
<input type="radio"/>	Erythromycin
<input type="radio"/>	Flucloxacillin
<input checked="" type="radio"/>	Minocycline Correct

Key Learning Points

Pharmacology, Respiratory Medicine

- Tetracyclines should not be given to children under the age of 12 or to pregnant or breastfeeding women.

Explanation

Tetracyclines can bind to calcium and deposit on growing bones and teeth. This may cause staining and occasionally dental hypoplasia.

Therefore, tetracyclines should not be given to children under the age of 12 or to pregnant or breastfeeding women.

However, doxycycline can be used (unlicensed) for the treatment of anthrax in children.

Dr Assem

A 35-year-old man is admitted following a serious attempt at paracetamol overdose.

Despite efforts to treat him he develops liver failure.

Which of the following is most likely with the ensuing liver failure?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | Better prognosis in older patients |
| <input type="radio"/> | Better prognosis in those with high alcohol consumption |
| <input type="radio"/> | Hypoglycaemia rarely happens within 12 hours of onset of encephalopathy |
| <input type="radio"/> | It is harmful to give N-acetylcysteine |
| <input type="radio"/> | Lactic acidosis is recognised complication |

(Please select 1 option)

<input type="radio"/>	Better prognosis in older patients
<input type="radio"/>	Better prognosis in those with high alcohol consumption
<input type="radio"/>	Hypoglycaemia rarely happens within 12 hours of onset of encephalopathy
<input type="radio"/>	It is harmful to give N-acetylcysteine
<input checked="" type="radio"/>	Lactic acidosis is recognised complication Correct

Key Learning Points

Toxicology

- After severe paracetamol overdose lactic acidosis is likely with the ensuing liver failure

Explanation

Use of intravenous N-acetylcysteine reduces morbidity and mortality in fulminant hepatic failure.

Severe hypoglycaemia affects 40% of patients with fulminant liver failure, which exacerbates encephalopathy.

It may develop rapidly and recur with sepsis.

Lactic acidosis is due to decreased hepatic lactate clearance, compounded by poor peripheral perfusion and increased lactate production.

The prognosis is poor in those with

- Blood PH less than 7.0
- Prolonged prothrombin time (more than 100s) and
- Serum creatinine more than 300 μM .

Mortality is greater if the patient is more than 40 years of age.

You would like to prescribe a selective serotonin reuptake inhibitor (SSRI) for a 14-year-old girl who has been diagnosed as being clinically depressed.

After much debate and intervention from various healthcare professionals, it was decided to prescribe her fluoxetine.

For which one of the following parameters should the patient be closely monitored, especially at the beginning of treatment?

(Please select 1 option)

<input type="radio"/>	Coldness of extremities
<input type="radio"/>	Hostility
<input type="radio"/>	Hyperglycaemia
<input type="radio"/>	Prothrombin time
<input type="radio"/>	Tachycardia

<input type="radio"/>	Coldness of extremities	
<input type="radio"/>	Hostility	This is the correct answer
<input type="radio"/>	Hyperglycaemia	
<input type="radio"/>	Prothrombin time	
<input checked="" type="radio"/>	Tachycardia	Incorrect answer selected

Key Learning Points

Pharmacology, Psychiatry

- The use of antidepressants has been linked with suicidal thoughts and behaviour. Where necessary patients should be monitored for suicidal behaviour, self harm or hostility, particularly at the beginning of treatment or when the dose is changed.

Explanation

Children and adolescents need to be monitored carefully. The use of antidepressants has been linked with suicidal thoughts and behaviour. Where necessary patients should be monitored for suicidal behaviour, self harm or hostility, particularly at the beginning of treatment or when the dose is changed.

The balance of risks and benefits for the treatment of depressive illness in individuals under the age of 18 years is considered unfavourable for citalopram, escitalopram, paroxetine and sertraline.

Clinical trials have failed to show efficacy and have shown an increase in harmful outcomes.

Only fluoxetine has shown to be effective in treating depressive illness in children, but careful monitoring for the above sign is required.

A 72-year-old female is diagnosed with giant cell arteritis and is treated with prednisolone 60 mg per day.

What is the most appropriate treatment for the prevention of steroid induced osteoporosis?

(Please select 1 option)

☐ Alendronic acid

☐ Calcium

☐ Raloxifene

☐ Tibolone

☐ Vitamin D

Please select 1 option

<input type="radio"/>	Alendronic acid	This is the correct answer
<input type="radio"/>	Calcium	
<input type="radio"/>	Raloxifene	
<input type="radio"/>	Tibolone	
<input checked="" type="radio"/>	Vitamin D	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Bisphosphonates are generally considered first line treatment for the prevention of steroid induced osteoporosis.

Explanation

Oral glucocorticoids are associated with significant increase in fracture risk, from doses as low as 5mg daily. Loss of bone-mineral density is greatest in the first few months of glucocorticoid therapy, but fracture risk declines rapidly after stopping. There is an increased risk of fracture over and above the effect of low bone mineral density.

Patients older than 65 years are considered at high risk of osteoporotic fractures as are those with a prior fragility fracture, and they should commence on bone-protective therapy at the time of starting glucocorticoid therapy. Measurement of bone density is not required before starting therapy. In patients younger than 65 years without risk factors, DEXA scan is recommended for assessment of fracture risk.

General measures to reduce bone loss include use of the lowest dose of glucocorticoids possible, and steroid-sparing agents. Dietary calcium should be increased and physical activity, with smoking and alcohol minimised. Daily intake 1,500 mg of calcium and 800U of vitamin D3 is recommended. Bone-protective therapy which can be used includes:

- alendronate
- alfacalcidol
- calcitonin
- calcitriol
- cyclic etidronate, and
- risedronate.

Bisphosphonates are generally considered first line. If unsuitable, then calcitriol or strontium ranelate may be considered.

Raloxifene is an selective oestrogen receptor modulator (SERM) that has oestrogenic actions and anti-oestrogenic actions on the uterus and breast. It can be used in the prevention of postmenopausal [osteoporosis](#) where bisphosphonates are not suitable, but not commonly in steroid-induced osteoporosis.

Tibolone is a form of hormone-replacement therapy which can be used in post-menopausal women. However, it should not be considered first-line therapy, and is only used where other therapies are contra-indicated, not tolerated, or there is a lack of response.

A 16-year-old female is admitted after taking an overdose of her mother's propranolol tablets approximately two hours ago.

On examination she is drowsy and has a pulse of 40 beats per minute with a blood pressure of 80/40 mmHg. She is treated with activated charcoal, IV fluids and IV atropine but her bradycardia and hypotension fail to respond.

Which of the following would be the most appropriate next stage in her management?

(Please select 1 option)



IV adrenaline



IV amiodarone



IV glucagon



IV phenytoin



Insertion of temporary pacemaker

- | | | |
|----------------------------------|----------------------------------|----------------------------|
| <input type="radio"/> | IV adrenaline | |
| <input type="radio"/> | IV amiodarone | |
| <input type="radio"/> | IV glucagon | This is the correct answer |
| <input type="radio"/> | IV phenytoin | |
| <input checked="" type="radio"/> | Insertion of temporary pacemaker | Incorrect answer selected |

Key Learning Points

Pharmacology, Toxicology

- In those in whom initial atropine is unsuccessful, IV glucagon is a recommended treatment for beta-blocker overdose,

Explanation

In those in whom initial atropine is unsuccessful, IV glucagon is a recommended treatment for beta blocker overdose, with some evidence indicating improvement in bradycardia and blood pressure.

A 58-year-old woman presents with early features of COPD. She is a heavy smoker and asks about drugs that may help her to stop smoking. In particular, she has heard about a drug that is now available called Champix (varenicline).

Varenicline is an agent used in the treatment of smokers to help them quit.

Which of the following best describes its mechanism of action?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | A tricyclic antidepressant with mostly noradrenergic properties |
| <input type="radio"/> | An α_2 -noradrenergic agonist that suppresses sympathetic activity |
| <input type="radio"/> | Is a nicotine replacement therapy |
| <input type="radio"/> | Is a partial agonist of the $\alpha_4\beta_2$ nicotinic receptor |
| <input type="radio"/> | Reduces uptake of dopamine, serotonin, and norepinephrine |

<input type="radio"/>	A tricyclic antidepressant with mostly noradrenergic properties	
<input type="radio"/>	An α_2 -noradrenergic agonist that suppresses sympathetic activity	
<input type="radio"/>	Is a nicotine replacement therapy	
<input type="radio"/>	Is a partial agonist of the $\alpha_4\beta_2$ nicotinic receptor	This is the correct answer
<input checked="" type="radio"/>	Reduces uptake of dopamine, serotonin, and norepinephrine	Incorrect answer selected

Key Learning Points

New Therapies, Pharmacology, Respiratory Medicine, Therapeutics

- Varenicline is a non-nicotine drug that is a partial agonist of the $\alpha_4\beta_2$ nicotinic receptor

Explanation

There are now many therapies that have been investigated for use in smoking cessation. Newer drugs are becoming available that have been specifically developed for smoking cessation. Varenicline is one of them.

Nicotine is a stimulant and releases dopamine in the brain that leads to addictive effects of smoking. Its effects can be replaced in other ways using nicotine replacement therapy and this reduces the addiction to cigarette smoking.

- Bupropion (Zyban) reduces the neuronal uptake of dopamine, serotonin, and norepinephrine.
- Clonidine, a second line agent in smoking cessation because of its side effects, is an α_2 -noradrenergic agonist that suppresses sympathetic activity.
- Nortriptyline is a tricyclic antidepressant with mostly noradrenergic properties and is an agent that appears to be effective.
- Varenicline is a non-nicotine drug that is a partial agonist of the $\alpha_4\beta_2$ nicotinic receptor.

Further Reading:

- Foulds J. The neurobiological basis for partial agonist treatment of nicotine dependence: varenicline. *Int J Clin Pract*.

A 17-year-old male presents to the Emergency Department after an overdose of alcohol and paracetamol.

He complained of abdominal discomfort and an intravenous infusion of N-Acetylcysteine was commenced. Fifteen minutes later he developed breathlessness, reported feeling flushed and developed a tachycardia.

What is the cause of this reaction?

(Please select 1 option)

<input type="radio"/>	A disulfiram-like (antabuse) reaction has occurred
<input type="radio"/>	The patient has developed pulmonary oedema
<input type="radio"/>	The patient has had a panic attack
<input type="radio"/>	The patient has received an overdose of N-Acetylcysteine
<input type="radio"/>	The patient has received N-Acetylcysteine previously

(Please select 1 option)

<input type="radio"/>	A disulfiram-like (antabuse) reaction has occurred
<input type="radio"/>	The patient has developed pulmonary oedema
<input type="radio"/>	The patient has had a panic attack
<input type="radio"/>	The patient has received an overdose of N-Acetylcysteine
<input checked="" type="radio"/>	The patient has received N-Acetylcysteine previously Correct

Key Learning Points

Pharmacology

- Dose-related adverse reactions are likely to be due to the patient having received the drug previously.

Explanation

This patient is having an acute hypersensitivity reaction the most common, dose independent adverse drug reaction. It is caused by previous exposure and being sensitised to the drug. The initial exposure induces the production of antibodies of Ig E class, subsequent exposure induces an immunological reaction - anaphylaxis. Some drugs can produce an similar pseudoallergic reaction on first exposure.

The majority of dose-related adverse reactions occur within the first hour of the initial infusion of acetylcysteine. The MHRA now recommends extending the time of the initial infusion from 15 minutes to 60 minutes in order to reduce the incidence of adverse reactions. Even if a patient has a history of a previous reaction to intravenous acetylcysteine, the benefits outweigh the risks and patient should receive treatment. Any 'hypersensitivity-like' reactions are more likely to be anaphylactoid in nature (i.e. not immunologically mediated) and therefore may not occur on repeated exposure.

Reference:

A 29-year-old man who is a keen amateur photographer with his own development studio presented to the Emergency department with confusion. His partner said he had been under a great deal of stress recently and she found him foolishly drinking a developer solution with a poison symbol on it. He is hypoxic and hypotensive.

The local poisons unit suggests a diagnosis of cyanide poisoning.

Which of the following would be the most appropriate treatment?

(Please select 1 option)

<input type="radio"/>	Desferrioxamine
<input type="radio"/>	Dicobalt EDTA
<input type="radio"/>	Gastric lavage with Fuller's earth
<input type="radio"/>	Haemodialysis
<input type="radio"/>	Penicillamine

<input type="radio"/>	Desferrioxamine	
<input type="radio"/>	Dicobalt EDTA	This is the correct answer
<input type="radio"/>	Gastric lavage with Fuller's earth	
<input type="radio"/>	Haemodialysis	
<input checked="" type="radio"/>	Penicillamine	Incorrect answer selected

Key Learning Points

Toxicology

- Kelocyanor (dicobalt EDTA), given by intravenous injection has been proven to be of use when administered to seriously ill victims of confirmed cyanide poisoning. It is itself toxic, however, and can kill if used wrongly.

Explanation

Potassium ferricyanide is used chiefly for blueprints in photography, for staining wood, in calico printing, and in electroplating.

Kelocyanor (dicobalt EDTA), given by intravenous injection has been proven to be of use when administered to seriously ill victims of confirmed cyanide poisoning. It is itself toxic, however, and can kill if used wrongly.

HSE knows of several cases of inappropriate use resulting in hospital treatment. Its administration is beyond the scope of first aid and a recommendation has been made in the past that a 'Kelocyanor kit' should be kept by users of cyanide and transported to hospital with the patient.

Unfortunately we are aware of cases where this has misled doctors to treat patients for cyanide poisoning when this diagnosis was not correct.

Reference:

Dr. Arshad

A 17-year-old woman presented six hours after taking 30 g of paracetamol.

Which of the following factors is most likely to predict an increased risk of hepatotoxicity from the paracetamol?

(Please select 1 option)

<input type="radio"/>	Anorexia nervosa
<input type="radio"/>	Consumption of 20 units of alcohol since taking the paracetamol
<input type="radio"/>	Gilbert's disease
<input type="radio"/>	Ingestion of amitriptyline with the paracetamol
<input type="radio"/>	Smoking 20 cigarettes per day

(Please select 1 option)

<input type="radio"/>	Anorexia nervosa	This is the correct answer
<input type="radio"/>	Consumption of 20 units of alcohol since taking the paracetamol	
<input type="radio"/>	Gilbert's disease	
<input type="radio"/>	Ingestion of amitriptyline with the paracetamol	
<input checked="" type="radio"/>	Smoking 20 cigarettes per day	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Malnourishment is an increased risk factor for hepatotoxicity from paracetamol overdose.

Explanation

The MHRA updated its guidelines on the treatment of paracetamol overdose in 2012. Previously, healthcare professionals were advised to assess for risk factors of hepatotoxicity and therefore were two lines on the treatment nomogram (one for patients with risk factors, and one for those without). A review found that the evidence base to support the use of risk factors was poor and inconsistent, and that many of the risk factors were imprecise and difficult to determine with sufficient certainty in clinical practice.

All patients with a timed plasma paracetamol level on or above a single treatment line joining points of 100 mg/L at 4 hours and 15 mg/L at 15 hours after ingestion should receive acetylcysteine based on the new treatment nomogram, regardless of risk factors for hepatotoxicity.

However, it is still important to know what the risk factors for hepatotoxicity are. These include:

- malnourished patients (anorexia nervosa/bulimia nervosa)
- patients taking enzyme inducing drugs (e.g. carbamazepine, phenytoin, rifampicin and St John's wort)
- patients with induced liver enzymes due to chronic ethanol abuse
- human immunodeficiency virus (HIV) positive patients.

It is true that tobacco smoking induces CYP1A2 (one of the P450 enzymes). However, it is not currently included in the list of high-risk situations.

Which of the following antiemetics functions as a cholinergic muscarinic antagonist?

(Please select 1 option)



Aprepitant



Domperidone



Hyoscine



Metoclopramide



Ondansetron

Dr. Assen

<input type="radio"/>	Aprepitant
<input type="radio"/>	Domperidone
<input type="radio"/>	Hyoscine This is the correct answer
<input checked="" type="radio"/>	Metoclopramide Incorrect answer selected
<input type="radio"/>	Ondansetron

Key Learning Points

Pharmacology

- Hyoscine acts as a competitive antagonist at muscarinic acetylcholine receptors.

Explanation

Scopolamine is named after the genus *Scopolia*.

The name 'hyoscine' is from the scientific name for henbane, *Hyoscyamus niger*.

It acts as a competitive antagonist at muscarinic acetylcholine receptors; it is thus classified as an anticholinergic or as an antimuscarinic drug.

A 67-year-old man is reviewed in oncology following surgery to remove a gastrointestinal stromal tumour (GIST). He had been losing weight over the past few months, suffering from night sweats, nausea, and early satiety, and an endoscopy had identified the tumour. A decision is made to commence adjuvant imatinib therapy.

Which of the following represents the mode of action of imatinib?

(Please select 1 option)

<input type="radio"/>	Alkylating agent
<input type="radio"/>	Nucleoside analogue
<input type="radio"/>	mTOR inhibitor
<input type="radio"/>	Serine threonine kinase inhibitor
<input type="radio"/>	Tyrosine kinase inhibitor

(Please select 1 option)

<input type="radio"/>	Alkylating agent
<input type="radio"/>	Nucleoside analogue
<input type="radio"/>	mTOR inhibitor
<input type="radio"/>	Serine threonine kinase inhibitor
<input checked="" type="radio"/>	Tyrosine kinase inhibitor Correct

Key Learning Points

Pharmacology

- Imatinib is a Bcr-Abl inhibitor originally developed for CML, but now has an extended role across a number of haematological malignancies, including gastric MALToma.

Explanation

The answer is Tyrosine kinase inhibitor. Imatinib is a small molecule protein-tyrosine kinase inhibitor that inhibits the activity of the Bcr-Abl tyrosine kinase (TK), as well as the KIT and PDGFR receptors. It was primarily developed for the treatment of chronic myeloid leukaemia, although now it has also proved useful in the treatment of a range of other myeloproliferative disorders including gastrointestinal stromal tumours. Studies suggest that in high risk patients it may reduce rate of recurrence after surgery.

Examples of alkylating agents include chlorambucil and cyclophosphamide, used as part of conventional chemotherapy regimens but not classically in the treatment of GISTs. Nucleoside analogues interfere with DNA replication and are primarily used as anti-virals including in the treatment of HIV, [Hepatitis B](#) and C. mTOR inhibitors are also used in the treatment of cancer, an example is everolimus, which is most commonly used in combination with exemestane for the treatment of metastatic breast cancer. A number of serine threonine kinase inhibitors are currently in development for the treatment of various malignancies.

A 68-year-old lady with mitral valve disease and atrial fibrillation is taking warfarin. Lately her INR has fallen and the dose of warfarin has had to be increased.

Which of the following new treatments may account for this change?

(Please select 1 option)

<input type="radio"/>	Allopurinol
<input type="radio"/>	Amiodarone
<input type="radio"/>	Clarithromycin
<input type="radio"/>	Sertraline
<input type="radio"/>	St John's wort

<input type="radio"/>	Allopurinol
<input type="radio"/>	Amiodarone
<input type="radio"/>	Clarithromycin
<input type="radio"/>	Sertraline
<input checked="" type="radio"/>	St John's wort Correct

Key Learning Points

Pharmacology

- St John's wort is an enzyme inducer and therefore can increase the metabolism of, for example, warfarin, and make it less effective

Explanation

Drugs that are metabolised in the liver can induce hepatic microsomal enzymes. Induction of enzymes by one drug can gradually increase the rate of metabolism of another, resulting in lower plasma concentrations and a reduced effect.

St John's wort is an enzyme inducer and therefore can increase the metabolism of warfarin and make it less effective. All the other options enhance the effect of warfarin.

Allopurinol can interact with warfarin to enhance the anticoagulant effect of warfarin.

Amiodarone inhibits metabolism of coumarins (enhanced anticoagulant effect).

Clarithromycin enhances anticoagulant effect of coumarins. This is because warfarin is metabolised by the same CYP3A isozyme as clarithromycin. Clarithromycin, known to inhibit CYP3A, and a drug primarily metabolised by CYP3A may be associated with elevations in drug concentrations that could increase or prolong both therapeutic and adverse effects of the concomitant drug.

Sertraline may interact with warfarin to enhance the anticoagulant effect.

A 17-year-old boy is admitted with a severe paracetamol overdose following an argument with his girlfriend.

He is treated with intravenous N-acetylcysteine.

Paracetamol is normally metabolised to harmless compounds except in overdose.

Which of the following compounds is the toxic metabolite that accumulates during paracetamol overdose and is reduced by treatment with N-acetylcysteine?

(Please select 1 option)

<input type="radio"/>	Glucuronide
<input type="radio"/>	Homocysteine
<input type="radio"/>	Methionine
<input type="radio"/>	N-acetyl-p-benzoquinoneimine
<input type="radio"/>	N-hydroxyacetaminophen

<input type="radio"/>	Glucuronide	
<input type="radio"/>	Homocysteine	
<input type="radio"/>	Methionine	
<input checked="" type="radio"/>	N-acetyl-p-benzoquinoneimine	This is the correct answer
<input type="radio"/>	N-hydroxyacetaminophen	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Paracetamol is predominantly metabolised to glucuronide and sulphate conjugates which are excreted in the urine.

