Which one of the following would shift the oxygen dissociation curve to the left?

○	Carboxyhaemoglobin
○	Acidosis
○	Raised pCO2
○	Pyrexia
○	Raised 2,3-DPG levels

Oxygen dissociation curve:

The oxygen dissociation curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood. It is not affected by haemoglobin concentration

Basics:

- shifts to left = for given oxygen tension there is increased saturation of Hb with oxygen i.e. decreased oxygen delivery to tissues
- shifts to right = for given oxygen tension there is reduced saturation of Hb with oxygen i.e. enhanced oxygen delivery to tissues

Shifts to Left = Lower oxygen delivery	**Shifts to Right = Raised oxygen delivery**
HbF, methaemoglobin, carboxyhaemoglobin Low [H+] (alkali) Low pCO2 Low 2,3-DPG Low temperature	Raised [H+] (acidic) Raised pCO2 Raised 2,3-DPG* Raised temperature

The L rule:
Shifts to L → Lower oxygen delivery, caused by

- **Low [H+] (alkali)**
- **Low pCO2**
- **Low 2,3-DPG**
- **Low temperature**

Another mnemonic is 'CADET, face Right!' for CO2, Acid, 2,3-DPG, Exercise and Temperature
*2,3-diphosphoglycerate

A		48.9%
B		14.7%
C		11%
D		8%
E		17.4%

A 22-year-old male with a history of familial adenomatous polyposis (FAP) has a total colectomy. What is the mode of inheritance of FAP?

○	Uniparental disomy of chromosome 12
○	Autosomal recessive
○	Uniparental disomy of chromosome 14
○	Autosomal dominant
○	X-linked recessive

Colorectal cancer: genetics

- It is currently thought there are three types of colon cancer:
  - sporadic (95%)
  - hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
  - familial adenomatous polyposis (FAP, <1%)
- Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene.
- It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC:

- an autosomal dominant condition, is the most common form of inherited colon cancer.
- Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive.
- Currently seven mutations have been identified, which affect genes involved in DNA mismatch repair leading to microsatellite instability.
- The most common genes involved are:
  - MSH2 (60% of cases)
  - MLH1 (30%)
- Patients with HNPCC are also at a higher risk of other cancers, with endometrial cancer being the next most common association, after colon cancer.
- **The Amsterdam criteria** are sometimes used to aid diagnosis:
  - at least 3 family members with colon cancer
  - the cases span at least two generations
  - at least one case diagnosed before the age of 50 years

FAP

- is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years.
- Patients inevitably develop carcinoma.
- It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5.
- Genetic testing can be done by analysing DNA from patients white blood cells.
- Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.
- Patients with FAP are also at risk from duodenal tumours.
- A variant of FAP called **Gardner's syndrome** can also feature
  - osteomas of the skull and mandible,
  - retinal pigmentation,
  - thyroid carcinoma and
  - epidermoid cysts on the skin

Answer: D **September 2007 exam**

Which one of the following diseases is most strongly associated with HLA antigen DR4?

○	Ankylosing spondylitis
○	Behcet's disease
○	Reiter's syndrome
○	Rheumatoid arthritis
○	Coeliac disease

Rheumatoid arthritis - HLA DR4

- Around 70% of patients with rheumatoid arthritis are HLA-DR4.
- Patients with Felty's syndrome (a triad of rheumatoid arthritis, splenomegaly and neutropaenia) are even more strongly associated with 90% being HLA-DR4

HLA associations:

- HLA antigens are encoded for by genes on chromosome 6.
- HLA A, B and C are class I antigens whilst
- HLA DP, DQ, DR are class II antigens.
- Questions are often based around which diseases have strong HLA associations.
- The most important associations are listed below:

HLA-A3:

- haemochromatosis

HLA-B5:

- Behcet's disease

HLA-B27:

- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DQ2/DQ8:

- coeliac disease

HLA-DR2:

- narcolepsy
- Goodpasture's

HLA-DR3:

- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4:

- type 1 diabetes mellitus*
- rheumatoid arthritis

*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Answer: D **January 2012 exam**

Which one of the following causes of primary immunodeficiency is a T-cell disorder?