Explanation

Paracetamol is predominantly metabolised to glucuronide and sulphate conjugates which are excreted in the urine.

Routledge et al. state¹:

"hepatotoxicity is related to the conversion of a small proportion of the ingested dose to N-acetyl-p-benzoquinoneimine. In therapeutic doses N-acetyl-p-benzoquinoneimine is detoxified by conjugation with glutathione in the liver, but once the protective intracellular glutathione stores are depleted hepatic and renal damage may ensue."

NAC and methionine replenish glutathione stores in the liver and may also act through its sulphhydryl (-SH) group as a direct reducing agent.

A 45-year-old male takes lithium for a bipolar affective disorder.

Which of the following drugs would be contraindicated in conjunction with lithium?

(Please select 1 option)

- | | |
|-----------------------|---------------------|
| <input type="radio"/> | Atenolol |
| <input type="radio"/> | Bendroflumethiazide |
| <input type="radio"/> | Codeine phosphate |
| <input type="radio"/> | Flucloxacillin |
| <input type="radio"/> | Thyroxine |

<input type="radio"/>	Atenolol
<input type="radio"/>	Bendroflumethiazide This is the correct answer
<input type="radio"/>	Codeine phosphate
<input checked="" type="radio"/>	Flucloxacillin Incorrect answer selected
<input type="radio"/>	Thyroxine

Key Learning Points

Pharmacology

- Caution should be exercised when taking lithium and diuretics as the latter may reduce renal clearance of lithium and increase serum lithium concentrations.

Explanation

Caution should be exercised when taking lithium and diuretics as the latter may reduce renal clearance of lithium and increase serum lithium concentrations.

Non-steroidal anti-inflammatory drugs (NSAIDs) also increase lithium concentrations.

Metronidazole, angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers also increase serum lithium concentrations.

A 62-year-old female presents with deteriorating arthralgia associated with longstanding rheumatoid arthritis. She was prescribed celecoxib in place of naproxen.

Which of the following concerning celecoxib is correct?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Anti-inflammatory effects of celecoxib are superior to those of naproxen |
| <input type="radio"/> | Celecoxib acts by inhibiting a different enzyme than naproxen |
| <input type="radio"/> | Celecoxib has a lower level of anti-platelet activity than naproxen |
| <input type="radio"/> | Celecoxib is associated with reduced hepatotoxicity compared with naproxen |
| <input type="radio"/> | Co-treatment with diuretic can be given more safely than with naproxen |

(Please select 1 option)

<input type="radio"/>	Anti-inflammatory effects of celecoxib are superior to those of naproxen	
<input type="radio"/>	Celecoxib acts by inhibiting a different enzyme than naproxen	
<input type="radio"/>	Celecoxib has a lower level of anti-platelet activity than naproxen	This is the correct answer
<input type="radio"/>	Celecoxib is associated with reduced hepatotoxicity compared with naproxen	
<input checked="" type="radio"/>	Co-treatment with diuretic can be given more safely than with naproxen	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Celecoxib has a lower level of anti-platelet activity than naproxen.

Explanation

Celecoxib is a selective cyclo-oxygenase(COX)-2 inhibitor differing from the other non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen which affects both COX-1 and COX-2.

COX-1 is involved in platelet aggregation and inhibition of this by the NSAIDs produces its beneficial cardiovascular effects. However platelet aggregation is not affected by COX-2.

Naproxen and celecoxib have been shown to be as effective at reducing inflammation. One of the benefits of celecoxib is its reduced incidence of upper gastrointestinal side effects.

As with the non-specific NSAIDs, hepatotoxicity may occur with the COX-2 specific inhibitors resulting in cholestatic, hepatocellular or mixed liver injury. Rates seem to be comparable between the traditional NSAIDs and the COX-2 selective inhibitors.

Co-administration of diuretics and COX-2 inhibitors should be avoided if possible, as COX-2 inhibitors may reduce the antihypertensive and diuretic effects of diuretics. This may be due to impaired prostaglandin synthesis, which results in salt and water retention. In addition, COX-2 inhibitors have nephrotoxic effects which can be exacerbated by diuretics.

Rofecoxib (Vioxx) has been withdrawn due to its increased cardiovascular events compared with naproxen. The cardiovascular effects of the COX-2 inhibitors remains under study, and care should be taken before prescribing them to patients with a past medical history of significant cardiovascular disease.

You are investigating a new anti-platelet agent which may have additional effects on top of clopidogrel. To investigate the effects of the new therapy you need to be aware of the mode of action of clopidogrel.

Which of the following best describes the action of clopidogrel?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | 5HT-2 receptor inhibition |
| <input type="radio"/> | Cox-1 inhibition |
| <input type="radio"/> | Cox-2 inhibition |
| <input type="radio"/> | Glycoprotein IIb IIIa inhibition |
| <input type="radio"/> | Inhibition of the platelet ADP receptor |

<input type="radio"/>	5HT-2 receptor inhibition
<input type="radio"/>	Cox-1 inhibition
<input type="radio"/>	Cox-2 inhibition
<input type="radio"/>	Glycoprotein IIb IIIa inhibition
<input checked="" type="radio"/>	Inhibition of the platelet ADP receptor Correct

Key Learning Points

Pharmacology

- Clopidogrel inhibits the platelet ADP receptor, which leads to decreased propensity to platelet aggregation.

Explanation

Clopidogrel inhibits the platelet ADP receptor, which leads to decreased propensity to platelet aggregation and is complementary to cyclo-oxygenase inhibition, which is the action of aspirin.

Aspirin is weakly selective for the COX-1 enzyme. Specific COX-2 inhibitors were developed, e.g. rofecoxib, as analgesics and were thought to be associated with reduced risk of peptic ulceration but post-marketing data suggested they were increased with a significantly increased risk of heart attack or stroke and so many have been withdrawn from the market.

5HT-2 receptor inhibition also reduces platelet aggregation; one example is sarpogrelate developed primarily as an alternative to aspirin because of its lower risk of haemorrhage.

Glycoprotein IIb IIIa inhibitors are used in patients with unstable angina/NSTEMI, an example being abciximab.

A 23-year-old man with known peanut allergy presented to the Emergency department with anaphylaxis. He has a swollen face and lips.

His BP is 90/60 mmHg, pulse 110 bpm and he is wheezy.

Which of the following formulations of adrenaline should be given?

(Please select 1 option)

<input type="radio"/>	0.5 ml of 1:10000 adrenaline IM
<input type="radio"/>	0.5 ml of 1:1000 adrenaline IM
<input type="radio"/>	5 ml of 1:1000 adrenaline IM
<input type="radio"/>	10 ml of 1:10000 adrenaline IV
<input type="radio"/>	Nebulised adrenaline

<input type="radio"/>	0.5 ml of 1:10000 adrenaline IM	
<input type="radio"/>	0.5 ml of 1:1000 adrenaline IM	This is the correct answer
<input type="radio"/>	5 ml of 1:1000 adrenaline IM	
<input checked="" type="radio"/>	10 ml of 1:10000 adrenaline IV	Incorrect answer selected
<input type="radio"/>	Nebulised adrenaline	

Key Learning Points

Pharmacology, Toxicology

- 0.5mL adrenaline 1:1000 solution should be administered intramuscularly in anaphylaxis. Another 0.5mL can be given after 5 minutes in the absence of clinical improvement.

Explanation

For adults, a dose of 0.5 mL adrenaline 1:1000 solution (500 micrograms) should be administered intramuscularly, and repeated after about five minutes in the absence of clinical improvement or if deterioration occurs after the initial treatment especially if consciousness becomes - or remains - impaired as a result of hypotension.

The intramuscular (IM) route for adrenaline is the route of choice for most healthcare providers. There is a much greater risk of causing harmful side effects by inappropriate dosage or misdiagnosis of anaphylaxis when using IV adrenaline.

Adult EpiPen which allergy sufferers can carry with them contains 0.3 mg or 0.15 mg adrenaline in a 1:1000 dilution for intramuscular (IM) injection.

A 23-year-old woman presents to the Emergency department with low grade fever and dysuria. Her only medication is the oral contraceptive pill.

On examination her temperature is 37.8°C, and she has suprapubic and left loin tenderness consistent with a urine infection and possible pyelonephritis.

Investigations show:

Haemoglobin	125 g/L	(115-165)
White cell count	$12.8 \times 10^9/L$	(4-11)
Platelets	$209 \times 10^9/L$	(150-400)
Serum sodium	139 mmol/L	(135-146)
Serum potassium	3.9 mmol/L	(3.5-5)
Creatinine	82 $\mu\text{mol/L}$	(79-118)

Which of the following antibiotics do SIGN guidelines recommend for this patient?

(Please select 1 option)

<input type="radio"/>	Amoxicillin
<input type="radio"/>	Ciprofloxacin
<input type="radio"/>	Co-trimoxazole
<input type="radio"/>	Nitrofurantoin
<input type="radio"/>	Trimethoprim

Please select 1 option

- | | | |
|----------------------------------|----------------|----------------------------|
| <input type="radio"/> | Amoxicillin | |
| <input checked="" type="radio"/> | Ciprofloxacin | This is the correct answer |
| <input type="radio"/> | Co-trimoxazole | |
| <input type="radio"/> | Nitrofurantoin | |
| <input type="radio"/> | Trimethoprim | Incorrect answer selected |

Key Learning Points

Pharmacology, Therapeutics

- Upper urinary tract infection is one area where resistance to antimicrobials is increasing. For this reason trimethoprim and amoxicillin are not recommended for treatment of upper urinary tract infections, and even resistance to quinolones such as ciprofloxacin is now beginning to prove problematic.

Explanation

Upper urinary tract infection is one area where resistance to antimicrobials is increasing.

For this reason trimethoprim and amoxicillin are not recommended for treatment of upper urinary tract infections, and even resistance to quinolones such as ciprofloxacin is now beginning to prove problematic.

Nitrofurantoin is not used for the treatment of upper urinary tract infections because of difficulty in achieving sufficient plasma concentration, and co-trimoxazole is a second line choice due to problems with blood dyscrasias.

HPA suggests patients started on ciprofloxacin should have urine sent for culture and patients admitted to hospital if there is no response to treatment in 24 hours.

A 74-year-old woman with chronic renal failure is admitted to the unit with infective endocarditis. You elect to begin treatment with IV benzylpenicillin and gentamicin.

On examination her temperature is 38.2°C, and she has a pansystolic murmur loudest at the left sternal edge, her BP is 125/82 mmHg, her pulse is 80 bpm and regular and she weighs 80 kg.

Investigations show:

Haemoglobin	105 g/L	(115-165)
White cell count	$7.0 \times 10^9/L$	(4-11)
Platelets	$202 \times 10^9/L$	(150-400)
Serum sodium	138 mmol/L	(135-146)
Serum potassium	4.8 mmol/L	(3.5-5)
Creatinine	190 $\mu\text{mol/L}$	(79-118)
Creatinine clearance	29 ml/min	(>60)

Which of the following is likely to represent the most appropriate dosing regime for the gentamicin?

(Please select 1 option)

<input type="radio"/>	0.75 mg/kg BD
<input type="radio"/>	1 mg/kg BD
<input type="radio"/>	1 mg/kg TDS
<input type="radio"/>	1.5 mg/kg OD
<input type="radio"/>	7 mg/kg OD

Dr. Assam

<input type="radio"/>	0.75 mg/kg BD	
<input type="radio"/>	1 mg/kg BD	
<input type="radio"/>	1 mg/kg TDS	
<input checked="" type="radio"/>	1.5 mg/kg OD	This is the correct answer
<input type="radio"/>	7 mg/kg OD	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- Aminoglycosides, such as gentamicin, have limited tissue distribution and are renally cleared. High plasma concentrations can cause ototoxicity, and dosing therefore needs to be carefully planned and monitored. Where gentamicin is used in patients with renal impairment, both ototoxicity and nephrotoxicity are potential concerns.

There are two commonly used regimens for dosing gentamicin. Both require the patient's body weight to ensure accurate dosing. For patients who are over their ideal body weight, this value rather than the patient's actual weight should be used. Ideal body weight can be calculated using age, sex and height on a number of online applications.

The most commonly used dosing regimen in the UK is the once daily regime, which is thought to be associated with reduced toxicity whilst being effective against gram-negative infections. It is not recommended for patients with a creatinine clearance of less than 60 ml/min. The dose used is 7 mg/kg IV every 24 hours. Levels should be monitored for patients on this regimen for 3 days or more, with a level taken 6-14 hours following the third dose. A nomogram is then used to determine whether the interval between doses should be altered.

Patients with creatinine clearance of less than 60 ml/min are usually given a reduced dose of gentamicin with a multiple-daily dosing regimen. This may also be recommended by microbiologists for the treatment of serious gram-negative infections such as *Pseudomonas*. Dosing is dependent on creatinine clearance.

- >60 ml/min - 1.5-1.7 mg/kg IV every 8 hours
- 40-60 ml/min - 1.2-1.5 mg/kg IV every 12 hours
- 20-40 ml/min - 1.2-1.5 mg/kg IV every 12-24 hours
- <20 ml/min - 2 mg/kg loading dose then discuss with microbiology and pharmacy

On this regimen monitoring is typically initiated after the 3rd or 4th dose, which allows a steady-state to be reached. Peak levels should be taken 30 minutes following the end of the infusion, and a trough level taken before the next dose. The desired trough level is less than 2 micrograms/ml, with a peak level of 5-8 micrograms/ml.

In this case, this lady has a creatinine clearance of 29 ml/min. As such the 7 mg/kg regimen is not appropriate. She should receive 1.2-1.5 mg/kg every 12-24 hours, so 1.5 mg/kg OD is the most correct here.

Three other drugs which require therapeutic monitoring are phenytoin, warfarin and clozapine.

Phenytoin is a highly effective anti-epileptic but is associated at toxic levels with neurological dysfunction including dizziness and nystagmus. Most warfarin therapy is directed towards a narrow therapeutic window between an INR of 2-3. Ineffective anticoagulation and excess coagulation can both be associated with significant adverse effects. Clozapine is effective in the treatment of psychotic disorders but is associated with blood cell dyscrasias, for this reason regular monitoring of full blood count is recommended.

Whereas monitoring of gentamicin and phenytoin involves PK monitoring (measuring the level of the drug in plasma), monitoring of warfarin and clozapine is essentially pharmacodynamic monitoring, looking for either over anticoagulation or abnormalities in the white blood cell count.

A 45-year-old woman has, approximately four hours ago, taken an unknown quantity of amitriptyline tablets that were being prescribed for her depression. She is feeling drowsy, agitated and has a dry mouth.

An ECG shows wide QRS complexes with arrhythmias.

Blood gas analysis revealed:

pH	7.2	(7.36-7.44)
PaO ₂	10 kPa	(11.3-12.6)
PaCO ₂	4 kPa	(4.7-6.0)

What is the most appropriate treatment?

(Please select 1 option)

<input type="radio"/>	Activated charcoal
<input type="radio"/>	Gastric lavage
<input type="radio"/>	Haemodialysis
<input type="radio"/>	Intravenous insulin
<input type="radio"/>	Intravenous sodium bicarbonate

Dr. Assem

<input type="radio"/>	Activated charcoal	
<input type="radio"/>	Gastric lavage	
<input type="radio"/>	Haemodialysis	
<input type="radio"/>	Intravenous insulin	
<input checked="" type="radio"/>	Intravenous sodium bicarbonate	Correct

Key Learning Points

Pharmacology, Psychiatry, Toxicology

- In TCA overdose, 50 ml of 8.4% sodium bicarbonate should be given if the pH is less than 7.1, QRS interval is more than 0.16 s, or there are cardiac arrhythmias or hypotension.

Explanation

There is no specific antidote for tricyclic antidepressant poisoning.

Management is initially by assessing ABCs and treating as appropriate. You should then check U&Es, looking specifically for hypokalaemia, and ABG looking for acidosis. Hypokalaemia should be corrected. ECG should be done to assess the QRS interval.

Gastric lavage should only be considered if it is within one hour of a potentially fatal overdose. 50 g of charcoal can be given if it is within one hour of ingestion.

50 ml of 8.4% sodium bicarbonate should be given if the pH is less than 7.1, QRS interval is more than 0.16 s, or there are cardiac arrhythmias or hypotension.

Antiarrhythmics should be avoided.

Hypotension should be treated with intravenous fluids, and inotropes can be considered.

In the case of **cardiac arrest**, prolonged resuscitation may be successful.

Patients who display signs of toxicity should be monitored for a minimum of 12 hours.

You are examining the mechanisms of various agents used in either platelet inhibition or anticoagulation in the management of cardiovascular disease.

Which of the following correctly describes a mechanism of action associated with warfarin therapy?

(Please select 1 option)

<input type="radio"/>	2b3a receptor inhibition
<input type="radio"/>	Cyclo-oxygenase inhibition
<input type="radio"/>	P2Y12 inhibition
<input type="radio"/>	Reduced levels of factor X
<input type="radio"/>	Selective COX-2 inhibition

(Please select 1 option)

<input type="radio"/>	2b3a receptor inhibition	
<input type="radio"/>	Cyclo-oxygenase inhibition	
<input type="radio"/>	P2Y12 inhibition	
<input type="radio"/>	Reduced levels of factor X	This is the correct answer
<input checked="" type="radio"/>	Selective COX-2 inhibition	Incorrect answer selected

Key Learning Points

Pharmacology

- Warfarin inhibits production of factors II, VII, IX and X, and it does this by restricting the activity and availability of vitamin K.

Explanation

Warfarin inhibits production of factors II, VII, IX and X, and it does this by restricting the activity and availability of vitamin K. This accounts for vitamin K administration being the treatment for warfarin toxicity.

2b3a receptor inhibitors are used in the treatment of acute coronary syndrome and they inhibit platelet aggregation.

P2Y12 is an adenosine diphosphate (ADP) dependent receptor involved in platelet aggregation which is inhibited by clopidogrel.

Cyclo-oxygenase inhibition is the mechanism of action of aspirin.

Selective COX-2 inhibitors have fallen out of favour due to potential increased risk of cardiovascular events.

A 45-year-old lady with a history of depression presented to the Emergency department drowsy.

Her repeat prescription says she is taking diazepam and dosulepin, and the ambulance crew say that she has taken an overdose of her medication. Her BP is 140/80 mmHg, pulse 130 bpm, respiratory rate 7 per minute and O₂ sats 98% on air.

Which of the following is the most appropriate next action?

(Please select 1 option)

<input type="radio"/>	Give flumazenil
<input type="radio"/>	Give naloxone
<input type="radio"/>	Obtain an ECG
<input type="radio"/>	Refer for urgent haemodialysis
<input type="radio"/>	Start N-acetylcysteine infusion

Please select 1 option)

<input type="radio"/>	Give flumazenil	
<input type="radio"/>	Give naloxone	
<input type="radio"/>	Obtain an ECG	This is the correct answer
<input type="radio"/>	Refer for urgent haemodialysis	
<input checked="" type="radio"/>	Start N-acetylcysteine infusion	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- In cases of suspected overdoses of tricyclic antidepressants, an electrocardiogram (ECG) would immediately indicate if there is a risk of significant tricyclic toxicity by showing a wide QRS complex or abnormal axis deviation.

Explanation

This is a tricky case and will catch those who go for the first answer they see that is reasonable.

The urge is quickly to treat the drowsy patient with respiratory depression with some sort of antidote, but there needs to be a diagnostic step first.

Tricyclic antidepressants can cause fatal arrhythmias and seizures which are very difficult to manage.

An electrocardiogram (ECG) would immediately indicate if there is a risk of significant tricyclic toxicity by showing a wide QRS complex or abnormal axis deviation.

A 58-year-old woman presented with unsteadiness and ataxia and gave a recent history of nausea and epigastric pain for which she had been prescribed an antacid and cimetidine.

She was an epileptic and had been well controlled with phenytoin for eight years. She had been also been prescribed amitriptyline for depression, was receiving post-menopausal hormone replacement therapy and was self-medicating with St John's wort.

Which of the following drugs is most likely to be responsible for her presentation?

(Please select 1 option)

<input type="radio"/>	Amitriptyline
<input type="radio"/>	Antacid
<input type="radio"/>	Cimetidine
<input type="radio"/>	Estradiol
<input type="radio"/>	St John's wort

<input type="radio"/>	Amitriptyline
<input type="radio"/>	Antacid
<input type="radio"/>	Cimetidine This is the correct answer
<input checked="" type="radio"/>	Estradiol Incorrect answer selected
<input type="radio"/>	St John's wort

Key Learning Points

Pharmacology, Toxicology

- Cimetidine can cause phenytoin toxicity.

Explanation

This patient has developed phenytoin toxicity which has been precipitated by cimetidine which inhibits cytochrome P₄₅₀ metabolism of phenytoin.

Phenytoin concentration is reduced by St John's wort and is unaffected by amitriptyline which would however reduce seizure threshold; antacids may reduce phenytoin absorption and oestradiol metabolism may be increased by phenytoin.

A 52-year-old woman takes lithium carbonate for manic depression and also takes codeine and diclofenac prescribed by her GP for osteoarthritis.

Which one of the following statements is correct?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Codeine will reduce the bioavailability of lithium |
| <input type="radio"/> | The analgesic effect of codeine will be reduced by co-administration of diclofenac |
| <input type="radio"/> | The nephrotoxicity of diclofenac will be increased in this patient |
| <input type="radio"/> | Plasma lithium concentration will be increased by codeine |
| <input type="radio"/> | Plasma lithium concentrations will be raised by diclofenac |

Please select 1 option.

<input type="radio"/>	Codeine will reduce the bioavailability of lithium	
<input type="radio"/>	The analgesic effect of codeine will be reduced by co-administration of diclofenac	
<input type="radio"/>	The nephrotoxicity of diclofenac will be increased in this patient	
<input type="radio"/>	Plasma lithium concentration will be increased by codeine	
<input checked="" type="radio"/>	Plasma lithium concentrations will be raised by diclofenac	Correct

Key Learning Points

Pharmacology, Toxicology

- Diclofenac decreases renal lithium clearance and increases lithium concentrations.

Explanation

Diclofenac decreases renal lithium clearance and increases lithium concentrations.

Codeine and diclofenac are frequently co-prescribed.

Dr Assem

A 71-year-old man with a history of chronic renal impairment and atrial fibrillation for which he takes warfarin, presents with an acutely tender and red left big toe.

Investigations reveal:

Serum creatinine	200 μ mol/L	(50-100)
Serum urate	0.5 mmol/L	(0.12-0.42)

Which of the following is the most appropriate treatment for this man's presentation?

(Please select 1 option)

- ☐ Allopurinol
- ☐ Colchicine
- ☐ Diclofenac
- ☐ Paracetamol
- ☐ Prednisolone

<input type="radio"/>	Allopurinol
<input type="radio"/>	Colchicine
<input type="radio"/>	Diclofenac
<input type="radio"/>	Paracetamol
<input checked="" type="radio"/>	Prednisolone Correct

Key Learning Points

Pharmacology, Rheumatology, Therapeutics

- Non-steroidal anti-inflammatory drugs (NSAIDs) may cause a deterioration in renal function and would be associated with an increased risk of bleeding in the elderly.

Explanation

This man presents with acute **gout**, has chronic renal impairment, AF and takes warfarin.

Non-steroidal anti-inflammatory drugs (NSAIDs) would be the treatment of choice but may cause a deterioration in renal function and would be associated with an increased risk of bleeding in the elderly.

The adverse effects of colchicine (especially gastrointestinal symptoms) would be more likely in the elderly and should probably be avoided in those with renal impairment of this degree.

Thus steroids are probably the best option.

Allopurinol may well precipitate/exacerbate acute **gout** and is used once the acute attack has settled following adequate treatment.

This is a classic MRCP question since it is hard to answer this by just looking in textbooks. Steroids are the last resort choice where NSAIDs and colchicine are deemed too dangerous to use and that is a matter of judgement applied by physicians. There is plenty of evidence for their efficacy.

Which one of the following drugs works by inhibiting the tumour necrosis factor?

(Please select 1 option)

☐ Cyclosporin

☐ Infliximab

☐ Methotrexate

☐ Montelukast

☐ Sulfasalazine

<input type="radio"/>	Cyclosporin	
<input type="radio"/>	Infliximab	This is the correct answer
<input type="radio"/>	Methotrexate	
<input type="radio"/>	Montelukast	
<input checked="" type="radio"/>	Sulfasalazine	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Infliximab is given with methotrexate and is associated with the development of tuberculosis. Other side effects include injection site reactions, infusion reactions, neutropenia, demyelinating disease and heart failure.

Explanation

Montelukast works as a leukotriene receptor antagonist and is used in the treatment of asthma.

Etanercept and infliximab inhibit TNF and are licensed in the treatment of rheumatoid arthritis.

Infliximab is given with methotrexate and is associated with the development of tuberculosis.

You are asked to review a 71-year-old woman who comes to the clinic complaining that her hearing is not as good as it was after a prolonged period of treatment in hospital for infective endocarditis.

On examination you find that she has significant sensorineural hearing impairment and you suspect this may be gentamicin related.

What is the mechanism of ototoxicity associated with gentamicin?

(Please select 1 option)

- | | |
|-----------------------|--------------------------------|
| <input type="radio"/> | Cell wall integrity disruption |
| <input type="radio"/> | DNA toxicity |
| <input type="radio"/> | Interruption of cell division |
| <input type="radio"/> | Nitric oxide reduction |
| <input type="radio"/> | Oxygen free radical generation |

Please select 1 option

<input type="radio"/>	Cell wall integrity disruption
<input type="radio"/>	DNA toxicity
<input type="radio"/>	Interruption of cell division
<input type="radio"/>	Nitric oxide reduction
<input checked="" type="radio"/>	Oxygen free radical generation Correct

Key Learning Points

Pharmacology

- Gentamicin is toxic to cochlear hair cells, and it is known to disrupt mitochondrial protein synthesis, which leads to increased oxygen free radical generation via inducible nitric oxide synthase activity.

Explanation

Gentamicin is toxic to cochlear hair cells, and it is known to disrupt mitochondrial protein synthesis, which leads to increased oxygen free radical generation via inducible nitric oxide synthase activity.

Peroxynitrite radicals are formed, which then leads to apoptosis.

It is thought that aminoglycosides take longer to clear from inner ear fluids, which may account for the site specific toxicity seen with this class of antibiotics.

A switch from BD dosing to OD dosing has reduced the susceptibility of patients to toxicity, and once daily regimes are now the preferred method of gentamicin administration.

Peak (one hour post dose), and trough, (pre-dose levels) are assayed to determine dose adjustments. A dose of 3 mg/kg/day is the usual starting level in adults with normal renal function.

Gentamicin may be used in patients with impaired renal function, but dose level and interval between doses needs to be adjusted to avoid toxicity.

A 59-year-old male presents with a three day history of marked muscle aches and weakness.

He has ischaemic heart disease for which he takes a number of drugs including simvastatin and has been taking these drugs for a number of years without any problem. On this occasion his CPK confirms a diagnosis of rhabdomyolysis with a level of 4200 IU/L (<200).

Which of the following health supplements is he most likely to have taken that would have contributed to the statin-induced rhabdomyolysis?

(Please select 1 option)

☐ Cod liver oil capsules

☐ Cranberry juice

☐ Ginseng

☐ Grapefruit juice

☐ Vitamin C

Please select 1 option.

<input type="radio"/>	Cod liver oil capsules
<input type="radio"/>	Cranberry juice
<input type="radio"/>	Ginseng
<input checked="" type="radio"/>	Grapefruit juice Correct
<input type="radio"/>	Vitamin C

Key Learning Points

Pharmacology

- Grapefruit juice significantly increases serum concentrations of some statins due to inhibition of the CYP3A4 mediated first pass metabolism.

Explanation

Grapefruit juice significantly increases serum concentrations of some statins. This is achieved by reducing the CYP3A4-mediated first-pass metabolism in the small intestine. Concomitant use of atorvastatin and large amounts of grapefruit juice should be avoided, or the dose of atorvastatin should be reduced accordingly. CYP3A4 is a member of the cytochrome P450 system.

Whilst an interaction is increasingly being recognised between cranberry juice and warfarin, there has as yet been no interaction with other drugs metabolised via the P450 system.

No interaction has been shown between statins, omega-3 fish oils, ginseng or vitamin C.

A 58-year-old male presents with painful breast tissue.

Six weeks previously he was treated for atrial fibrillation and had a number of drugs commenced.

Which one of the following drugs may have caused this problem?

(Please select 1 option)

- | | |
|-----------------------|----------------|
| <input type="radio"/> | Aspirin |
| <input type="radio"/> | bisoprolol |
| <input type="radio"/> | Flecainide |
| <input type="radio"/> | Spironolactone |
| <input type="radio"/> | Warfarin |

<input type="radio"/>	Aspirin
<input type="radio"/>	bisoprolol
<input type="radio"/>	Flecainide
<input checked="" type="radio"/>	Spironolactone Correct
<input type="radio"/>	Warfarin

Key Learning Points

Pharmacology, Therapeutics

- Spironolactone causes gynaecomastia can block androgen production by inhibiting enzymes in the testosterone synthetic pathway, and can also block receptor binding of testosterone and dihydrotestosterone.

Explanation

In the setting of atrial fibrillation spironolactone may be used if the patient is thought to be in heart failure (which is fairly common with atrial fibrillation). In addition, spironolactone has been shown to reduce the recurrence rate of atrial fibrillation following cardioversion and so it is possible it would be started for this reason.

Spironolactone causes gynaecomastia by several mechanisms. It can block androgen production by inhibiting enzymes in the testosterone synthetic pathway, and can also block receptor binding of testosterone and dihydrotestosterone. In addition, it displaces oestradiol from sex hormone binding globulin (SHBG), which increases free oestrogen levels.

A 76-year-old man with a recent history of cerebral haemorrhage is admitted with a cough, worsening breathlessness and right pleuritic chest pain. He is also mildly pyrexial.

His ventilation-perfusion scan reveals several areas of perfusion deficit in the right lower zone, with a normal ventilation scan.

What is the most appropriate line of management?

(Please select 1 option)

<input type="radio"/>	Aspirin therapy
<input type="radio"/>	Antibiotics
<input type="radio"/>	Inferior vena cava (IVC) filter
<input type="radio"/>	Low molecular weight heparin treatment
<input type="radio"/>	Warfarin treatment

<input type="radio"/>	Aspirin therapy	
<input type="radio"/>	Antibiotics	
<input type="radio"/>	Inferior vena cava (IVC) filter	This is the correct answer
<input type="radio"/>	Low molecular weight heparin treatment	
<input checked="" type="radio"/>	Warfarin treatment	Incorrect answer selected

Key Learning Points

Pharmacology, Respiratory Medicine, Therapeutics

- IVC filters are indicated in the treatment of emboli where there are contraindications to systemic anticoagulation.

Explanation

This patient has a pulmonary embolism (PE) following a recent haemorrhagic stroke.

The risk of rebleeding into the stroke area is too high with anticoagulation.

The best action would be percutaneous insertion of IVC filter which may be as effective as anticoagulation. It is used in cases where anticoagulation is a contraindication or in those in whom anticoagulation alone fails.

A 62-year-old male presented to the urologists with symptoms of urinary hesitancy and dribbling.

They diagnose benign prostatic hyperplasia and he is commenced on finasteride.

Through which of the following mechanisms does finasteride function?

(Please select 1 option)

- | | |
|-----------------------|----------------------------------|
| <input type="radio"/> | 5-alpha-reductase inhibitor |
| <input type="radio"/> | Alpha receptor antagonist |
| <input type="radio"/> | LHRH analogue |
| <input type="radio"/> | LHRH antagonist |
| <input type="radio"/> | Testosterone receptor antagonist |

<input type="radio"/>	5-alpha-reductase inhibitor	This is the correct answer
<input type="radio"/>	Alpha receptor antagonist	
<input type="radio"/>	LHRH analogue	
<input type="radio"/>	LHRH antagonist	
<input checked="" type="radio"/>	Testosterone receptor antagonist	Incorrect answer selected

Key Learning Points

Pharmacology

- Finasteride is a 5-alpha-reductase inhibitor preventing the conversion of testosterone to the active dihydrotestosterone (DHT).

Explanation

Finasteride is a 5-alpha-reductase inhibitor preventing the conversion of testosterone to the active dihydrotestosterone (DHT).

Consequently this agent opposes testosterone, so gynaecomastia and reduced libido are common side effects.

It is also taken orally (under the brand name Propecia) for the treatment of male pattern hair loss.

A patient has just received intravenous ceftazidime. He immediately became flushed and wheezy, with a blood pressure of 80/40 mmHg.

Which of the following is the most appropriate immediate management for this patient?

(Please select 1 option)

- | | |
|-----------------------|--------------------------------|
| <input type="radio"/> | Chlorphenamine 10 mg IV |
| <input type="radio"/> | Adrenaline 0.2 ml of 1:1000 IV |
| <input type="radio"/> | Adrenaline 0.5 mg IV |
| <input type="radio"/> | Adrenaline 0.5 mg IM |
| <input type="radio"/> | Hydrocortisone 100 mg IV |

- | | | |
|----------------------------------|--------------------------------|----------------------------|
| <input type="radio"/> | Chlorphenamine 10 mg IV | |
| <input type="radio"/> | Adrenaline 0.2 ml of 1:1000 IV | |
| <input type="radio"/> | Adrenaline 0.5 mg IV | |
| <input type="radio"/> | Adrenaline 0.5 mg IM | This is the correct answer |
| <input checked="" type="radio"/> | Hydrocortisone 100 mg IV | Incorrect answer selected |

Key Learning Points

Pharmacology, Toxicology

- Immediate treatment of anaphylaxis includes cessation of the causative agent, then oxygen, fluids and adrenaline 0.5 mg intramuscularly.

Explanation

Immediate treatment of [anaphylaxis](#) includes cessation of whatever caused it.

Then give oxygen, fluids and adrenaline 0.5mg intramuscularly.

Checking concentrations of adrenaline is very important especially in high pressure situations. Intravenous adrenaline is potentially hazardous unless diluted appropriately, and should only be used in [cardiac arrest](#) situations unless the clinician has experience of using it regularly.

A 45-year-old female is admitted with fatigue, nausea and weight loss. She is known to have abused alcohol for many years and has previously developed delirium tremens. She stopped drinking alcohol two days ago.

On examination, she is thin, alert and orientated. She is slightly icteric, with features of chronic liver disease but there is no flapping tremor. Pulse is 88 bpm regular, blood pressure is 106/74 mmHg and temperature is 37°C.

She is treated with IV thiamine.

Which of the following agents would be recommended for the prevention of acute alcohol withdrawal?

(Please select 1 option)

<input type="radio"/>	IM haloperidol
<input type="radio"/>	IV diazepam
<input type="radio"/>	Oral diazepam
<input type="radio"/>	Oral quetiapine
<input type="radio"/>	Oral lorazepam

Please select 1 option

<input type="radio"/>	IM haloperidol	
<input type="radio"/>	IV diazepam	
<input type="radio"/>	Oral diazepam	
<input type="radio"/>	Oral quetiapine	
<input checked="" type="radio"/>	Oral lorazepam	Correct

Key Learning Points

Pharmacology

- In hepatic impairment benzodiazepines with a shorter half life are preferred.

Explanation

This patient with features of alcoholic chronic liver disease would be regarded at high risk of developing acute alcohol withdrawal, particularly in view of her past history of delirium tremens.

Benzodiazepines are appropriate agents in preventing acute alcohol withdrawal and oral agents such as lorazepam and diazepam are recommended.

Patients with liver cirrhosis are at risk of hepatic encephalopathy with benzodiazepines. However, it is not known that she has cirrhosis and the potential for alcohol withdrawal is a real risk. She should therefore be given benzodiazepines and monitored closely for any signs of encephalopathy. In hepatic impairment benzodiazepines with a shorter half life (e.g. lorazepam and oxazepam) are preferred

A 19-year old girl has been brought to the Emergency department by her friends following a night out at a party. Her friends comment that she has been talking to herself about 'irrelevant things'. She seems agitated and restless.

On examination, her reflexes are increased and an electrocardiogram (ECG) demonstrates ventricular ectopics.

What kind of substance abuse do you suspect at this point?

(Please select 1 option)

<input type="radio"/>	Alcohol
<input type="radio"/>	Barbituate
<input type="radio"/>	Cannabis
<input type="radio"/>	Ecstasy
<input type="radio"/>	Glue sniffing

<input type="radio"/>	Alcohol
<input type="radio"/>	Barbiturate
<input type="radio"/>	Cannabis
<input checked="" type="radio"/>	Ecstasy Correct
<input type="radio"/>	Glue sniffing

Key Learning Points

Pharmacology

- Ecstasy (3,4-methylenedioxymethamphetamine, MDMA) can cause tachycardia and hypertension.

Explanation

This is a case of [ecstasy overdose](#).

Ecstasy (3,4-methylenedioxymethamphetamine, MDMA) stimulates the central nervous system.

It causes:

- Increased alertness and self-confidence
- Euphoria
- Extrovert behaviour
- Increased talkativeness with rapid speech
- Lack of desire to eat or sleep
- Tremor
- Dilated pupils
- Tachycardia, and
- Hypertension.

More severe intoxication is associated with:

- Excitability
- Agitation
- Paranoid delusions
- Hallucinations with violent behaviour
- Hypertonia, and
- Hyperreflexia.

Convulsions, rhabdomyolysis, hyperthermia, and cardiac arrhythmias may also develop.

In severe cases of MDMA poisoning the following are also observed:

- Hyperthermia
- Disseminated intravascular coagulation
- Rhabdomyolysis
- Acute renal failure, and
- Hyponatraemia

Hepatic damage has also been reported.

Rarely, poisoning due to amphetamines may result in intracerebral and subarachnoid haemorrhage and acute cardiomyopathy; these complications may be fatal.

Hyperthyroxaemia may be found in chronic amphetamine users.

Which of the listed medications has a thiazide-like action?

(Please select 1 option)

☐ Acetazolamide

☐ Bumetanide

☐ Furosemide

☐ Metolazone

☐ Triamterene

<input type="radio"/>	Acetazolamide	
<input type="radio"/>	Bumetanide	
<input type="radio"/>	Furosemide	
<input type="radio"/>	Metolazone	This is the correct answer
<input checked="" type="radio"/>	Triamterene	Incorrect answer selected

Key Learning Points

Pharmacology

- Thiazide diuretics act on the distal convoluted tubule of the nephron to prevent sodium and chloride reabsorption. Of the above diuretics, metolazone has a thiazide-like action.

Explanation

Metolazone is an example of a diuretic with a thiazide-like action.

Bumetanide and furosemide are loop diuretics, blocking reabsorption of sodium at the loop of Henle.

Acetazolamide is a carbonic anhydrase inhibitor and has no relation to thiazide-like action.

Triamterene is a potassium-sparing diuretic with no thiazide-like activity.

A 16-year-old male is brought to the Emergency department with a Glasgow coma scale (GCS) rating of 3/15.

Within 10 minutes he regained consciousness with a GCS of 15/15, is sitting up and talking.

What is he likely to have taken?

(Please select 1 option)

☐ Inhaled solvent glue

☐ Smoked heroin

☐ Smoked marijuana

☐ Snorted cocaine

☐ Taken ecstasy

<input type="radio"/>	Inhaled solvent glue	This is the correct answer
<input type="radio"/>	Smoked heroin	
<input type="radio"/>	Smoked marijuana	
<input type="radio"/>	Snorted cocaine	
<input checked="" type="radio"/>	Taken ecstasy	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Inhaled solvents are rapidly absorbed through the lungs and then quickly distributed, meaning their effects are short-lived.

Explanation

This patient was markedly comatose on arrival but quickly regains consciousness. This suggests a short acting (probably) inhaled anaesthetic-like agent - glue.

Marijuana would not be expected to produce this level of coma and the effects of cocaine would last much longer.

The inhaled solvents, due to their lipophilicity, are rapidly absorbed through the lungs and then quickly distributed to the brain and other organs. The effects therefore appear within minutes of inhalation.

It's much less common to get such a low GCS with just smoking heroin, you tend to see this with intravenous drug use. Also, the recovery is far less rapid (unless you give the patient naloxone, which you are not told here).

Typical substances that are inhaled include toluene, aromatic hydrocarbons and butane.

A 35-year-old woman with known seafood allergy presented after developing an itchy rash at a restaurant. She had widespread urticaria which spared her neck and face.

On examination, her blood pressure was 130/70 mmHg, pulse 95 bpm, respiratory rate 24/min and O₂ saturation 99% on air.

Intravenous hydrocortisone and intramuscular antihistamine have been given.

What is the next most appropriate step in the management of this patient?

(Please select 1 option)

<input type="radio"/>	Inhaled adrenaline
<input type="radio"/>	Intramuscular adrenaline
<input type="radio"/>	Intravenous adrenaline
<input type="radio"/>	Observe
<input type="radio"/>	Subcutaneous adrenaline

(Please select 1 option)

<input type="radio"/>	Inhaled adrenaline
<input type="radio"/>	Intramuscular adrenaline
<input type="radio"/>	Intravenous adrenaline
<input type="radio"/>	Observe This is the correct answer
<input checked="" type="radio"/>	Subcutaneous adrenaline Incorrect answer selected

Key Learning Points

Pharmacology

- Adrenaline is indicated in allergic reactions if there is stridor, wheeze, respiratory distress or cardiogenic shock.

Explanation

Where there is a history of a typical allergic reaction, as here, current United Kingdom resuscitation guidelines suggest adrenaline if there is:

- Stridor
- Wheeze
- Respiratory distress, or
- Clinical evidence of shock.