○	Chediak-Higashi syndrome
○	Chronic granulomatous disease
○	Common variable immunodeficiency
○	DiGeorge syndrome
○	Wiskott-Aldrich syndrome

DiGeorge syndrome - a T-cell disorder

DiGeorge syndrome is a primary immunodeficiency disorder caused by T-cell deficiency and dysfunction. It is an example of a microdeletion syndrome. Patients are consequently at increased risk of viral and fungal infections.

Primary immunodeficiency:

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. *Staphylococcus aureus* and fungi (e.g. *Aspergillus*)
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Hypogammaglobulinemia is seen. May predispose to autoimmune disorders and lymphoma
Bruton's congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen *Live vaccines should be avoided*
Selective Ig A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4^{th} pharyngeal pouches	Common features include congenital heart disease, learning difficulties, hypocalcaemia, recurrent viral/fungal diseases

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. 1) Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. 2) Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. TTT: Stem cell transplantation may be successful
Ataxia telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia, recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopaenia, low IgM levels

Answer: D

A 60-year-old woman with a history of hypothyroidism and inflammatory arthritis is admitted after slipping on ice and falling over. Some routine blood tests are performed:

Na^+	141 mmol/l
K^+	2.9 mmol/l
Chloride	114 mmol/l
Bicarbonate	16 mmol/l
Urea	5.2 mmol/l
Creatinine	75 µmol/l

Which one of the following is most likely to explain these results?

○	Renal tubular acidosis (type 1)
○	Diabetic ketoacidosis
○	Renal tubular acidosis (type 4)
○	Aspirin overdose
○	Conn's syndrome

Renal tubular acidosis causes a normal anion gap

- The low bicarbonate suggests an acidosis.
- The anion gap is however normal, (141 + 2.9) - (114 + 16) = 13.9 mmol/l. The different diagnosis is therefore causes of a metabolic acidosis with a normal anion gap.
- Aspirin and diabetic ketoacidosis causes a metabolic acidosis associated with a raised anion gap.
- Conn's syndrome would explain the hypokalaemia but it does not cause a metabolic acidosis.
- Renal tubular acidosis type 4 is associated with hyperkalaemia.
- The correct answer is therefore renal tubular acidosis type 1, which is likely to be secondary to this patient's inflammatory arthritis.

Metabolic acidosis:

- Metabolic acidosis is commonly classified according to the anion gap.
- If a question supplies the chloride level then this is often a clue that the anion gap should be calculated.

Anion gap:

- The anion gap is calculated by:
  (sodium + potassium) - (bicarbonate + chloride)
- A normal anion gap is 8-14 mmol/L.
- It is useful to consider in patients with a metabolic acidosis:

Causes of a normal anion gap or hyperchloraemic metabolic acidosis:

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Causes of a raised anion gap metabolic acidosis:

- lactate:
  - Lactic acidosis type A: shock, hypoxia, burns.
  - Lactic acidosis type B: metformin.
- ketones: diabetic ketoacidosis, alcohol, starvation
- urate: renal failure
- acid poisoning: salicylates, methanol

Answer: A

Which of the following is deficient in patients with hereditary angioedema?

○	C1-INH
○	C3
○	Heat shock protein type 1
○	C6
○	Histamine degradation protein (HDP)

Next question

Hereditary angioedema - C1-INH deficiency

Hereditary angioedema:

- autosomal dominant condition
- associated with low plasma levels of the C1 inhibitor (C1-INH) protein.
- C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation:

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks.
- Serum C4 is the most reliable and widely used screening tool

Symptoms:

- attacks may be proceeded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management:

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help

A		56.7%
B		15.5%
C		7.6%
D		7.3%
E		13%

56.7% of users answered this question correctly

September 2012 exam

Patients with deficiencies of which one of the following complement proteins are most predisposed to disseminated meningococcal infection?

○	C1
○	C2
○	C3
○	C4
○	C5

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection

Complement deficiencies:

- Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body.
- Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency:

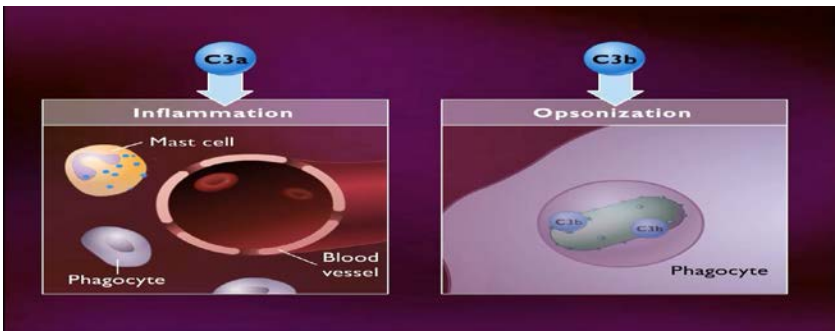
- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency:

- causes recurrent bacterial infections



C5 deficiency:

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency:

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

January 2013 exam

Answer E

Which of the following conditions is inherited in an autosomal recessive fashion?

○	Hypokalaemic periodic paralysis
○	Adult polycystic disease
○	Huntington's disease
○	Friedreich's ataxia
○	Ehlers-Danlos syndrome

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Autosomal recessive conditions

- **Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural',**
- **notable exceptions:**

  - **some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst**
  - **others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant**
  - **some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive**

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Friedreich's ataxia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Gilbert's syndrome*
- Glycogen storage disease
- Haemochromatosis
- Wilson's disease
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's
- PKU
- Sickle cell anaemia
- Thalassaemias

*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Answer D

Which one of the following occurs during reverse transcriptase polymerase chain reaction?

○	Proteins are converted to DNA
○	DNA is converted to RNA
○	Used to amplify DNA
○	RNA is converted to DNA
○	Proteins are converted to RNA

PCR:

- Polymerase chain reaction (PCR) is a molecular genetic investigation technique.
- The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence.
- It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections.
- PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep:

- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added
- The following cycle then takes place:
  - mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
  - mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

- The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR:

- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

A	6.3%
B	22.4%
C	13.9%
D	48.4%
E	8.9%

48.4% of users answered this question correctly

January 2009 exam

Which of the following is true regarding rheumatoid factor?

○	It is usually an IgM molecule reacting against patient's own IgG
○	High titres are not associated with severe disease
○	Rose-Waaler test involves agglutination of IgG coated latex particles
○	80% of SLE patients are RF positive
○	50% of patients with Sjogren's syndrome are RF positive

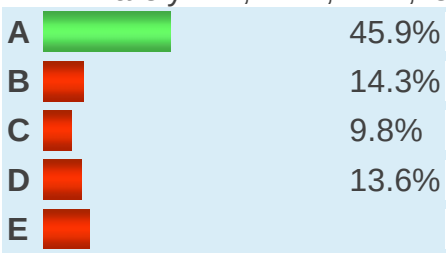
Rheumatoid factor is an IgM antibody against IgG

Rheumatoid factor

- Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG
- RF can be detected by either:
  - Rose-Waaler test: sheep red cell agglutination
  - Latex agglutination test (less specific)
- RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy



A 19-year-old female with a history of anorexia nervosa is admitted to hospital. Her BMI has dropped to 16. She has agreed to be fed by nasogastric tube. Which one of the following electrolyte disturbances is most likely to occur?