A literature review in the BMJ includes a copy of the algorithm and a discussion of the evidence for adrenaline¹.

A 48-year-old man is admitted with nausea and excessive drowsiness after taking an antihistamine tablet. He has previously used the antihistamine but on this occasion he has recently been drinking large amounts of grapefruit juice for his health.

Grapefruit juice is suspected of causing a drug interaction in this man.

Which of the following liver enzyme systems is affected by grapefruit juice?

(Please select 1 option)

<input type="radio"/>	Cytochrome p450 3A4
<input type="radio"/>	Glucuronidation
<input type="radio"/>	Glutathione S-transferase
<input type="radio"/>	Glycine decarboxylase
<input type="radio"/>	Sulfation

Please select 1 option.

<input type="radio"/>	Cytochrome p450 3A4	This is the correct answer
<input type="radio"/>	Glucuronidation	
<input type="radio"/>	Glutathione S-transferase	
<input checked="" type="radio"/>	Glycine decarboxylase	Incorrect answer selected
<input type="radio"/>	Sulfation	

Key Learning Points

Pharmacology

- Bergamottin is a constituent of grapefruit juice and is metabolised by the cytochrome p450 3A4 pathway.

Explanation

Bergamottin is a constituent of grapefruit juice and is metabolised by the cytochrome p450 3A4 pathway.

Dr Assem

A 63-year-old man was found collapsed.

A department of psychiatry outpatient card was found in his jacket, together with a bottle of procyclidine tablets.

He was febrile (38.2°C), conscious but unresponsive to commands. The blood pressure was 160/105 mmHg and there was marked muscle rigidity.

What is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Acute catatonic schizophrenia
<input type="radio"/>	Bacterial meningitis
<input type="radio"/>	Cerebral malaria
<input type="radio"/>	Neuroleptic malignant syndrome
<input type="radio"/>	Procyclidine overdose

(Please select 1 option)

<input type="radio"/>	Acute catatonic schizophrenia	
<input type="radio"/>	Bacterial meningitis	
<input type="radio"/>	Cerebral malaria	
<input type="radio"/>	Neuroleptic malignant syndrome	This is the correct answer
<input checked="" type="radio"/>	Procyclidine overdose	Incorrect answer selected

Key Learning Points

Psychiatry, Toxicology

- Neuroleptic malignant syndrome (NMS) is characterised by fever, muscular rigidity, altered mental status, and autonomic dysfunction.

Explanation

The symptoms are typical of neuroleptic malignant syndrome (NMS).

NMS is characterised by:

- Fever
- Muscular rigidity
- Altered mental status
- Autonomic dysfunction.

Procyclidine is used to treat the Parkinsonian side effects of neuroleptics; its presence in the patient's pocket implies that he was taking neuroleptics.

Signs of procyclidine overdose include:

- Agitation
- Confusion
- Sleeplessness lasting up to 24 hours or more
- Pupils are dilated and unreactive to light.

Visual and auditory hallucinations and tachycardia have also been reported.

A 45-year-old woman presents to the oncology clinic with metastatic carcinoma of the breast.

She wants to take an active role in deciding on the optimal chemotherapy regime for herself, and wants to discuss the relative advantages of capecitabine versus 5-fluorouracil (5-FU).

What would you advise her about capecitabine?

(Please select 1 option)

<input type="radio"/>	Can be orally administered
<input type="radio"/>	Has a greater period of progression free survival than 5-FU
<input type="radio"/>	Is associated with less blood dyscrasias than 5-FU
<input type="radio"/>	Is not dependent on renal function
<input type="radio"/>	Is not usually associated with diarrhoea

<input type="radio"/>	Can be orally administered	This is the correct answer
<input type="radio"/>	Has a greater period of progression free survival than 5-FU	
<input type="radio"/>	Is associated with less blood dyscrasias than 5-FU	
<input type="radio"/>	Is not dependent on renal function	
<input checked="" type="radio"/>	Is not usually associated with diarrhoea	Incorrect answer selected

Key Learning Points

Pharmacology

- The major difference between capecitabine and 5-FU is that capecitabine is an oral prodrug of 5-FU.

Explanation

The major difference between capecitabine and 5-FU is that capecitabine is an oral prodrug of 5-FU. The final step in metabolism to 5-FU is thymidine phosphorylase, higher activity of thymidine phosphorylase occurring in tumour tissues.

Evidence suggests that efficacy of capecitabine versus 5-FU is broadly similar, with minor, insignificant differences occurring in progression free survival in comparative studies across a range of primary tumour types.

Whilst activation of capecitabine to 5-FU occurs after a number of steps, metabolites are still renally excreted, so in this sense, no significant advantage over 5-FU is conferred.

Which of the following antiemetics functions through inhibition of neurokinin (NK)1 receptor?

(Please select 1 option)

- | | |
|-----------------------|-------------|
| <input type="radio"/> | Aprepitant |
| <input type="radio"/> | Domperidone |
| <input type="radio"/> | Hyoscine |
| <input type="radio"/> | Granisetron |
| <input type="radio"/> | Ondansetron |

Please select 1 option.

<input type="radio"/>	Aprepitant	This is the correct answer
<input type="radio"/>	Domperidone	
<input type="radio"/>	Hyoscine	
<input type="radio"/>	Granisetron	
<input checked="" type="radio"/>	Ondansetron	Incorrect answer selected

Key Learning Points

Pharmacology

- Aprepitant is a neurokinin receptor blocker used in the prevention of chemotherapy induced nausea.

Explanation

Aprepitant is a neurokinin receptor blocker used in the prevention of chemotherapy induced nausea.

Ondansetron and granisetron are 5HT₃ antagonists.

Hyoscine is an anticholinergic/antihistaminergic.

Domperidone is an antidopaminergic agent.

Dr. Assem

A 17-year-old male was found by the police in an acutely confused state in the early hours of the morning.

He was taken to the local Emergency department where he is a frequent attendee with a history of schizophrenia and deliberate self-harm. He is found to be have dilated pupils and was somewhat agitated with visual hallucinations and a sinus tachycardia of 110 beats per minute on electrocardiogram.

He later told the nursing staff that he had taken some acid of unknown quantity because the voice had told him to, so that he can be protected against other people poisoning him. He was observed overnight in hospital where he became less agitated and his heart rate had returned to normal. Prior to discharge, he was reviewed by the on-call psychiatric team and his anti-psychotic medication was changed to olanzapine.

A week later, his mother found him semiconscious in his flat. His admission electrocardiogram showed a sinus tachycardia of 115 beats per minute, his pupils were dilated and he had a temperature of 39°C. His muscle tone was globally increased and diminished reflexes throughout with equivocal plantars. He had a palpable bladder and was catheterised.

Investigations showed:

Haemoglobin	145 g/L	(120-160)
White cell count	$8.4 \times 10^9/L$	(4-11)
Platelets	$310 \times 10^9/L$	(150-400)
Serum sodium	145 mmol/L	(137-144)
Serum potassium	5.5 mmol/L	(3.5-4.9)
Serum urea	32.3 mmol/L	(2.5-7.5)
Serum creatinine	410 μ mol/L	(60-110)
Serum chloride	108 mmol/L	(95-107)
Serum bicarbonate	15 mmol/L	(20-28)
Urine dipstick	Protein ++	
	Blood +++	

What is the most likely cause for his biochemical abnormalities?

(Please select 1 option)

<input type="radio"/>	Amphetamine overdose
<input type="radio"/>	Neuroleptic malignant syndrome
<input type="radio"/>	Rhabdomyolysis
<input type="radio"/>	Serotonin syndrome
<input type="radio"/>	Urinary tract infection

<input type="radio"/>	Amphetamine overdose	
<input checked="" type="radio"/>	Neuroleptic malignant syndrome	This is the correct answer
<input type="radio"/>	Rhabdomyolysis	
<input type="radio"/>	Serotonin syndrome	
<input type="radio"/>	Urinary tract infection	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Neuroleptic malignant syndrome is a potentially fatal idiosyncratic reaction to neuroleptic drugs that antagonise the central dopamine D2 receptors or result in dopamine depletion.

Explanation

Neuroleptic malignant syndrome is a potentially fatal idiosyncratic reaction to neuroleptic drugs that antagonise the central dopamine D2 receptors or result in dopamine depletion. It is rarer with the newer anti-psychotic drugs such as olanzapine, but can occur. It results in an elevated temperature set-point, impairment of normal thermal homeostasis, extrapyramidally-induced muscular rigidity and **rhabdomyolysis**, altered mental status and autonomic dysfunction.

Diagnosis can be made if neuroleptics have been taken within 1-4 weeks, temperature above 38°C, muscle rigidity and five of the following features:

- Altered mental status
- Tachycardia
- Hypotension or hypertension
- Tremor
- hyporeflexia but lead pipe rigidity
- Incontinence
- Diaphoresis or sialorrhoea
- Increased creatine phosphokinase or urinary myoglobin
- Metabolic acidosis
- Leucocytosis, and
- Exclusion of other illnesses.

This patient does have **rhabdomyolysis**, but the over-riding cause is neuroleptic malignant syndrome. **Rhabdomyolysis** is isolated in most commonly seen following trauma or following prolonged immobilisation. NMS presents with hyporeflexia and lead pipe rigidity whereas **Serotonin syndrome** will present with hyperreflexia.

Urinary tract infection would not explain all the signs seen above.

Many of the features of **serotonin syndrome** are the same as those of **neuroleptic malignant syndrome**, but the medications this patient is on make the latter more likely.

Amphetamine overdose could lead to the symptoms described above, but the stem given should lead you more towards the use of neuroleptics rather than amphetamines.

Which of the following is the mechanism of action of Ivabradine?

(Please select 1 option)

☐ L-Type calcium channel blocker

☐ Beta blocker

☐ Alpha blocker

☐ If channel inhibitor

☐ Sodium channel blocker

Dr. Assem

<input type="radio"/>	L-Type calcium channel blocker	
<input type="radio"/>	Beta blocker	
<input type="radio"/>	Alpha blocker	
<input type="radio"/>	If channel inhibitor	This is the correct answer
<input checked="" type="radio"/>	Sodium channel blocker	Incorrect answer selected

Key Learning Points

Pharmacology

- Ivabradine is a novel agent which blocks the I_f channel in the sinoatrial node, resulting in a reduced heart rate and a subsequent anti-anginal effect.

Explanation

Ivabradine is a novel agent which blocks the I_f channel in the sinoatrial node, resulting in a reduced heart rate. It is used as an anti-anginal agent as a second-line alternative to the rate-slowing calcium-channel blockers verapamil and diltiazem.

L-Type calcium channels are found in the cardiac muscle cells as well as skeletal and smooth muscle cells, and are blocked by verapamil and diltiazem.

Labetalol and atenolol are both beta blockers which can be used in the treatment of angina.

Sodium channel blockers, such as flecainide, are anti-arrhythmics which can be used in the treatment of tachyarrhythmias such as AF.

Alpha blockers, such as doxazosin, are mainly used to treat hypertension but can also be used in the management of lower urinary tract symptoms.

A 45-year-old female presents with a six month history of exertional dyspnoea and is diagnosed with pulmonary fibrosis (PF).

Over the last one year she has received a variety of medications.

Which of the following drugs could be responsible?

(Please select 1 option)

☐ Dexamethasone

☐ Ibuprofen

☐ Nalidixic acid

☐ Penicillamine

☐ Sulphasalazine

Dr Assen

Please select 1 option

<input type="radio"/>	Dexamethasone
<input type="radio"/>	Ibuprofen
<input type="radio"/>	Nalidixic acid
<input type="radio"/>	Penicillamine
<input checked="" type="radio"/>	Sulphasalazine Correct

Key Learning Points

Respiratory Medicine, Therapeutics

- Sulphasalazine pulmonary toxicity typically presents with new-onset dyspnoea and pulmonary infiltrates visible on chest radiograph. There may be peripheral blood eosinophilia.

Explanation

The drugs which can classically cause pulmonary fibrosis include:

- Cytotoxics: busulphan, bleomycin, methotrexate, cyclophosphamide, carmustine
- Antibiotics: e.g. nitrofurantoin
- Cardiac drugs: hydralazine, amiodarone, tocainide
- Opiates: e.g. heroin abuse

Sulphasalazine pulmonary toxicity is rare, but is increasingly recognised. It typically presents with new-onset dyspnoea and pulmonary infiltrates visible on chest radiograph. There may be peripheral blood eosinophilia. Histology most commonly demonstrates an eosinophilic pneumonia with interstitial inflammation and fibrosis. Drug withdrawal is standard treatment, with or without the addition of corticosteroids.

Dexamethasone can be used to treat pulmonary fibrosis, and is not a recognised cause. Neither is ibuprofen nor nalidixic acid (a synthetic quinolone antibiotic).

Penicillamine is associated with pulmonary toxicity in the form of diffuse alveolar damage, hypersensitivity pneumonitis and obliterative bronchitis. It does not cause pulmonary fibrosis however, and D-penicillamine has actually been shown to stabilise pulmonary fibrosis in the setting of systemic sclerosis.

Mr VU is taking amitriptyline for depressive illness.

He comes to see you at a routine outpatient appointment and informs you that he has been experiencing some side effects with his amitriptyline therapy.

Which of the following is the most commonly recognised side effect of this drug?

(Please select 1 option)

- | | |
|-----------------------|--------------------|
| <input type="radio"/> | Gout |
| <input type="radio"/> | Hypokalaemia |
| <input type="radio"/> | Renal stones |
| <input type="radio"/> | Taste disturbances |
| <input type="radio"/> | Urinary retention |

○	Effect 1 (gland)
○	Gout
○	Hyokalaemia
○	Renal stones
○	Taste disturbances
●	Urinary retention Correct

Key Learning Points

Pharmacology, Psychiatry

- Urinary retention is a known side effect of amitriptyline and similar tricyclic antidepressants.

Explanation

Many adverse effects of amitriptyline and similar tricyclic antidepressants are caused by their antimuscarinic actions.

Antimuscarinic effects are relatively common and occur before an antidepressant effect is obtained. They include:

- Dry mouth
- **Orthostatic hypotension** occasionally leading to paralytic **legs**
- Urinary retention
- Blurred vision and disturbances in accommodation
- Increased intraocular pressure, and
- Hyperthermia.

Tolerance is often achieved if treatment is continued and adverse effects may be less troublesome if treatment is begun with small doses and then increased gradually, although this may delay the clinical response.

Drowsiness may also be common, although a few tricyclic antidepressants possess little or no sedative potential and may produce nervousness and insomnia.

Other neurological adverse effects include:

- Headache
- Peripheral neuropathy
- Tremor
- Ataxia
- Epileptiform seizures
- **Tinnitus**, and
- Occasional extrapyramidal symptoms including speech difficulties (dysarthria).

Confusion, hallucinations, or delirium may occur, particularly in the elderly, and mania or hypomania, and behavioural disturbances (particularly in children) have been reported.

Gastrointestinal complaints include:

- Sour or metallic taste
- Stomatitis, and
- Gastric irritation with nausea and vomiting.

Orthostatic hypotension and tachycardia can occur in patients without a history of cardiovascular disease, and may be particularly troublesome in the elderly.

Hypersensitivity reactions, such as urticaria and angioedema, and photosensitisation have been reported and, rarely, cholestatic jaundice and blood disorders, including:

- Eosinophilia
- Bone marrow depression
- Thrombocytopenia
- Leucopenia, and
- Agnucitocytosis

Endocrine effects include testicular enlargement, **gynecomastia** and breast enlargement, and galactorrhoea. Sexual dysfunction may also occur.

Changes in blood sugar concentrations may also occur, and, very occasionally, **hypernatraemia** associated with inappropriate secretion of antidiuretic hormone.

Other adverse effects that have been reported are increased appetite with weight gain for occasionally anorexia with weight loss. Sweating may be a problem.

A 55-year-old male who is being treated with lithium for a bipolar disorder has a long history of hypertension for which he is receiving escalating doses of medication. On his most recent visit to clinic his blood pressure was noted to be 166/102 mmHg and a new antihypertensive was added to his current antihypertensive therapy.

Five days later he presents with features of lithium toxicity including tremor, nausea and weakness.

The addition of which of the following drugs was likely to have precipitated the lithium toxicity?

(Please select 1 option)

<input type="radio"/>	Doxazosin
<input type="radio"/>	Hydralazine
<input type="radio"/>	Irbesartan
<input type="radio"/>	Minoxidil
<input type="radio"/>	Moxonidine

<input type="radio"/>	Doxazosin
<input type="radio"/>	Hydralazine
<input type="radio"/>	Irbesartan This is the correct answer
<input checked="" type="radio"/>	Minoxidil Incorrect answer selected
<input type="radio"/>	Moxonidine

Key Learning Points

Pharmacology

- ACE inhibitors and angiotensin antagonists are also capable of precipitating lithium toxicity through reduced lithium clearance.

Explanation

The precipitation of lithium toxicity by diuretics is well appreciated. Yet [ACE inhibitors](#) and angiotensin antagonists are also capable of precipitating lithium toxicity through reduced lithium clearance.

Other drugs that may precipitate [lithium toxicity](#) include:

- NSAIDs
- Tetracycline
- Phenytoin, and
- Ciclosporin.

A 45-year-old female with chronic schizophrenia was recently converted to a new antipsychotic agent. She presented two weeks later with a sore throat and fever.

Her full blood count shows:

Haemoglobin	125 g/L	(115-165)
White cell count	$1.3 \times 10^9/L$	(4-11)
Platelets	$135 \times 10^9/L$	(150-400)

What drug is she likely to have commenced?

(Please select 1 option)

<input type="radio"/>	Clozapine
<input type="radio"/>	Haloperidol
<input type="radio"/>	Olanzapine
<input type="radio"/>	Quetiapine
<input type="radio"/>	Risperidone

Dr. Assem

Please select 1 option)



Clozapine

This is the correct answer



Haloperidol



Olanzapine



Quetiapine



Risperidone

Incorrect answer selected

Key Learning Points

Pharmacology, Psychiatry, Therapeutics

- A serious side effect of clozapine is agranulocytosis. Leukopaenia is an indication to permanently stop clozapine treatment.

Explanation

Clozapine is associated with agranulocytosis and granulocytopenia in approximately 1-2% of patients, which can result in fatal sepsis. The mechanism through which this happens remains unclear.

In order to safeguard against harm a UK Clozaril Patient Monitoring System ensures strict monitoring of all patients on this treatment. A white cell count with differential is checked prior to treatment, then weekly for the first 18 weeks, then two weekly from week 18 to 52, and then four weekly after one year of clozapine with stable blood results. They are then checked for four weeks after discontinuation of treatment.

Olanzapine has been associated with agranulocytosis in the form of case reports in the literature. However, unlike clozapine, this link is not well established.

None of the other medications listed are commonly associated with agranulocytosis.

Dr. Arsen

A 76-year-old man attended the outpatient clinic for a routine follow up appointment.

He had presented to hospital with acute dyspnoea six months previously and had been diagnosed with severe aortic regurgitation. During his admission he had undergone aortic valve replacement with a mechanical valve.

During the consultation he does not report any residual dyspnoea or ankle swelling. His INR is stable and is checked regularly by his general practitioner. His only complaint is of difficulty sleeping, which he says started when his wife died suddenly one year previously. He wakes at 4 am and has difficulty getting back to sleep. He lives alone and has no enjoyment in life since the death of his wife. In recounting his wife's death he is very tearful and says that he often cries without any apparent reason.

What would be the best choice of antidepressant in this case?

(Please select 1 option)

<input type="radio"/>	Amitriptyline
<input type="radio"/>	Citalopram
<input type="radio"/>	Fluoxetine
<input type="radio"/>	St John's wort
<input type="radio"/>	Venlafaxine

<input type="radio"/>	Amitriptyline	
<input type="radio"/>	Citalopram	This is the correct answer
<input type="radio"/>	Fluoxetine	
<input type="radio"/>	St John's wort	
<input checked="" type="radio"/>	Venlafaxine	Incorrect answer selected

Key Learning Points

Psychiatry, Therapeutics

- Citalopram is the safest antidepressant to use in patients who are also prescribed warfarin.

Explanation

Warfarin has a narrow therapeutic index which is affected by a number of drugs, primarily through the cytochrome P450 isoenzyme system. Selective serotonin re-uptake inhibitors (SSRIs) may enhance the anticoagulant effect of warfarin, as may the serotonin and noradrenaline re-uptake inhibitor (SNRI) venlafaxine. However, current data suggests that sertraline and citalopram appear to be the safest antidepressants to prescribe with warfarin. Fluvoxamine and fluoxetine appear to pose the highest potential risk. The remaining antidepressants appear to lie somewhere in between.

St John's wort (*Hypericum perforatum*), a herbal antidepressant available over the counter in the United Kingdom, reduces the anticoagulant effect of warfarin and concomitant use should be avoided. In cases of true depression, as here, an antidepressant is indicated.

Tricyclic antidepressants are used much less frequently now, as safer antidepressants have been introduced. Their use in cardiac patients is associated with a number of potential complications, due to antimuscarinic and quinidine-like properties. There is a dose-dependent increase in the plasma half-life of warfarin.