○	Hyperkalaemia
○	Hypocalcaemia
○	Metabolic acidosis
○	Hypophosphataemia
○	Hypermagnesemia

Next question

Refeeding syndrome causes hypophosphataemia

This patient is at risk of refeeding syndrome, which can lead to profound hypophosphataemia

Hypophosphataemia:

Causes:

- alcohol excess
- acute liver failure
- diabetic ketoacidosis
- refeeding syndrome
- primary hyperparathyroidism
- osteomalacia

Consequences:

- red blood cell haemolysis
- white blood cell and platelet dysfunction
- muscle weakness and rhabdomyolysis
- central nervous system dysfunction

A	9.3%
B	8.6%
C	7.2%
D	64.9%
E	9.9%

64.9% of users answered this question correctly

May 2013 exam

Which one of the following statements regarding gastrin is true?

○	Secreted by D cells in the stomach
○	Secretion is inhibited by high antral pH
○	Reduces acid secretion in the stomach
○	Increases gastric motility
○	Distension of the stomach inhibits secretion

Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
Gastrin	G cells in antrum of the stomach	➢ Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), ➢ luminal peptides/amino acids ➢ Inhibited by: low antral pH, somatostatin	➢ Increase HCL, pepsinogen and IF secretion, ➢ increases gastric motility, ➢ stimulates parietal cell maturation
CCK	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
Secretin	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
VIP	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
Somatostatin	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Answer D

January 2007 exam

The nicotinic acetylcholine receptor is an example of a:

○	Ligand-gated ion channel
○	Tyrosine kinase receptor
○	Guanylate cyclase receptor
○	G protein-coupled receptor
○	Intracellular receptor

Membrane receptors:

- There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

1) Ligand-gated ion channel receptors:

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

2) Tyrosine kinase receptors:

- intrinsic tyrosine kinase: insulin, insulin-like growth factor (IGF), epidermal growth factor (EGF)
- receptor-associated tyrosine kinase: growth hormone, prolactin, interferon, interleukin

3) Guanylate cyclase receptors:

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor, brain natriuretic peptide

4) G protein-coupled receptors:

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- 7-helix membrane-spanning domains
- consist of 3 main subunits: alpha, beta and gamma
- the alpha subunit is linked to GDP.Ligand binding causes conformational changes to receptor, GDP is phosphorylated to GTP,and the alpha subunit is activated
- G proteins are named according to the alpha subunit (G_s, G_i, G_q)

	G_s	G_i	G_q
Mechanism	Activates adenylate cyclase → increases cAMP → activates protein kinase A	Inhibits adenylate cyclase → decreases cAMP → inhibits protein kinase A	Activates phospholipase C → splits PIP_2 to IP_3 & DAG → activates protein kinase C
Examples	➢ Beta-1 receptors (epinephrine, norepinephrine, dobutamine) ➢ Beta-2 receptors (epinephrine, salbuterol) ➢ H2 receptors (histamine) ➢ D1 receptors	➢ M2 receptors (acetylcholine) ➢ Alpha-2 receptors (epinephrine, norephinephrine) ➢ D2 receptors (dopamine) ➢ GABA-B receptor	➢ Alpha-1 receptors (epinephrine, norepinephrine) ➢ H1 receptors (histamine) ➢ V1 receptors (vasopressin) ➢ M1, M3 receptors (acetylcholine)

	G_s	G_i	G_q
	(dopamine) ➢ V2 receptors (vasopressin) ➢ Receptors for ACTH, LH, FSH, glucagon, PTH, calcitonin, prostaglandins		

Answer : A

A 72-year-old woman who takes bendroflumethiazide for hypertension is admitted to the Emergency Department. Admission bloods show the following:

Na^+	131 mmol/l
K^+	2.2 mmol/l
Urea	3.1 mmol/l
Creatinine	56 µmol/l
Glucose	4.3 mmol/l

Which one of the following ECG features is most likely to be seen?