Venlafaxine has been reported to enhance warfarin, and it must be used with caution in patients with cardiac disease. As with tricyclics, NICE recommends that it should not be used in patients with a high risk of serious cardiac arrhythmias or a recent myocardial infarction.

A 45-year-old male attends for an insurance medical and is in good health.

Examination was normal but investigations reveal that he has a serum urate concentration of 0.55 mmol/L (0.25-0.45).

Which of the following is the most appropriate management for this patient?

(Please select 1 option)

<input type="radio"/>	Lifestyle advice
<input type="radio"/>	Start allopurinol
<input type="radio"/>	Start colchicine
<input type="radio"/>	Start diclofenac
<input type="radio"/>	Start prednisolone

(Please select 1 option)

<input type="radio"/>	Lifestyle advice	This is the correct answer
<input type="radio"/>	Start allopurinol	
<input type="radio"/>	Start colchicine	
<input type="radio"/>	Start diclofenac	
<input checked="" type="radio"/>	Start prednisolone	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- For asymptomatic patients with isolated slightly elevated urate is lifestyle advice with an appropriately reduced purine diet.

Explanation

The most appropriate treatment for this asymptomatic man with an isolated slightly elevated urate is lifestyle advice with an appropriately reduced purine diet, increased exercise and reduced alcohol consumption.

A 62-year-old woman presents with a one year history of worsening bilateral, anterior knee pain. The pain is increased by climbing stairs. Both knees are stiff for five to 10 minutes in morning. There is no history of knee swelling. The pain is partially controlled by paracetamol 1 g up to four times a day. She has a history of diabetes, and angina.

On examination, she is overweight. There is crepitus and during active and passive movement of both knees. There is no knee effusion. A recent knee x ray shows joint space narrowing in the medial tibio-femoral joint.

What is the next step in her management?

(Please select 1 option)

<input type="radio"/>	Acupuncture
<input type="radio"/>	Oral NSAIDs
<input type="radio"/>	Rest
<input type="radio"/>	Topical NSAIDs
<input type="radio"/>	Transcutaneous electrical nerve stimulation (TENS)

Please select 1 option

<input type="radio"/>	Acupuncture	
<input checked="" type="radio"/>	Oral NSAIDs	
<input type="radio"/>	Rest	
<input type="radio"/>	Topical NSAIDs	This is the correct answer
<input checked="" type="radio"/>	Transcutaneous electrical nerve stimulation (TENS)	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Treatment of knee OA

Explanation

This lady has osteoarthritis.

NICE guidelines recommend formulating individualised management plans for patients with osteoarthritis.

Behavioural change, such as exercise, weight loss and suitable footwear should be encouraged. Comorbidities which compound the effect of osteoarthritis symptoms should be identified and their treatment optimised.

Paracetamol and/or topical NSAIDs (for knee or hand OA) should be offered before considering oral NSAIDs.

If symptoms are not controlled with the above strategies, oral NSAIDs or COX-2 inhibitors (but not etoricoxib) can be used. A proton pump inhibitor should be co-prescribed. The lowest effective dose should be prescribed for the shortest period possible. If the patient is already taking low-dose aspirin, an alternative analgesic should be considered.

Treatments which are not recommended include rubefacients, intra-articular hyaluronan, electro-acupuncture and chondroitin or glucosamine products.

Adjuvants which can be used include opioid analgesics, topical capsaicin and intra-articular corticosteroids.

Application of heat or cold packs, or TENS, can be considered if other strategies are ineffective. Manipulation and stretching can be helpful, particularly for hip osteoarthritis. Bracing/joint supports can be used for patients with biomechanical joint pain or instability.

Patients should be referred for joint surgery if they have already been offered all of the core treatments or if they have refractory joint symptoms which have a substantial impact on their quality of life.

If there is a clear history of mechanical locking, referral for arthroscopic lavage and debridement should be considered.

You are discussing the optimal medication for use in a patient who needs to withdraw from heroin. He seems motivated and would like to try tablet therapy. He failed to stay clean during the last month, having used street heroin on up to five occasions.

Which of the following is the most effective in preventing use of heroin?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Buprenorphine |
| <input type="radio"/> | Buprenorphine and naloxone combination tablets |
| <input type="radio"/> | Codeine phosphate |
| <input type="radio"/> | Dihydrocodeine |
| <input type="radio"/> | Morphine |

(Please select 1 option)

<input type="radio"/>	Buprenorphine	
<input checked="" type="radio"/>	Buprenorphine and naloxone combination tablets	This is the correct answer
<input type="radio"/>	Codeine phosphate	
<input type="radio"/>	Dihydrocodeine	
<input type="radio"/>	Morphine	Incorrect answer selected

Key Learning Points

Pharmacology

- The purpose of combining buprenorphine and naloxone for the treatment of opioid action is that it prevents addicts from achieving a high if they try to create an IV preparation from the tablets for injection.

Explanation

Buprenorphine is a partial opiate agonist which binds mu and kappa opiate receptors in the brain. A partial agonist occupies and modulates the receptor without exerting the euphoric effects that would be gained by injecting IV heroin, a full agonist, because it does not exert the full effect.

Naloxone is an opioid antagonist which binds at mu opioid receptors. This means that it blocks the action of opioid agonists such as morphine.

The purpose of combining buprenorphine and naloxone for the treatment of opioid action is that it prevents addicts from achieving a high if they try to create an IV preparation from the tablets for injection.

Dr Assem

A 60-year-old female suffers from bipolar affective disorder and is being treated with lithium. She also has a long history of hypertension for which she is on treatment.

During a recent clinic visit her blood pressure was noted to be 170/94 mmHg and a new antihypertensive agent was added. A week later she presents with features of lithium toxicity including tremor, nausea and weakness.

The addition of which one of the following drugs was likely to have precipitated the lithium toxicity?

(Please select 1 option)

<input type="radio"/>	Doxazosin
<input type="radio"/>	Hydralazine
<input type="radio"/>	Lisinopril
<input type="radio"/>	Minoxidil
<input type="radio"/>	Moxonidine

<input type="radio"/>	Doxazosin	
<input type="radio"/>	Hydralazine	
<input type="radio"/>	Lisinopril	This is the correct answer
<input type="radio"/>	Minoxidil	
<input checked="" type="radio"/>	Moxonidine	Incorrect answer selected

Key Learning Points

Pharmacology

- ACE inhibitors and angiotensin antagonists are capable of precipitating lithium toxicity through reduced lithium clearance.

Explanation

The precipitation of lithium toxicity by diuretics is well appreciated. Yet [ACE inhibitors](#) [log-in required for full text] and angiotensin antagonists are also capable of precipitating lithium toxicity through reduced lithium clearance.

Other drugs that may precipitate [lithium toxicity](#) include:

- NSAIDs
- Tetracycline
- Phenytoin, and
- Ciclosporin.

A 38-year-old male is admitted with an hour history of chest pain, confusion and agitation commencing shortly after taking a recreational drug.

On examination, he is confused, has a temperature of 38.3°C and a blood pressure of 188/102 mmHg.

Which of the following drugs is most likely to be responsible for his presentation?

(Please select 1 option)

<input type="radio"/>	Cocaine
<input type="radio"/>	Ecstasy (MDMA)
<input type="radio"/>	Gamma hydroxybutyrate (GHB)
<input type="radio"/>	LSD
<input type="radio"/>	Opiates

Please select 1 option

<input type="radio"/>	Cocaine	This is the correct answer
<input type="radio"/>	Ecstasy (MDMA)	
<input type="radio"/>	Gamma hydroxybutyrate (GHB)	
<input checked="" type="radio"/>	LSD	Incorrect answer selected
<input type="radio"/>	Opiates	

Key Learning Points

Toxicology

- The risk of a myocardial infarction is increased 24 times in the first hour after cocaine use.

Explanation

In this scenario, the young male presents with confusion and agitation following drug abuse. The most likely agent is cocaine.

Through central effects, cocaine induces sweating, pyrexia and also adrenergic mediated hypertension. It may also be responsible for coronary and cerebral artery spasm causing infarction.

Dr. Assen

A 18-year-old female is brought to the Emergency department unconscious after having taken an overdose.

On examination she has a Glasgow coma score of 6, a respiratory rate of 8 breaths per minute, a heart rate of 52 beats per minute and her blood pressure is 84/62 mmHg. Her pupils are small but are reactive to light, muscle tone is reduced and plantar responses are flexor.

Which of the following is she most likely to have taken in overdose?

(Please select 1 option)

<input type="radio"/>	Diazepam
<input type="radio"/>	Dihydrocodeine
<input type="radio"/>	Diphenhydramine
<input type="radio"/>	Ecstasy (MDMA)
<input type="radio"/>	Methanol

<input type="radio"/>	Diazepam
<input type="radio"/>	Dihydrocodeine This is the correct answer
<input type="radio"/>	Diphenhydramine
<input type="radio"/>	Ecstasy (MDMA)
<input checked="" type="radio"/>	Methanol Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- Dihydrocodeine is an opiate analgesic and when taken in overdose, acts as a respiratory depressant leading to reduced respiratory rate. It can cause bradycardia and hypotension in large doses. Pupillary constriction is a diagnostic feature in opiate overdose.

Explanation

Dihydrocodeine is an opiate analgesic and when taken in overdose has a number of toxic effects. It acts as a respiratory depressant leading to reduced respiratory rate. It can cause bradycardia and hypotension in large doses. Pupillary constriction is a diagnostic feature in opiate overdose.

It is also a central nervous system depressant and therefore causes coma in overdose.

Benzodiazepines and antihistamines tend not to have the same cardiorespiratory effects as opiates.

MDMA is a stimulant and can cause delirium, convulsions and ventricular arrhythmias.

Diazepam would be less likely here due to the bradycardia and the hypotension.

Which of the following does N-acetylcysteine replenish?

(Please select 1 option)

- | | |
|-----------------------|------------------------|
| <input type="radio"/> | Cystathionine |
| <input type="radio"/> | Cytochrome P450 |
| <input type="radio"/> | Glucuronyl transferase |
| <input type="radio"/> | Glutathione |
| <input type="radio"/> | Sulfatase |

Dr. Assem

(Please select 1 option)

<input type="radio"/>	Cystathionine	
<input type="radio"/>	Cytochrome P450	
<input type="radio"/>	Glucuronyl transferase	
<input type="radio"/>	Glutathione	This is the correct answer
<input checked="" type="radio"/>	Sulfatase	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- N-Acetylcysteine is an antidote for paracetamol overdose.

Explanation

Acetylcysteine, the N-acetyl derivative of the naturally occurring amino acid L-cysteine, is a mucolytic agent and sulfhydryl donor acting as an antidote for paracetamol overdose.

A 51-year-old female has rheumatoid arthritis.

She states that she is allergic to penicillin and co-trimoxazole.

Therefore, which of the following drugs is contraindicated?

(Please select 1 option)

- | | |
|-----------------------|----------------|
| <input type="radio"/> | Azathioprine |
| <input type="radio"/> | Ciclosporin |
| <input type="radio"/> | Gold therapy |
| <input type="radio"/> | Methotrexate |
| <input type="radio"/> | Sulphasalazine |

(Please select 1 option)

<input type="radio"/>	Azathioprine
<input type="radio"/>	Ciclosporin
<input type="radio"/>	Gold therapy
<input type="radio"/>	Methotrexate
<input checked="" type="radio"/>	Sulphasalazine Correct

Key Learning Points

Pharmacology, Rheumatology

- An allergy to co-trimoxazole would be a contraindication to the use of sulphasalazine.

Explanation

Both co-trimoxazole and sulphasalazine contain sulphonamide groups and hence an allergy to co-trimoxazole would be a contraindication to the use of sulphasalazine.

Co-trimoxazole is a mixture of trimethoprim and sulfamethoxazole.

Sulphasalazine is a combination of 5-aminosalicylic acid and sulfapyridine. It is commonly used in the treatment of inflammatory bowel disease, and can also be used in rheumatoid and psoriatic arthritis.

Azathioprine is a purine analogue which is commonly used as a steroid-sparing agent.

Ciclosporin is a calcineurin inhibitor, used for the prevention of transplant rejection.

Gold therapy was previously used as a disease modifying agent in rheumatoid arthritis, but this has now been replaced by methotrexate which is a dihydrofolate reductase inhibitor.

A 30-year-old male presented with a paranoid psychosis accompanied by visual hallucinations which resolved over the next three days.

Which one of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Alcohol withdrawal
<input type="radio"/>	Diazepam dependence
<input type="radio"/>	Fluoxetine overdose
<input type="radio"/>	Heroin withdrawal
<input type="radio"/>	Smoking cannabis

<input checked="" type="radio"/>	Alcohol withdrawal	This is the correct answer
<input type="radio"/>	Diazepam dependence	
<input type="radio"/>	Fluoxetine overdose	
<input type="radio"/>	Heroin withdrawal	
<input checked="" type="radio"/>	Smoking cannabis	Incorrect answer selected

Key Learning Points

Pharmacology, Psychiatry

- Alcoholic hallucinosis can appear 12-24 hours after stopping alcohol and includes visual, auditory and tactile hallucinations

Explanation

The key points in the history are that, firstly, these are visual hallucinations and secondly that they resolve over 72 hours. Of all the options given, **alcohol withdrawal** is the most likely. The fact that this patient has paranoid psychosis makes it even more likely.

Symptoms typically present about 8 hours after a significant fall in blood alcohol levels. The peak is on day two, and by day five the symptoms are significantly better. Minor withdrawal symptoms appear 6-12 hours after cessation of alcohol and include:

- Insomnia
- Fatigue
- Tremor
- Anxiety
- Nausea
- Vomiting
- Headache
- Sweating
- Palpitations
- Anorexia
- Depression, and
- Craving

Alcoholic hallucinosis can appear 12-24 hours after stopping alcohol and includes visual, auditory and tactile hallucinations. Withdrawal seizures can appear 24-28 hours after cessation and are generalised tonic-clonic seizures. **Alcohol withdrawal** delirium (delirium tremens) can appear 48-72 hours after cessation. Mortality without treatment is approximately 35%.

Benzodiazepines can cause a protracted withdrawal syndrome, with symptoms persisting for 6 months or more. It is characterised by anxiety, irritability, **insomnia** and sensory disturbance. In severe cases it can resemble mania and schizophrenia.

Fluoxetine overdose typically causes few symptoms, but can be associated with arrhythmias.

Heroin withdrawal has significant physical symptoms, including tremors, cramps, muscle and bone pain, rhinitis, tachycardia and diarrhoea and vomiting, in addition to psychiatric symptoms.

Cannabis use causes relaxation, euphoria, short-term memory loss and dry mouth and eyes. A withdrawal syndrome is recognised but not well defined. Long-term use has been linked with paranoia and **schizophrenia**, but these symptoms do not resolve quickly and visual hallucinations are unlikely.

A 49-year-old woman presents to the Emergency department with right sided pleuritic chest pain. She has had two previous pulmonary emboli (PE) and is on lifelong warfarin therapy.

On examination she is short of breath and in pain. Her BP is 105/70 mmHg and her pulse is 92. Auscultation of the chest is normal. She has a swollen left leg, but she tells you this is chronic since an extensive DVT a few years earlier.

Investigations reveal:

Haemoglobin	125 g/L	(115-165)
White cell count	$7.2 \times 10^9/L$	(4-11)
Platelets	$203 \times 10^9/L$	(150-400)
Serum sodium	137 mmol/L	(135-146)
Serum potassium	4.2 mmol/L	(3.5-5)
Creatinine	82 $\mu\text{mol/L}$	(79-118)
INR	2.2	(2-3)
CXR	No focal changes	-
CTPA	Subsegmental pulmonary emboli	-
PaO ₂	8.2 kPa	(10-13.3)
PaCO ₂	4.2 kPa	(4.8-6.1)

Which of the following is the most appropriate next step?

(Please select 1 option)

<input type="radio"/>	Add aspirin to her therapy
<input type="radio"/>	Add clopidogrel to her therapy
<input type="radio"/>	Increase the INR target to 3-4
<input type="radio"/>	Increase the INR target to 4-5
<input type="radio"/>	Refer for an IVC filter

Please select 1 option

<input type="radio"/>	Add aspirin to her therapy
<input type="radio"/>	Add clopidogrel to her therapy
<input type="radio"/>	Increase the INR target to 3-4
<input type="radio"/>	Increase the INR target to 4-5
<input checked="" type="radio"/>	Refer for an IVC filter Correct

Key Learning Points

Pharmacology, Therapeutics

- In this situation, where she is anticoagulated yet has sustained a further PE, there are two potential choices, either to consider increasing her INR target to 3-4, or considering an IVC filter.

Explanation

In this situation, where she is anticoagulated yet has sustained a further PE, there are two potential choices, either to consider increasing her INR target to 3-4, or considering an IVC filter.

Contraindications to anticoagulation where an IVC filter may be considered include:

- Haemorrhagic stroke
- Recent neurosurgery or other major surgery
- Major trauma, and
- Evidence of active internal bleeding.

Other contraindications include:

- Pregnancy
- Frequent falls, and
- Poor potential compliance with warfarin.

In these situations an IVC filter may be the most appropriate option. Given her young age and the potential for further PEs, a filter may be considered ahead of increased warfarin dose.

IVC filters may also be considered for prophylaxis in patients who have a diagnosis of cancer or who have a DVT and are about to undergo surgery. In this case, anticoagulation may result in more problems than filter placement.

A previous relative contraindication to filter placement was the need to undergo MRI, but now, MRI proof filters are available and this is no longer a problem.

Reference:

British Committee for Standards in Haematology Writing Group, et al. [Guidelines on use of vena cava filters](#). *Br J Haematol*.

2006;124:100-5

A 55-year-old gentleman has been taking methotrexate 7.5 mg weekly for seronegative erosive rheumatoid arthritis with considerable clinical and symptomatic improvement. He has been on this dose for three months.

His most recent investigations, performed two days ago, reveal the following:

Haemoglobin	129 g/L	(120-165)
White cell count	$5.3 \times 10^9/L$	(4-11)
Platelets	$183 \times 10^9/L$	(150-400)
Urea	4.2 mmol/L	(2.5-7.5)
Creatinine	88 $\mu\text{mol/L}$	(60-110)
Alkaline phosphatase	92 U/L	(60-110)
AST	22 U/L	(1-31)
ALT	15 U/L	(5-35)

When should the next FBC be performed?

(Please select 1 option)

<input type="radio"/>	One week
<input type="radio"/>	Two weeks
<input type="radio"/>	One month
<input type="radio"/>	Six months
<input type="radio"/>	One year

(Please select 1 option)

<input type="radio"/>	One week	
<input type="radio"/>	Two weeks	
<input type="radio"/>	One month	This is the correct answer
<input type="radio"/>	Six months	
<input checked="" type="radio"/>	One year	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Clinicians are recommended to check FBC fortnightly until 6 weeks after the last dose increase. Provided it is stable, it can be checked monthly thereafter until the dose and disease is stable for one year.

Explanation

His results are normal and he is receiving a stable dose of methotrexate.

The most appropriate time interval for monitoring his full blood count (FBC) according to current UK guidance would therefore be in one month.

Clinicians are recommended to check FBC fortnightly until 6 weeks after the last dose increase. Provided it is stable, it can be checked monthly thereafter until the dose and disease is stable for one year.

Thereafter, monitoring is guided by clinical judgement. If white cell count is less than 3.5, neutrophils less than 2 or platelets less than 150, methotrexate should be withheld pending discussion with the specialist team. An MCV greater than 105 fL warrants checking B12, folate and TSH and treating any abnormality. If these are normal, discuss with the specialist team.

Liver function tests should be checked three monthly. If there is an unexplained decrease in albumin, or AST/ALT twice the upper limit of normal, the specialist team should be informed.

Urea, creatinine and electrolytes should be checked six monthly. If the estimated glomerular filtration rate falls below 50 mL/minute, methotrexate should be withheld until the result has been discussed with the specialist team.

In addition to this monitoring, any clinical signs of toxicity should be monitored for. If the patient develops rash, oral ulceration, nausea, vomiting or diarrhoea, methotrexate should be withheld until discussed with the specialist team. Any new or increasing dyspnoea or dry cough should be urgently discussed with secondary care, and methotrexate withheld. A sore throat or abnormal bruising should be investigated with an FBC, and methotrexate withheld until the results available.

Reference:

A 79-year-old male with critical ischaemia of his foot is awaiting below knee amputation and has lower limb pain despite IV paracetamol.

He is awake and lucid with normal observations.

His full blood count shows:

Haemoglobin	120 g/L	(130-180)
White cell count	$14.0 \times 10^9/L$	(4-11)
Platelets	$67 \times 10^9/L$	(150-400)

Which of the following is the next most appropriate option for pain relief?

(Please select 1 option)

<input type="radio"/>	Diclofenac 50 mg per oram
<input type="radio"/>	Epidural analgesia
<input type="radio"/>	A single shot femoral nerve block
<input type="radio"/>	Morphine PCA
<input type="radio"/>	Tramadol

Dr. Assem

Please select 1 option

<input type="radio"/>	Diclofenac 50 mg per oram
<input type="radio"/>	Epidural analgesia
<input type="radio"/>	A single shot femoral nerve block
<input type="radio"/>	Morphine PCA
<input checked="" type="radio"/>	Tramadol Correct

Key Learning Points

Pharmacology

- Analgesia should be given as per the WHO ladder - paracetamol, NSAIDs (if not contraindicated), weak opiates, strong opiates.

Explanation

Of the options given, tramadol is the best and follows the WHO analgesic ladder.

In a 79-year-old arteriopath diclofenac is best avoided for fear of renal damage. It is now contraindicated for use in those with heart disease which must be assumed in a patient with limb ischaemia.

Epidural analgesia may confer benefits, especially pre-operatively for below knee amputation and would be appropriate if the operation were to be delayed. However with platelets of $67 \times 10^9/L$ most anaesthetists would be reluctant to site one.

Femoral nerve block is a relatively simple procedure which may help, but will give incomplete cover (not much effect on ischaemic foot pain) and will only provide transient pain relief.

A morphine PCA would be appropriate if the patient was unable to take analgesia orally or if oral opiates proved ineffective. A PCA is generally only used for a short period but would be suitable for pain relief before and after the amputation as the delay before surgery should be short.

A 42-year-old man presented with confusion following a seizure.

He has a history of epilepsy and is also known to the community psychiatry team.

Examination reveals that he has a temperature of 37°C, BP 138/84 mmHG, coarse tremor and a pulse of 90 bpm. On examination he has brisk reflexes, and 7 beats of nystagmus on lateral gaze.

Which of the following is the most likely underlying diagnosis?

(Please select 1 option)

- | | |
|-----------------------|--------------------------------|
| <input type="radio"/> | Benzodiazepine overdose |
| <input type="radio"/> | Carbamazepine toxicity |
| <input type="radio"/> | Lithium toxicity |
| <input type="radio"/> | Neuroleptic malignant syndrome |
| <input type="radio"/> | Tricyclic overdose |

Lowest 1 point
Severe hypoxia, anoxia
Cardiomyogenic toxicity
Lithium toxicity Severe hypoxia, anoxia
Neuroleptic malignant syndrome
Toxicity overdose Severe hypoxia, anoxia

Key Learning Points

Pharmacology, Psychiatry, Toxicology

- Lithium toxicity occurs at levels above 1.4 mmol/L, and can result in hypoxia, anoxia, vomiting, ataxia, hyperreflexia, dysreflexia, confusion and seizures.

Explanation

The correct answer and comment should note the possibility of lithium toxicity which is the condition that best fits this clinical picture.

Lithium toxicity occurs at levels above 1.4 mmol/L, and can result in:

- Ataxia
- Diarrhoea
- Vomiting
- Anis
- Hyperreflexia
- Dysreflexia
- Confusion, and
- Seizures.

In the acute range it can be associated with a triad, which can become coarser in toxicity. If allowed to progress, toxicity will result in coma with hyperreflexia and increased tone. Neurological damage can be irreversible. At high can also cause, concerning but doesn't complete heart block is also seen.

Generally, treatment is supportive and attention must be paid to electrolytes, fluid balance, renal function and seizure control. Treatment should be considered, as blood regulation can be used in significant acute overdose. Diuretics should be avoided. Haemodialysis may be required, and charcoal adsorption can control agitation.

Severe hypoxia, anoxia presents with:

- Seizures
- Diarrhoea
- Anis
- Impaired motor function
- Arrhythmia
- Seizures
- Hyperreflexia
- Dysreflexia
- Vomiting

In severe hypoxia there can be:

- Diarrhoea
- Anis
- **Severe hypoxia, anoxia**
- Hyperreflexia
- Dysreflexia, and
- Cardiac arrest

Severe hypoxia, anoxia presents with:

- Seizures
- Seizures
- Anis
- Hyperreflexia
- Seizures
- Vomiting
- Seizures
- Seizures
- Seizures
- Seizures

The presence of hyperreflexia and hyperreflexia in this case make lithium more likely than they do share a number of features in toxicity.

Severe hypoxia, anoxia results in rigidity, tremor, automatic instability, decline and altered plasma membrane phospholipase.

Toxicity antidepressants are very toxic to overdose and result in:

- Tachycardia
- Seizures
- Dry mouth
- Flushing and sweating
- Urinary retention
- Confusion
- Agitation, and
- Headache

Severe cases result in hyperreflexia, hyperreflexia, tachycardia, QT prolongation, widening of the QRS, hyperreflexia and seizures.

A 52-year-old Afro-Caribbean gentleman is diagnosed with hypertension after having three blood pressure measurements greater than 160/100 mmHg.

On examination his BMI is 24 kg/m², and he looks well. There is no significant past medical history of note.

According to the NICE guidelines, which of the following is the most appropriate to prescribe first line for this patient?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Atenolol
<input type="radio"/>	Diltiazem
<input type="radio"/>	Ramipril
<input type="radio"/>	Valsartan

<input type="radio"/>	Amlodipine	This is the correct answer
<input type="radio"/>	Atenolol	
<input type="radio"/>	Diltiazem	
<input checked="" type="radio"/>	Ramipril	Incorrect answer selected
<input type="radio"/>	Valsartan	

Key Learning Points

Pharmacology

- Amlodipine is the most effective in reducing systolic and diastolic blood pressures over a range of doses widely used in clinical practice.

Explanation

Patients of African origin are more likely to have low renin hypertension. This means that they are more likely to respond to initial therapy with either a calcium antagonist or diuretic, usually a thiazide. A number of studies have shown that although both amlodipine and diltiazem are well tolerated, amlodipine is more effective in reducing systolic and diastolic blood pressures over a range of doses widely used in clinical practice.

Thiazides and beta blockers have been implicated in a meta-analysis as being associated with increased risk of developing insulin resistance, but given his BMI is in the normal range this is unlikely to be a significant problem.

In contrast those patients of Caucasian origin who tend to have higher levels of renin respond much more readily to angiotensin-converting enzyme (ACE) inhibition, or if they fail to tolerate an ACE inhibitor because of cough, to an angiotensin receptor blocker. For these patients, ACE inhibition is seen by NICE as the first line treatment.

Combination therapies were designed originally around the ABCD guidelines from the British Hypertension Society, but because of the analysis which suggested increased risk of diabetes when beta blockade is combined with a thiazide, the combination of these two is no longer recommended.

Following the ASCOT study however, the ACE inhibitor calcium antagonist combination has been the one preferred by many clinicians.

A 64-year-old woman presented 10 hours after ingestion of 12 g of quinine sulphate.

Which of the following is the most common characteristic clinical feature in this situation?

(Please select 1 option)

- | | |
|-----------------------|----------------|
| <input type="radio"/> | Blindness |
| <input type="radio"/> | Bradycardia |
| <input type="radio"/> | Hyperacusis |
| <input type="radio"/> | Hyperglycaemia |
| <input type="radio"/> | Hypotension |

<input type="radio"/>	Blindness	This is the correct answer
<input type="radio"/>	Bradycardia	
<input type="radio"/>	Hyperacusis	
<input type="radio"/>	Hyperglycaemia	
<input checked="" type="radio"/>	Hypotension	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- The major toxic effects of quinine are on the nervous system, in particular the optic and auditory nerve.

Explanation

The major toxic effects of quinine are on the nervous system, in particular the optic and auditory nerve. It is also particularly toxic on retinal photoreceptor cells, and causes vasoconstriction and spasm of the retinal artery. Blurred vision can proceed to complete blindness, which is characteristic of overdose. Initial signs are narrowing of the retinal arterioles on fundoscopy. Later there is retinal oedema, and the pupils become dilated and unresponsive to light.

Effects on the auditory nerve may cause **tinnitus** and deafness, but not hyperacusis.

Initially quinine causes generalised stimulation of the central nervous system, leading to tachycardia, fever, delirium and tachypnoea. In severe overdose it can then cause myocardial depression, peripheral vasodilatation and widened QRS with prolonged QTc and risk of VT, torsade and VF.

In addition, renal failure, **haemolytic anaemia** and gastrointestinal disturbance can develop. At very high plasma levels, sinoatrial block and high-degree **atrioventricular block** may be seen. Hypotension may occur secondary to quinine's alpha-blocking effect, but is not as characteristic as blindness.

Additional features include:

- nausea
- vomiting
- headache
- seizures
- fatigue
- tremor, and
- ataxia.

Hyperglycaemia is not characteristic.

Management is with activated charcoal and gastric lavage, if presentation is early enough. **Bradycardia** can be treated with atropine or pacing. Bicarbonate is considered for a prolonged QRS (>120 ms), aiming for a pH of 7.45-5. Haemodialysis can also be used to clear the quinine. There is no specific treatment for visual disturbance.

A 46-year-old lady with rheumatoid arthritis whose regular medications include methotrexate, folic acid, Adcal-D3, ibuprofen and paracetamol attends the GP surgery with a sore throat.

On examination she has enlarged tonsils with pus, tender cervical lymphadenopathy and a fever of 38.5°C. There is no cough.

Which of the following options represents the most appropriate management plan?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | Admit the patient to hospital as an emergency with suspected neutropaenic sepsis |
| <input type="radio"/> | Commence benzylpenicillin 500 mg QDS for 10 days |
| <input type="radio"/> | Give the patient advice about self-management of sore throat and advise to return if she does not improve in the next five days |
| <input type="radio"/> | Send an urgent venous blood sample for full blood count and commence phenoxymethylpenicillin 500 mg QDS for 10 days |
| <input type="radio"/> | Send an urgent venous blood sample for full blood count and give the patient advice about self-management of sore throat |

<input type="radio"/>	Admit the patient to hospital as an emergency with suspected neutropaenic sepsis
<input type="radio"/>	Commence benzylpenicillin 500 mg QDS for 10 days
<input type="radio"/>	Give the patient advice about self-management of sore throat and advise to return if she does not improve in the next five days
<input type="radio"/>	Send an urgent venous blood sample for full blood count and commence phenoxymethylpenicillin 500 mg QDS for 10 days This is the correct answer
<input checked="" type="radio"/>	Send an urgent venous blood sample for full blood count and give the patient advice about self-management of sore throat Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology, Therapeutics

- Marrow failure in patients taking methotrexate can present with fever and sore throat.

Explanation

Marrow failure in patients taking methotrexate can present with fever and sore throat. A full blood count to exclude this serious complication of methotrexate therapy is required. However, there are clear signs of **tonsillitis** making this the most likely diagnosis.

The patient meets the Centor criteria for antibiotic treatment of sore throat and as she is on immunosuppressant medication treatment with antibiotics would be reasonable.

The Centor criteria indicate that **tonsillitis** is more likely to be bacterial in origin if four of the following features are present:

- Anterior cervical adenopathy
- Tonsillar exudates
- Fever and
- Absence of cough.

Methotrexate must be stopped in the setting of infection and should only be restarted once all symptoms have resolved.

If the full blood count showed significant cytopenia hospital admission may be warranted, but otherwise the patient can be managed in the community.

A 68-year-old man with a history of type 2 diabetes, chronic renal failure and epilepsy is admitted to the Emergency department with anorexia, nausea, and increasing lethargy.

He also developed tremor and nystagmus, with truncal ataxia and strange choreoathetoid movements. He takes BD mixed insulin for his diabetes, phenytoin for his epilepsy, ramipril and amlodipine for his hypertension.

On examination his BP is 159/88 mmHg, his pulse is 90. He has bilateral crackles on auscultation of his chest consistent with fluid overload.

Investigations reveal:

Haemoglobin	105 g/L	(135-177)
White cells	$7.8 \times 10^9/L$	(4-11)
Platelets	$182 \times 10^9/L$	(150-400)
Sodium	139 mmol/L	(135-146)
Potassium	5.7 mmol/L	(3.5-5)
Creatinine	231 $\mu\text{mol/L}$	(79-118)
HbA _{1c}	53 mmol/mol	(<35)
Phenytoin levels	Within the therapeutic range	

Which of the following is the most likely reason for his phenytoin toxicity?

(Please select 1 option)

<input type="radio"/>	Decreased GI absorption of phenytoin
<input type="radio"/>	Decreased hydroxylation of phenytoin
<input type="radio"/>	Decreased protein binding of phenytoin
<input type="radio"/>	Increased protein binding of phenytoin
<input type="radio"/>	Increased renal cycling of phenytoin metabolites

<input type="radio"/>	Decreased GI absorption of phenytoin	
<input type="radio"/>	Decreased hydroxylation of phenytoin	
<input type="radio"/>	Decreased protein binding of phenytoin	This is the correct answer
<input type="radio"/>	Increased protein binding of phenytoin	
<input checked="" type="radio"/>	Increased renal cycling of phenytoin metabolites	Incorrect answer selected

Key Learning Points

Pharmacology

- In patients with renal failure, dose reduction of drugs that are usually highly protein bound is required to reduce the risk of toxicity.

Explanation

This patient has renal failure, a state in which drugs that are usually highly protein bound, such as phenytoin, lose some of their affinity for protein binding. This results in increased availability of free drug at any given dose, which then increases the risk of toxicity.

Because laboratory assays for phenytoin usually measure total drug concentration, this gives a degree of false reassurance.

In patients with renal failure, dose reduction of phenytoin is therefore required.

Other drugs where this may be a problem include sodium valproate and warfarin.

In the treatment of hyperlipidaemia, what is the mechanism of action of ezetimibe?

(Please select 1 option)

<input type="radio"/>	Inhibit hepatic secretion of VLDL
<input type="radio"/>	Prevent cholesterol absorption from the intestine
<input type="radio"/>	Reduced cholesterol synthesis through inhibition of the enzyme HMG CoA reductase
<input type="radio"/>	Reduced expression of LDL receptors in the liver surface
<input type="radio"/>	Stimulate increased action of the enzyme lipoprotein lipase

(Please select 1 option)

<input type="radio"/>	Inhibit hepatic secretion of VLDL	
<input type="radio"/>	Prevent cholesterol absorption from the intestine	This is the correct answer
<input type="radio"/>	Reduced cholesterol synthesis through inhibition of the enzyme HMG CoA reductase	
<input type="radio"/>	Reduced expression of LDL receptors in the liver surface	
<input checked="" type="radio"/>	Stimulate increased action of the enzyme lipoprotein lipase	Incorrect answer selected

Key Learning Points

Pharmacology

- Ezetimibe reduces the absorption of cholesterol through the gut, although the exact mechanism of action is unclear. Unlike bile acid sequestrants, ezetimibe is systemically absorbed.

Explanation

Ezetimibe reduces the absorption of cholesterol through the gut.

Although its exact mechanism of action is unclear, it probably downregulates proteins in the brush border of enterocytes to reduce lipid absorption. Unlike bile acid sequestrants, ezetimibe is systemically absorbed.

Ezetimibe is a useful medication for patients who are:

- intolerant of statins
- failing targets on statins alone, and
- have a history of serious adverse events with statin use.

When used as a monotherapy at a dose of 10 mg daily, ezetimibe reduces LDL cholesterol by around 20%. Increasing the dose further generally does not improve efficacy.

When used in conjunction with statins much greater LDL cholesterol reductions are seen.

A mother brings her 3-year-old child to the Emergency department because she is complaining of earache. You collect her from the waiting room where she is happily playing with toys. This is the second episode over the past year.

On examination her temperature is 37.4°C and her right ear drum is pink and bulging consistent with otitis media.

According to the SIGN national guidelines, how will you manage the child?

(Please select 1 option)

<input type="radio"/>	Advise paracetamol and or ibuprofen to relieve her pain
<input type="radio"/>	Prescribe clarithromycin for the child and advise her to start it immediately
<input type="radio"/>	Prescribe penicillin V for the child and advise she starts it immediately
<input type="radio"/>	Prescribe penicillin V for the child and advise she starts it in 24 hours if the pain does not improve
<input type="radio"/>	Refer to the ENT surgeons as this is the second episode

Please select 1 option

<input type="radio"/>	Advise paracetamol and or ibuprofen to relieve her pain	This is the correct answer
<input type="radio"/>	Prescribe clarithromycin for the child and advise her to start it immediately	
<input type="radio"/>	Prescribe penicillin V for the child and advise she starts it immediately	
<input type="radio"/>	Prescribe penicillin V for the child and advise she starts it in 24 hours if the pain does not improve	
<input checked="" type="radio"/>	Refer to the ENT surgeons as this is the second episode	Incorrect answer selected

Key Learning Points

Pharmacology, Therapeutics

- SIGN guidelines point out that in children without significant systemic features of infection such as fever and generalised illness apart from pain, there is no significant benefit of antibiotics.

Explanation

Advise her to take paracetamol and or ibuprofen to relieve her pain.

SIGN guidelines point out that in children without significant systemic features of infection such as fever and generalised illness apart from pain, there is no significant benefit of antibiotics. The guidelines state that if all children were treated with antibiotics, then the number needed to treat (NNT) would be 17 to avoid one clinical failure.

Unfortunately practice in the management of otitis media in children varies considerably in children across the world, from 31% in the Netherlands to 98% in the USA and Australia.

Additionally, for a very common condition, the number of well conducted clinical trials is small. This is one area which could have benefited from better randomised controlled trials of antibiotics at the outset, but on available evidence, rationalisation of antibiotic use to guard against the development of resistance is sensible.

A 22-year-old male is admitted after drinking engine coolant in an apparent suicide attempt after finding his wife in bed with the postman.

Investigations reveal:

pH	7.1	(7.36-7.44)
pO ₂	15.3 kPa	(11.3-12.6)
pCO ₂	3.2 kPa	(4.7-6.0)
Standard bicarbonate	2.2 mmol/L	(20-28)
Serum calcium	1.82 mmol/L	(2.2-2.6)

After replacing calcium which of the following is the most urgent treatment for this man?

(Please select 1 option)

<input type="radio"/>	8.4% bicarbonate infusion
<input type="radio"/>	Alcohol infusion
<input type="radio"/>	Fomepizole infusion
<input type="radio"/>	Gastric lavage
<input type="radio"/>	Haemodialysis

(Please select 1 option)

<input type="radio"/>	8.4% bicarbonate infusion	This is the correct answer
<input type="radio"/>	Alcohol infusion	
<input type="radio"/>	Fomepizole infusion	
<input type="radio"/>	Gastric lavage	
<input checked="" type="radio"/>	Haemodialysis	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- IV fluids with bicarbonate is used to correct the metabolic acidosis

Explanation

Engine coolant contains [ethylene glycol](#). Ingestion of as little as 30-60 ml is capable of causing death.

Traditional management of poisoning includes the use of ethanol, with or without haemodialysis.

Activated charcoal is not indicated and gastric lavage may be beneficial only in the first hour after ingestion.

However fomepizole has recently been approved for use and is a competitive inhibitor of alcohol dehydrogenase. However it is very expensive and the evidence supporting its use over alcohol is lacking. Also, this patient already has a severe metabolic acidosis.

In these circumstances, antidotal therapy to block alcohol dehydrogenase with ethanol or 4-MP alone is insufficient to treat the poisoning. Data suggest that a severe lactic acidosis needs initial correction and in this patient the most appropriate treatment would be IV fluids with bicarbonate to correct the metabolic acidosis.

Then haemodialysis is probably required.

A 16-year-old boy reports palpitations, excessive sweating and tremor occurring almost daily when he walks past a car park where he was mugged four weeks ago.

He is finding the symptoms very troublesome and has started missing school to avoid the car park.

Which of the following psychiatric illnesses does he have?

(Please select 1 option)

<input type="radio"/>	Adjustment disorder
<input type="radio"/>	Agoraphobia
<input type="radio"/>	Anorexia nervosa
<input type="radio"/>	Cynophobia
<input type="radio"/>	Generalised anxiety disorder

(Please select 1 option)

<input type="radio"/>	Adjustment disorder	This is the correct answer
<input type="radio"/>	Agoraphobia	
<input type="radio"/>	Anorexia nervosa	
<input type="radio"/>	Cynophobia	
<input checked="" type="radio"/>	Generalised anxiety disorder	Incorrect answer selected

Key Learning Points

Pharmacology

- Adjustment disorder occurs within three months of an identifiable stressor and lasts six months from the withdrawal of the stressor

Explanation

Adjustment disorder occurs within three months of an identifiable stressor and lasts six months from the withdrawal of the stressor. The patient will show either distress in excess of that expected or a disruption of their day to day life.

The criteria for diagnosing generalised anxiety disorder are anxiety/tension, occasionally accompanied by physical symptoms, on more days than not for more than six months. It is more a diagnosis of exclusion however, as it may be due to prescription medication or another psychiatric illness.

Anxiety disorders can be treated with selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase inhibitor (MAOI).

Benzodiazepines and beta blockers can be used on a PRN basis for patients who suffer with panic attacks.

Cognitive behavioural therapy can also be of help.

Anorexia nervosa is an eating disorder with altered body image.

Agoraphobia is phobia of open spaces.

Cynophobia is phobia of dogs.

A 55-year-old woman is attending clinic a number of months after having had a myocardial infarction.

She has been commenced on appropriate drugs to reduce cardiovascular risk and has made dietary modifications for healthy living. Recently, however, she complains of muscle aches and pains and is found to have an elevated CPK.

Consumption of which of the following is likely to have contributed to increased statin-associated myotoxicity?

(Please select 1 option)

<input type="radio"/>	Carrot juice
<input type="radio"/>	Cranberry juice
<input type="radio"/>	Garlic cloves
<input type="radio"/>	Grapefruit juice
<input type="radio"/>	Omega-3 fish oils

(Please select 1 option)

<input type="radio"/>	Carrot juice	
<input type="radio"/>	Cranberry juice	
<input type="radio"/>	Garlic cloves	
<input checked="" type="radio"/>	Grapefruit juice	This is the correct answer
<input type="radio"/>	Omega-3 fish oils	Incorrect answer selected

Key Learning Points

Pharmacology

- Grapefruit juice significantly increases serum concentrations of some statins

Explanation

Grapefruit juice significantly increases serum concentrations of some statins. This is achieved by reducing the CYP3A4-mediated first-pass metabolism in the small intestine. Concomitant use of atorvastatin and large amounts of grapefruit juice should be avoided, or the dose of atorvastatin should be reduced accordingly. CYP3A4 is a member of the cytochrome P450 system.

Whilst a interaction is increasingly being recognised between cranberry juice and warfarin, there has as yet been no interaction with other drugs metabolised via the P450 system.

No interaction has been shown between statins, carrot juice, garlic or omega-3 fish oils. According to NICE CG172, patients should no longer be advised omega-3 supplementation to prevent another MI, although your knowledge about that is not tested in this question.

A 22-year-old woman attends the GP concerned that she has a positive pregnancy test. She maintains that she never missed a pill over the course of the last three months.

Which of the following, when taken concurrently with the combined contraceptive pill, is most likely to increase the risk of pregnancy?

(Please select 1 option)

- | | |
|-----------------------|----------------|
| <input type="radio"/> | Cimetidine |
| <input type="radio"/> | Erythromycin |
| <input type="radio"/> | Fluconazole |
| <input type="radio"/> | Fluoxetine |
| <input type="radio"/> | St John's wort |

Please select 1 option

<input type="radio"/>	Cimetidine
<input type="radio"/>	Erythromycin
<input type="radio"/>	Fluconazole
<input type="radio"/>	Fluoxetine
<input checked="" type="radio"/>	St John's wort Correct

Key Learning Points

Pharmacology

- St John's wort is a potent CYP-450 inducer, and use can lead to rapid decreases in sex steroids administered as the combined pill.

Explanation

St John's wort is a potent CYP-450 inducer, and use can lead to rapid decreases in sex steroids administered as the combined pill.

- Fluconazole is a 2C9 inhibitor
- Fluoxetine a 2C19 inhibitor
- Erythromycin a 3A4 inhibitor
- Cimetidine an inhibitor of 1A2 and 2D6.

As such all four of the other potential choices should not affect contraceptive effectiveness because they do not lead to a decrease in sex steroid levels.

Potent enzyme inducers which may cause significantly decreased pill effectiveness include rifampicin and carbamazepine.

Other antibiotics such as the tetracyclines which may be used in this population for example in the treatment of acne, are known to lead to decreased pill efficacy.

Dr. Baber

A 68-year-old woman comes to the cardiology clinic for review.

She complains of pitting oedema of both ankles and is concerned that some of her medication for heart disease or hypertension may be responsible.

On examination her blood pressure is 142/72 mmHG, pulse is 78 and regular. Her chest is clear, but there is pitting oedema of both lower legs, which she says gets worse towards the end of each day.

Which of the following medications is most likely to be responsible?

(Please select 1 option)

<input type="radio"/>	Diltiazem
<input type="radio"/>	Indapamide
<input type="radio"/>	Isosorbide dinitrate
<input type="radio"/>	Nicorandil
<input type="radio"/>	Ramipril

<input type="radio"/>	Diltiazem	This is the correct answer
<input type="radio"/>	Indapamide	
<input type="radio"/>	Isosorbide dinitrate	
<input type="radio"/>	Nicorandil	
<input checked="" type="radio"/>	Ramipril	Incorrect answer selected

Key Learning Points

Pharmacology

- Diltiazem, like dihydropyridine calcium channel antagonists is associated with ankle swelling due to peripheral venous dilatation.

Explanation

Diltiazem, like dihydropyridine calcium channel antagonists is associated with ankle swelling due to peripheral venous dilatation.

Swelling is seen to worsen during the course of the day, and is recognised to improve when patients keep their legs up.

Peripheral oedema is not a common problem in patients prescribed nitrates such as isosorbide dinitrate or nitrate donors such as nicorandil.

It is not reported with indapamide, a thiazide-like diuretic, or with ramipril, an ACE inhibitor.

A 19-year old student is diagnosed with bipolar disorder and is started on olanzapine.

Which of the following is the most common side effect that she may experience?

(Please select 1 option)

<input type="radio"/>	Cardiac arrhythmia
<input type="radio"/>	Elevated transaminases
<input type="radio"/>	Thrombocytopaenia
<input type="radio"/>	Urinary retention
<input type="radio"/>	Weight gain

<input type="radio"/>	Cardiac arrhythmia
<input type="radio"/>	Elevated transaminases
<input type="radio"/>	Thrombocytopaenia
<input type="radio"/>	Urinary retention
<input checked="" type="radio"/>	Weight gain Correct

Key Learning Points

Pharmacology

- Olanzapine can cause significant weight gain, and the management of this should be carefully considered prior to treatment initiation.

Explanation

The answer is weight gain. Weight gain can be clinically significant, and in the trials was seen regardless of the patient's baseline BMI. Approximately 65% of patients treated with olanzapine experienced some degree of weight gain, and so it is important to discuss management strategies for this with patients prior to initiating therapy.

All of the other side effects listed are also seen with olanzapine therapy, although arrhythmias and urinary retention are uncommon. Raised transaminases are seen in between 1 in 10 and 1 in 100 of patients treated, and thrombocytopaenia is rare.

Mrs HV is taking an antidepressant. Her husband recently passed away and she was diagnosed as being clinically depressed. Since taking the antidepressants, she has been complaining of drowsiness, confusion and fatigue.

Depletion of which of the following electrolytes may be causing Mrs HV's symptoms?

(Please select 1 option)

<input type="radio"/>	Chloride
<input type="radio"/>	Magnesium
<input type="radio"/>	Phosphate
<input type="radio"/>	Potassium
<input type="radio"/>	Sodium

<input type="radio"/>	Chloride
<input type="radio"/>	Magnesium
<input type="radio"/>	Phosphate
<input type="radio"/>	Potassium
<input checked="" type="radio"/>	Sodium Correct

Key Learning Points

Pharmacology, Psychiatry

- The Committee on Safety of Medicines (CSM) have reported that hyponatraemia is associated with all types of antidepressants.

Explanation

The Committee on Safety of Medicines (CSM) have reported that hyponatraemia is associated with all types of antidepressants; however it has been reported more frequently with selective serotonin reuptake inhibitors (SSRIs) than with other antidepressants.

Hyponatraemia should be considered in all patients who develop drowsiness, confusion or convulsions whilst taking an antidepressant.

A 72-year-old woman comes to the Emergency department.

She takes warfarin, an anticoagulant for chronic atrial fibrillation, and is usually on a stable warfarin dose of 5 mg every morning. She has had a number of trips to the GP over past weeks for management of her hypertension, a respiratory tract infection, and for treatment of depression.

On examination her BP is 142/72 mmHg, her pulse is 80 bpm and regular, she has extensive bruising over her arms and legs.

Investigations show:

Haemoglobin	131 g/L	(115-165)
White cell count	$8.1 \times 10^9/L$	(4-11)
Platelets	$160 \times 10^9/L$	(150-400)
Serum sodium	140 mmol/L	(135-146)
Serum potassium	4.7 mmol/L	(3.5-5)
Creatinine	106 $\mu\text{mol/L}$	(79-118)
INR	6.1	(2-3)

Which of the following medications is most likely to have caused an increased propensity to bruising?

(Please select 1 option)

<input type="radio"/>	Azithromycin
<input type="radio"/>	Digoxin
<input type="radio"/>	Fluoxetine
<input type="radio"/>	Ramipril
<input type="radio"/>	Simvastatin

Please select 1 option

<input type="radio"/>	Azithromycin
<input type="radio"/>	Digoxin
<input type="radio"/>	Fluoxetine This is the correct answer
<input type="radio"/>	Ramipril
<input checked="" type="radio"/>	Simvastatin Incorrect answer selected

Key Learning Points

Pharmacology

- Fluoxetine is a CYP450 enzyme inhibitor. Both inhibitors and inducers of CYP450 enzymes may lead to changes in the anti-coagulant effect of warfarin.

Explanation

Warfarin is subject to both pharmacodynamic and pharmacokinetic interactions which may lead to increased INR.

Pharmacodynamic interactions are those which may increase the propensity to bleeding without actually altering the absorption, metabolism, distribution or excretion of warfarin. Examples include concomitant use of clopidogrel or aspirin in combination with warfarin, or concomitant use of acute therapies like 2b3a receptor antagonists.

Pharmacokinetic interactions are those which impact on the absorption, metabolism, distribution or excretion of the drug.

Fluoxetine is a CYP450 enzyme inhibitor. Both inhibitors and inducers of CYP450 enzymes may lead to changes in the anti-coagulant effect of warfarin.

Co-prescription of antibiotics often inadvertently leads to increases in INR, examples of antibiotic P450 inhibitors include clarithromycin and erythromycin.

As per the list of recognised interactions with Warfarin in the BNF Fluoxetine causes a severe risk of increasing ones risk of bleeding. The interactions with Azithromycin is not list even as a minor risk. <https://bnf.nice.org.uk/interaction/warfarin.html>

A farmer on treatment for depression is admitted acutely one hour following an intentional overdose of an unidentified substance.

On examination he is bradycardic, hypotensive, disorientated, hypersalivating, and has small pupils.

Which of the following is he most likely to have ingested ?

(Please select 1 option)

<input type="radio"/>	A tricyclic antidepressant (TCA)
<input type="radio"/>	An organophosphate insecticide
<input type="radio"/>	Cyanide
<input type="radio"/>	Paracetamol
<input type="radio"/>	Paraquat

<input type="radio"/>	A tricyclic antidepressant (TCA)	
<input type="radio"/>	An organophosphate insecticide	This is the correct answer
<input type="radio"/>	Cyanide	
<input type="radio"/>	Paracetamol	
<input checked="" type="radio"/>	Paraquat	Incorrect answer selected

Key Learning Points

Toxicology

- Hypersalivation and miosis are specific clues to acetylcholine overactivity.

Explanation

Hypersalivation and miosis are the specific clues to acetylcholine overactivity.

The patient has occupational access to organophosphate insecticides.

Pupils tend to be dilated with TCA overdose. Paracetamol, cyanide, and paraquat should not affect pupils.

A 52-year-old woman with a three year history of sero-positive erosive rheumatoid arthritis has recently commenced methotrexate therapy initiated at the rheumatology clinic.

Which one of the following agents should she also be receiving in conjunction with her methotrexate?

(Please select 1 option)

<input type="radio"/>	Folic acid
<input type="radio"/>	Omeprazole
<input type="radio"/>	Thiamine
<input type="radio"/>	Vitamin C
<input type="radio"/>	Zinc supplements

<input type="radio"/>	Folic acid	This is the correct answer
<input type="radio"/>	Omeprazole	
<input type="radio"/>	Thiamine	
<input type="radio"/>	Vitamin C	
<input checked="" type="radio"/>	Zinc supplements	Incorrect answer selected

Key Learning Points

Pharmacology, Rheumatology

- Methotrexate is a chemotherapeutic agent; it acts through inhibition of dihydrofolate reductase thus depleting folate concentrations.

Explanation

Methotrexate is a chemotherapeutic agent as well as being an immunosuppressant used as a disease-modifying antirheumatic drug (DMARD). It acts through inhibition of dihydrofolate reductase thus depleting folate concentrations.

To reduce the impact of **folate deficiency**, a dose of 5 mg of folic acid weekly* is recommended in conjunction with methotrexate taking the agent at least two days prior to commencing the methotrexate. Its action in arthritides is not entirely understood but may relate to both anti-inflammatory as well as immunomodulation.

*Some local variations may exist regarding dose and frequency of folate therapy. Please be aware of your local guidelines.

A 16-year-old female attends the Emergency department 15 hours after ingesting approximately 30 g of paracetamol and 2 g of dihydrocodeine.

On examination, she is drowsy with a Glasgow coma scale of 15. Her pulse is 100 beats per minute, blood pressure is 110/66 mmHg and she has pinpoint pupils, with saturations of 96% on air.

What is the most appropriate treatment for this patient?

(Please select 1 option)

<input type="radio"/>	10% Dextrose infusion
<input type="radio"/>	Activated charcoal by mouth
<input type="radio"/>	Gastric lavage
<input type="radio"/>	N-acetylcysteine intravenously
<input type="radio"/>	Naloxone intravenously

<input type="radio"/>	10% Dextrose infusion	
<input type="radio"/>	Activated charcoal by mouth	
<input type="radio"/>	Gastric lavage	
<input type="radio"/>	N-acetylcysteine intravenously	This is the correct answer
<input checked="" type="radio"/>	Naloxone intravenously	Incorrect answer selected

Key Learning Points

Pharmacology, Toxicology

- N-acetylcysteine intravenously is the most appropriate treatment for paracetamol overdose. The need to consider transplant is based on the Kings College Criteria.

Explanation

This patient has taken a significant overdose of paracetamol, and is presenting late at 15 hours.

She is at risk of hepatocellular damage and needs to be commenced on an infusion of intravenous N-acetylcysteine immediately. It is continued for 30 hours and sometimes beyond this, depending on results of prothrombin time, liver function tests, urea and electrolytes, and glucose.

Activated charcoal is given to patients presenting within one hour of overdose.

Flumazenil is reserved for reversal of benzodiazepine-induced respiratory depression.

Naloxone is used for opiate-induced respiratory depression.

A 41-year-old female is brought into the Emergency department after taking an uncertain quantity of paracetamol two hours previously and trying to hang herself.

She becomes agitated and insists that she wants to go home immediately. You judge that she is at high risk of suicide.

Which of the following is the most appropriate course of action for this patient?

(Please select 1 option)

<input type="radio"/>	Ask her to sign a 'discharge against medical advice' form and let her go
<input type="radio"/>	Call the duty psychiatrist, but let the patient go if she insists and the duty psychiatrist does not arrive in time to see her
<input type="radio"/>	Call the hospital security services, restrain her and sedate her
<input type="radio"/>	Detain her under section 5(2) of the Mental Health Act
<input type="radio"/>	Detain the patient under common law, seeking the help of hospital security services

<input type="radio"/>	Ask her to sign a 'discharge against medical advice' form and let her go	
<input type="radio"/>	Call the duty psychiatrist, but let the patient go if she insists and the duty psychiatrist does not arrive in time to see her	
<input type="radio"/>	Call the hospital security services, restrain her and sedate her	
<input type="radio"/>	Detain her under section 5(2) of the Mental Health Act	
<input checked="" type="radio"/>	Detain the patient under common law, seeking the help of hospital security services	Correct

Key Learning Points

Pharmacology, Psychiatry, Toxicology

- In situations involving attempted suicide, you need to assess whether the patient has capacity.

Explanation

This patient has taken an unknown quantity of paracetamol tablets, and continues to have suicidal ideation. In situations such as these you need to assess whether the patient has capacity.

Taking a paracetamol overdose in itself does not mean the patient has no capacity, but often capacity is lacking. The chance of suffering severe consequences if a paracetamol overdose goes untreated is high. Often, therefore these patients do not possess the level of capacity required for a decision of this importance. Family should be involved if possible.

In cases such as this the patient, if found to lack capacity, should be held under common law until the appropriate time to take a blood sample (four hours after the overdose).

Psychiatric team advice can be sought, but they need the patient to be 'medically fit' to be able to do a full assessment. In general this means they must have completed all treatment necessary (for example, NAC infusion) prior to mental health assessment.

Allowing self-discharge in this situation would be inappropriate.

Sedation is inappropriate in this situation.

Section 5(2) of the Mental Health Act is used for patients who are already admitted to the hospital who have a mental illness, to allow compulsory detention for up to 72 hours. Formal assessment under the Mental Health Act should be undertaken as soon as possible. It is not used in the Emergency department.

A 53-year-old woman is started on a capecitabine based regime for the treatment of metastatic carcinoma.

Which of the following is true of capecitabine?

(Please select 1 option)

<input type="radio"/>	Capecitabine is more effective than IV agents
<input type="radio"/>	Diarrhoea is rarely seen with therapy
<input type="radio"/>	It is a way to deliver 5 fluorouracil orally
<input type="radio"/>	It is a way to deliver cisplatin orally
<input type="radio"/>	It is not effective in the treatment of coloncarcinoma

<input type="radio"/>	Capecitabine is more effective than IV agents	
<input type="radio"/>	Diarrhoea is rarely seen with therapy	
<input type="radio"/>	It is a way to deliver 5 fluorouracil orally	This is the correct answer
<input type="radio"/>	It is a way to deliver cisplatin orally	
<input checked="" type="radio"/>	It is not effective in the treatment of coloncarcinoma	Incorrect answer selected

Key Learning Points

Pharmacology

- Capecitabine is a way to deliver 5 fluorouracil orally.

Explanation

The answer is that it is a way to deliver 5 fluorouracil orally.

Capecitabine is a prodrug, which is metabolised to produce 5-fluorouracil, a chemotherapeutic agent used intravenously in the treatment of cancer. Damage to rapidly dividing cells in the GI tract leads to symptoms of diarrhoea and vomiting as a result of capecitabine treatment. Studies of efficacy suggest no major differences in clinical remission when capecitabine is compared to 5-fluorouracil given IV.

A 52-year-old woman who complains of exertional breathlessness presents to the clinic as she is desperate to stop smoking. She has had a number of unsuccessful attempts to stop smoking over the years and has tried nicotine patches.

Which of the following would be an appropriate choice to assist in her attempts at smoking cessation?

(Please select 1 option)

<input type="radio"/>	Acupuncture
<input type="radio"/>	Hypnotism
<input type="radio"/>	Nicotine gum
<input type="radio"/>	Nortriptyline
<input type="radio"/>	Varenicline

<input type="radio"/>	Acupuncture
<input type="radio"/>	Hypnotism
<input type="radio"/>	Nicotine gum
<input type="radio"/>	Nortriptyline
<input checked="" type="radio"/>	Varenicline Correct

Key Learning Points

Pharmacology, Respiratory Medicine

- Varenicline is recommended as a possible treatment to help smokers who have said they want to stop smoking

Explanation

Varenicline (Champix) is an oral anti-smoking agent with dual action, reducing the craving for cigarettes and also making the smoking of cigarettes less pleasurable. Action on Smoking and Health (ASH) have released [guidance](#) on its use. It appears to be effective and safe with the main side effect being nausea.

Varenicline appears to be more effective in clinical trials than either bupropion or placebo and is prescribed for 12 weeks in the first instance with further 12 week course if craving still persists.

A 50-year-old male has a blood pressure of 160/90 mmHg on two consecutive days.

You decide that you are going to initiate drug therapy.

Which of the following statements regarding your decision is correct?

(Please select 1 option)

- | | |
|-----------------------|---|
| <input type="radio"/> | ACE inhibitors should not be used as first line treatment in Afro-Caribbean patients |
| <input type="radio"/> | An alpha-blocker would be a first line agent in this patient |
| <input type="radio"/> | If the patient is non-caucasian a beta blocker would be an appropriate first line treatment |
| <input type="radio"/> | Potassium monitoring is not required if an ACE inhibitor is prescribed without the addition of spironalactone |
| <input type="radio"/> | Spironalactone would be an appropriate second line agent in this patient |

- | | | |
|----------------------------------|---|----------------------------|
| <input type="radio"/> | ACE inhibitors should not be used as first line treatment in Afro-Caribbean patients | This is the correct answer |
| <input type="radio"/> | An alpha-blocker would be a first line agent in this patient | |
| <input type="radio"/> | If the patient is non-caucasian a beta blocker would be an appropriate first line treatment | |
| <input type="radio"/> | Potassium monitoring is not required if an ACE inhibitor is prescribed without the addition of spironalactone | |
| <input checked="" type="radio"/> | Spironalactone would be an appropriate second line agent in this patient | Incorrect answer selected |

Key Learning Points

Pharmacology, Therapeutics

- ACE inhibitors have low efficacy in black patients in the clinical trials of ACE inhibitors.

Explanation

ACE inhibitors have low efficacy in black patients in the clinical trials of ACE inhibitors.

According to the British Hypertension Society guidelines (J Hum Hypertension 2003;17:81-86) first line treatment in black patients and patients older than 55 years of age should be with a diuretic or a calcium channel blocker.

An alpha blocker or spironalactone should only be used as an adjunct treatment in resistant hypertension.

A 45-year-old female attends the clinic complaining of headache and vomiting for five days. She has a history of scleroderma complicated by stage V chronic kidney disease.

On examination, she is tachycardic and has a blood pressure of 240/130 mmHg. Fundoscopy reveals grade 3 hypertensive retinopathy.

Which of the following is a centrally acting antihypertensive agent?

(Please select 1 option)

- | | |
|-----------------------|----------------------|
| <input type="radio"/> | Diazoxide |
| <input type="radio"/> | Hydralazine |
| <input type="radio"/> | Minoxidil |
| <input type="radio"/> | Moxonidine |
| <input type="radio"/> | Sodium nitroprusside |

Please select 1 option

<input type="radio"/>	Diazoxide	
<input type="radio"/>	Hydralazine	
<input type="radio"/>	Minoxidil	
<input type="radio"/>	Moxonidine	This is the correct answer
<input checked="" type="radio"/>	Sodium nitroprusside	Incorrect answer selected

Key Learning Points

Pharmacology

- Moxonidine is a centrally acting anti-hypertensive which is a selective agonist at the imidazoline-1 receptor in the medulla oblongata.

Explanation

Moxonidine is centrally acting and is licensed for mild to moderate hypertension not controlled by beta blockers, ACE inhibitors, calcium channel antagonists and thiazides. It is a selective agonist at the imidazoline subtype 1 receptor. This receptor subtype is found in the medulla oblongata, and by acting on it moxonidine causes a decrease in sympathetic nervous system activity and therefore a decrease in blood pressure.

The other drugs listed are vasodilators in action.

Diazoxide and sodium nitroprusside can be used intravenously in hypertensive emergencies.

Minoxidil is reserved for when hypertension is resistant to other treatments; it causes fluid retention and oedema, however, it is effective in combination with a beta blocker and loop diuretic.

Hydralazine can be given orally also in combination with a diuretic and beta blocker. Side effects include reflex tachycardia and fluid retention.

You are asked to advise on analgesia for a 44-year-old woman with acute intermittent porphyria who has undergone wisdom teeth extraction.

Which of the following drugs is safe for use in her treatment?

(Please select 1 option)

<input type="radio"/>	Cephalexin
<input type="radio"/>	Cetirizine
<input type="radio"/>	Diclofenac
<input type="radio"/>	Erythromycin
<input type="radio"/>	Ibuprofen

<input type="radio"/>	Cephalexin
<input type="radio"/>	Cetirizine
<input type="radio"/>	Diclofenac
<input type="radio"/>	Erythromycin
<input checked="" type="radio"/>	Ibuprofen Correct

Key Learning Points

Therapeutics

- Many drugs may induce acute porphyric crises thus great care must be taken when prescribing for patients with acute porphyria. Ibuprofen is safe for patients with acute porphyria.

Explanation

Many drugs may induce acute porphyric crises thus great care must be taken when prescribing for patients with acute porphyria.

Drugs unsafe for use in acute porphyria include

- Barbiturates
- Tricyclic antidepressants
- Monoamine oxidase inhibitor (MAOIs)
- Amphetamines
- Anabolic steroids
- Hormone replacement therapy
- Benzodiazepines
- Diuretics
- Captopril
- Cephalosporins
- Erythromycin
- Isoniazid
- Sulphonamides
- Sulphonylureas
- Theophylline
- Antihistamines
- Nifedipine
- Verapamil
- Amiodarone
- Simvastatin

Ibuprofen is safe for use in acute intermittent porphyria, but diclofenac should be avoided.

A patient is treated with hydralazine for the management of her blood pressure. Unfortunately she suffers profound hypotension after only five doses of medication.

Which of the following characteristics does she most likely possess?

(Please select 1 option)

<input type="radio"/>	CYP 2D6 polymorphism
<input type="radio"/>	Fast acetylation
<input type="radio"/>	HLA-DR2 genotype
<input type="radio"/>	G6-PD deficiency
<input type="radio"/>	Slow acetylation

<input type="radio"/>	CYP 2D6 polymorphism
<input type="radio"/>	Fast acetylation
<input type="radio"/>	HLA-DR2 genotype
<input type="radio"/>	G6-PD deficiency
<input checked="" type="radio"/>	Slow acetylation Correct

Key Learning Points

Pharmacology

- Slow acetylators often experience toxicity from drugs such as isoniazid, sulfonamides, procainamide, and hydralazine, whereas fast acetylators may not respond to isoniazid and hydralazine in the management of tuberculosis and hypertension.

Explanation

Slow acetylators often experience toxicity from drugs such as isoniazid, sulfonamides, procainamide, and hydralazine, whereas fast acetylators may not respond to isoniazid and hydralazine in the management of tuberculosis and hypertension.

Sulphonamides are now rarely used due to problems with blood dyscrasias.

Patients with G6-PD deficiency suffer from toxicity when they are prescribed drugs which are also oxidising agents, such as anti-malarials.

A 45-year-old publican is brought to the Emergency department by ambulance.

He is extremely agitated and says that he can see a number of dogs at the door of the side room and they are barking fiercely. On further questioning his wife tells you that he drinks some eight to ten pints of beer and glasses of wine and whisky each day. They have recently had an argument about his drinking and he has not touched any alcohol for the past 12-18 hours.

On examination he is agitated and sweating, his BP is 145/84 mmHg, his pulse is 85 and regular. He has changes consistent with chronic liver disease and is tender in the right upper quadrant of his abdomen.

Investigations show:

Haemoglobin	101 g/L	(135-177)
White cell count	$8.3 \times 10^9/L$	(4-11)
Platelets	$151 \times 10^9/L$	(150-400)
Sodium	138 mmol/L	(135-146)
Potassium	4.0 mmol/L	(3.5-5)
Creatinine	90 $\mu\text{mol/L}$	(79-118)
Alanine aminotransferase	92 IU/L	(5-40)
Bilirubin	54 $\mu\text{mol/L}$	(<17)

Which of the following is the most likely diagnosis?

(Please select 1 option)

<input type="radio"/>	Alcoholic hallucinosis
<input type="radio"/>	Delirium tremens
<input type="radio"/>	Hypomanic episode
<input type="radio"/>	Minor alcohol withdrawal symptoms
<input type="radio"/>	Stimulant overdose

(Please select 1 option)

<input type="radio"/>	Alcoholic hallucinosis	This is the correct answer
<input type="radio"/>	Delirium tremens	
<input type="radio"/>	Hypomanic episode	
<input type="radio"/>	Minor alcohol withdrawal symptoms	
<input checked="" type="radio"/>	Stimulant overdose	Incorrect answer selected

Key Learning Points

Pharmacology

- Alcoholic hallucinosis is known to appear some 12-24 hours after the last alcoholic drink has been taken and hallucinations may be visual, auditory or tactile in nature.

Explanation

Alcoholic hallucinosis is known to appear some 12-24 hours after the last alcoholic drink has been taken and hallucinations may be visual, auditory or tactile in nature.

More minor withdrawal symptoms which patients experience may include:

- a degree of agitation and restlessness
- sweating
- nausea and vomiting, and
- feelings of depression.

Withdrawal seizures are seen 24-48 hours after alcohol withdrawal, and two to three days after stopping drinking withdrawal delirium (delirium tremens 'DTs') is seen.

Management includes the use of anti-withdrawal medication such as chlordiazepoxide, and thiamine replacement.

A 55-year-old gentleman is suffering with erectile dysfunction.

He has a past medical history of type 2 diabetes and angina.

Which of the following medications would be a contraindication to prescribing sildenafil?

(Please select 1 option)

<input type="radio"/>	Clopidogrel
<input type="radio"/>	GTN spray used once per month
<input type="radio"/>	Metoprolol
<input type="radio"/>	Nicorandil
<input type="radio"/>	Propranolol

Please select 1 option

<input type="radio"/>	Clopidogrel	
<input type="radio"/>	GTN spray used once per month	
<input type="radio"/>	Metoprolol	
<input checked="" type="radio"/>	Nicorandil	This is the correct answer
<input type="radio"/>	Propranolol	Incorrect answer selected

Key Learning Points

Pharmacology

- The phosphodiesterase 5 inhibitors should be avoided in patients taking nitrates or nicorandil. This is due to vasodilatation potentially causing hypotension and precipitating a myocardial event.

Explanation

The phosphodiesterase 5 inhibitors should be avoided in patients taking nitrates or nicorandil. This is due to vasodilatation potentially causing hypotension and precipitating a myocardial event.

The gentleman using a GTN spray less than once per week could be prescribed sildenafil, although it is worth warning him that should he have chest pain requiring the Emergency department after having taken sildenafil, he should warn his health care providers so that they can avoid nitrates whilst treating his symptoms.

Myocardial infarction is a contraindication to the use of sildenafil; however cardiovascular disease (that is, angina) requires cautious prescribing.

Other patients in which PDE5 inhibitors should be used with caution are those with risk of priapism, such as sickle cell or multiple myeloma.

None of the other drugs, aspirin, clopidogrel, ACE inhibitors and beta blockers are contraindications to the use of sildenafil.

A 59-year-old male with type 2 diabetes is attending the foot clinic regularly. He has a neuropathic ulcer complicated by osteomyelitis. A deep wound swab has grown *Staphylococcus aureus* and *Escherichia coli*.

He also takes warfarin for atrial fibrillation.

Which of the following antibiotics will reduce the anticoagulant effect of warfarin?

(Please select 1 option)

<input type="radio"/>	Ciprofloxacin
<input type="radio"/>	Co-trimoxazole
<input type="radio"/>	Erythromycin
<input type="radio"/>	Metronidazole
<input type="radio"/>	Rifampicin

<input type="radio"/>	Ciprofloxacin
<input type="radio"/>	Co-trimoxazole
<input type="radio"/>	Erythromycin
<input type="radio"/>	Metronidazole
<input checked="" type="radio"/>	Rifampicin Correct

Key Learning Points

Pharmacology

- Rifampicin is known to induce the action of some enzymes, therefore increasing the metabolism of warfarin and so reducing its anticoagulant effect.

Explanation

The anticoagulant effect of warfarin can be affected by drugs, which induce or inhibit the action of enzymes involved in the metabolism of warfarin.

Rifampicin is known to induce the action of such enzymes, therefore increasing the metabolism of warfarin and so reducing its anticoagulant effect.

Erythromycin and ciprofloxacin inhibit the effect of these enzymes, therefore enhancing the anticoagulant effect of warfarin.

Metronidazole and co-trimoxazole inhibit the clearance of the active S isomer of warfarin, therefore enhancing its anticoagulant effect.

A 73-year-old woman with a history of chronic lymphocytic leukaemia (CLL) is treated with fludarabine as single agent chemotherapy to control her symptoms. You counsel her as to the increased risk of infections.

The risk of which infection is particularly increased in patients treated with fludarabine?

(Please select 1 option)

<input type="radio"/>	<i>Candida albicans</i>
<input type="radio"/>	Herpes simplex
<input type="radio"/>	<i>Pseudomonas aeruginosa</i>
<input type="radio"/>	<i>Staphylococcus aureus</i>
<input type="radio"/>	Tuberculosis

Please select 1 option

<input type="radio"/>	<i>Candida albicans</i>	
<input checked="" type="radio"/>	Herpes simplex	This is the correct answer
<input type="radio"/>	<i>Pseudomonas aeruginosa</i>	
<input type="radio"/>	<i>Staphylococcus aureus</i>	
<input checked="" type="radio"/>	Tuberculosis	Incorrect answer selected

Key Learning Points

Pharmacology

- Fludarabine use is associated with defective T cell function and thus increased risk of herpes virus reactivation.

Explanation

The answer is Herpes simplex. Fludarabine has the greatest effect on T cell function. There is inhibition of cytokine-induced activation of STAT-1 and STAT-1-dependent gene transcription, which results in decreased peripheral blood T cell counts. These occur early in treatment and persist for up to two years after discontinuation of therapy. A greater impact is seen on CD4+ T cells than CD8+ T cells or NK cells. Decreased B cell and monocyte counts are also seen. This alteration in T cell function leads to increased susceptibility to the herpes family of viruses, including herpes simplex and varicella zoster virus.

Chlorambucil is most associated with increased risk of common bacterial infections including pseudomonas, staphylococcus and streptococcus. Increased risk of fungal infections is also seen. TNF-alpha inhibitors used in the treatment of **rheumatoid arthritis** and inflammatory bowel disease are particularly associated with tuberculosis reactivation.

A 35-year-old business man presents with anxiety and palpitations after 'snorting' cocaine. The patient denies any prior use and has also consumed some alcohol.

On examination, he is distressed and sweating with a temperature of 38°C, pulse of 138 beats per minute (regular) and a blood pressure of 216/110 mmHg. His ECG reveals a sinus tachycardia.

Which of the following is the most appropriate initial treatment for this man?

(Please select 1 option)

<input type="radio"/>	Dantrolene
<input type="radio"/>	Diazepam
<input type="radio"/>	Lidocaine
<input type="radio"/>	Propranolol
<input type="radio"/>	Verapamil

<input type="radio"/>	Dantrolene	
<input checked="" type="radio"/>	Diazepam	This is the correct answer
<input type="radio"/>	Lidocaine	
<input checked="" type="radio"/>	Propranolol	Incorrect answer selected
<input type="radio"/>	Verapamil	

Key Learning Points

Pharmacology, Toxicology

- Initial treatment of cocaine poisoning involves intravenous administration of diazepam to control agitation, and cooling measures for hyperthermia.

Explanation

Cocaine abuse is quite common and neurological and cardiovascular side effects predominate.

Delirium, hyperthermia, arrhythmias, myocardial and cerebral infarction are reported.

In this patient, the first consideration should be to establish adequate ventilation and support the circulation, and also to remove any residual cocaine from the nostrils.

Generally, the toxic effects of cocaine are short-lived and relate to sympathetic stimulation, as in this case with tachycardia, pyrexia and hypertension.

Initial treatment of cocaine poisoning involves intravenous administration of diazepam to control agitation, and cooling measures for hyperthermia.

Sedation with diazepam may also be appropriate initial therapy for hypertension and tachycardia in this situation since the excessive sympathetic tone is largely centrally mediated.

Control of anxiety and agitation with diazepam when combined with rapid cooling may also decrease heat production in hyperthermic patients.

If further treatment is required, an intravenous nitrate is particularly useful for associated coronary artery spasm.

Further Reading:

Which of the following antiemetics functions through antagonism of the 5-hydroxytryptamine 3A receptor?

(Please select 1 option)

- | | |
|-----------------------|----------------|
| <input type="radio"/> | Aprepitant |
| <input type="radio"/> | Domperidone |
| <input type="radio"/> | Hyoscine |
| <input type="radio"/> | Metoclopramide |
| <input type="radio"/> | Ondansetron |

Dr. Assem

<input type="radio"/>	Aprepitant
<input type="radio"/>	Domperidone
<input type="radio"/>	Hyoscine
<input type="radio"/>	Metoclopramide
<input checked="" type="radio"/>	Ondansetron Correct

Key Learning Points

Pharmacology

- Ondansetron is a serotonin 5-HT₃ receptor antagonist used mainly to treat nausea and vomiting following chemotherapy.

Explanation

Ondansetron is a serotonin 5-HT₃ receptor antagonist used mainly to treat nausea and vomiting following chemotherapy.

Its effects are thought to be on both peripheral and central nerves. One part is to reduce the activity of the vagus nerve, which is a nerve that activates the vomiting center in the medulla oblongata, the other is a blockage of serotonin receptors in the chemoreceptor trigger zone.

It does not have much effect on vomiting due to motion sickness.

This drug does not have any effect on dopamine receptors or muscarinic receptors.

A 60-year-old woman has a fracture of the wrist following a fall. Dual energy x ray absorptiometry (DEXA) scan shows osteoporosis in her lumbar spine and hips.

She is treated with once weekly alendronate 70 mg and Calcichew.

Which is the mechanism of action of biphosphonates in the treatment of osteoporosis?

(Please select 1 option)

- | | |
|-----------------------|--|
| <input type="radio"/> | Enhancing the absorption and action of vitamin D |
| <input type="radio"/> | Enhancing the absorption of calcium from the gut |
| <input type="radio"/> | Enhancing the survival and function of osteoblasts |
| <input type="radio"/> | Enhancing the survival and function of osteoclasts |
| <input type="radio"/> | Reducing the survival and function of osteoclasts |

<input type="radio"/>	Enhancing the absorption and action of vitamin D	
<input type="radio"/>	Enhancing the absorption of calcium from the gut	
<input type="radio"/>	Enhancing the survival and function of osteoblasts	
<input type="radio"/>	Enhancing the survival and function of osteoclasts	
<input checked="" type="radio"/>	Reducing the survival and function of osteoclasts	Correct

Key Learning Points

Pharmacology, Rheumatology

- The mechanism of action of bisphosphonates involves the inhibition of osteoclasts

Explanation

The mechanism of action of bisphosphonates involves the inhibition of farnesyl diphosphate synthase within osteoclasts. In doing this they interfere with geranylgeranylation (attachment of the lipid to regulatory proteins), which causes osteoclast inactivation. This leads to reduced bone turnover, increased bone mass and improved mineralisation.

Bisphosphonates licensed for the prevention and treatment of osteoporosis include alendronate, risedronate and ibandronate.

The bisphosphonates zoledronate and pamidronate are used for the treatment of metastatic bone disease and short term management of hypercalcaemia.

Dr Asseel

A 23-year-old man who presented to the gastroenterology clinic with bloody diarrhoea has been diagnosed with inflammatory bowel disease after endoscopy and biopsy. Although he has improved significantly with the combination of mesalazine and prednisolone, he now requires a steroid sparing agent, and it is recommended that he start azathioprine.

Which of the following tests should be undertaken before starting azathioprine?

(Please select 1 option)

<input type="radio"/>	Catechol o-methyl transferase (COMT) activity
<input type="radio"/>	Chest radiograph
<input type="radio"/>	Serum folate
<input type="radio"/>	Quantiferon gamma test
<input type="radio"/>	Thiopurine methyl transferase (TPMT) activity

<input type="radio"/>	Catechol o-methyl transferase (COMT) activity
<input type="radio"/>	Chest radiograph
<input type="radio"/>	Serum folate
<input type="radio"/>	Quantiferon gamma test
<input checked="" type="radio"/>	Thiopurine methyl transferase (TPMT) activity Correct

Key Learning Points

Pharmacology

- TPMT activity is a useful screening test with respect to reducing risks of toxicity from azathioprine, and is recommended prior to treatment initiation.

Explanation

The correct answer is TPMT activity. TPMT is the main enzyme responsible for metabolising the active metabolite of azathioprine, (6-mercaptopurine). Naturally occurring polymorphisms which reduce TPMT activity are recognised, and these are associated with significant azathioprine toxicity (especially bone marrow suppression), and testing is therefore recommended before initiating therapy with azathioprine. In patients with reduced TPMT activity, half dose therapy or an alternative can be given.

COMT is responsible for degradation of adrenaline, nor-adrenaline and dopamine, and as such is not relevant in this case. Chest radiograph and quantiferon gamma testing can be considered as screening tests for tuberculosis, which should be done before initiation of anti-TNF therapy. Serum folate should be checked prior to starting methotrexate if folate deficiency is suspected.

A 49-year-old woman with a history of hypertension comes to the clinic for review.

She has noticed that she has become jaundiced and is concerned one of her medications may be responsible. She has recently had a second anti-hypertensive added to her regime, and is taking an antibiotic for a respiratory tract infection.

Investigations show

Haemoglobin	123 g/L	(115-160)
White cell count	$6.2 \times 10^9/L$	(4-11)
Platelets	$195 \times 10^9/L$	(150-400)
Serum sodium	138 mmol/L	(135-146)
Serum potassium	4.0 mmol/L	(3.5-5)
Creatinine	105 $\mu\text{mol/L}$	(79-118)
Alanine aminotransferase	85 U/L	(5-40)
Alkaline phosphatase	420 U/L	(39-117)
Bilirubin	189 $\mu\text{mol/L}$	(<17)

Which of the following medications is the most likely cause?

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input type="radio"/>	Co-amoxiclav
<input type="radio"/>	Enalapril
<input type="radio"/>	Paracetamol
<input type="radio"/>	Penicillin V

(Please select 1 option)

<input type="radio"/>	Amlodipine
<input checked="" type="radio"/>	Co-amoxiclav This is the correct answer
<input type="radio"/>	Enalapril
<input type="radio"/>	Paracetamol
<input type="radio"/>	Penicillin V Incorrect answer selected

Key Learning Points

Pharmacology

- Amoxicillin is an important cause of cholestatic jaundice.

Explanation

Amoxicillin clavulanate is an important cause of cholestatic jaundice.

Other common drugs associated with cholestatic jaundice include:

- Chlorpromazine
- Ciprofloxacin
- Ofloxacin
- Cimetidine
- Phenytoin
- Naproxen
- Captopril
- Erythromycin, and
- Azithromycin.

In this case the co-amoxiclav should be withdrawn, and the combination avoided in future.

Because of cholestatic jaundice, prescription of co-amoxiclav is not recommended for longer than 14 days.