○	Short PR interval
○	Short QT interval
○	Flattened P waves
○	J waves
○	U waves

Hypokalaemia - U waves on ECG

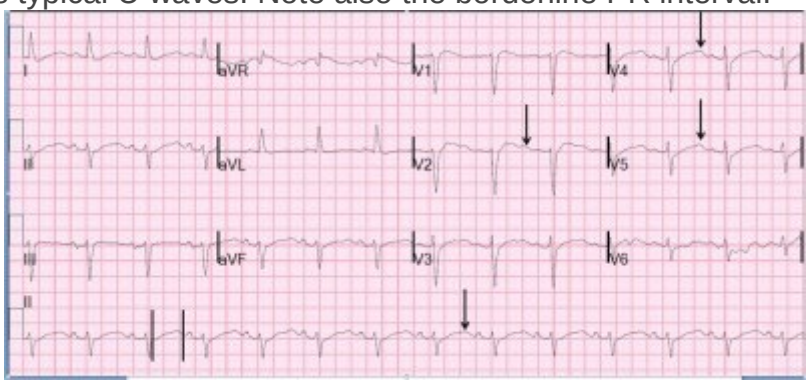
J waves are seen in hypothermia whilst delta waves are associated with Wolff Parkinson White syndrome.

ECG: hypokalaemia:

ECG features of hypokalaemia

- U waves
- small or absent T waves (occasionally inversion)
- prolong PR interval
- ST depression
- long QT

The ECG below shows typical U waves. Note also the borderline PR interval.



One registered user suggests the following rhyme

- In Hypokalaemia, U have no Pot and no T, but a long PR and a long QT

ANSWER : E

Which one of the following is least associated with hypercalcaemia?

○	Sarcoidosis
○	Primary hyperparathyroidism
○	Thiazide diuretics
○	Squamous cell lung cancer
○	Monoclonal gammopathy of uncertain significance

One of the key differentiating features between monoclonal gammopathy of uncertain significance (MGUS) and myeloma is the absence of complications such as immune paresis, hypercalcaemia and bone pain

Hypercalcaemia: causes

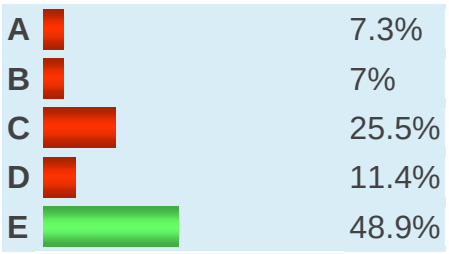
- The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

**usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation



Which one of the following serum proteins is most likely to increase in a patient with severe pneumococcal pneumonia?

○	Transferrin
○	Transthyretin
○	Ferritin
○	Albumin
○	Cortisol binding protein

Acute phase proteins

Acute phase proteins

- CRP
- procalcitonin
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:

- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

*plays a more significant role in other mammals such as mice

A	13.4%
B	7.7%
C	60.9%
D	7.5%
E	10.4%

60.9% of users answered this question correctly

September 2013 exam

A 79-year-old man is admitted with congestive cardiac failure. Bloods on admission show:

BNP	354 pg/ml

Which one of the following would result from elevated BNP levels?

○	Decreased sodium diuresis
○	Vasoconstriction of the coronary arteries
○	Inhibition of the renin-angiotensin-aldosterone system
○	Vasoconstriction of the pulmonary vessels
○	Increased sympathetic tone

BNP - actions:

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

B-type natriuretic peptide:

- B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.
- Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels.
- Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease.
- Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP:

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

Clinical uses of BNP

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

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

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

4) Screening for cardiac dysfunction:
   - not currently recommended for population screening

Answer :c

Which one of the following causes of primary immunodeficiency is due to a defect in both B-cell and T-cell function?

○	Common variable immunodeficiency
○	Chronic granulomatous disease
○	Wiskott-Aldrich syndrome
○	Chediak-Higashi syndrome
○	Di George syndrome

Combined B- and T-cell disorders: SCID WAS ataxic (SCID, Wiskott-Aldrich syndrome, ataxic telangiectasia)

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction.
It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene.
Features include recurrent bacterial infections (e.g. chest), eczema and thrombocytopenia

Primary immunodeficiency:
Primary immunodeficiency disorders may be classified according to which component of the immune system they affect.

Neutrophil disorders

Disorder	Underlying defect	Notes
Chronic granulomatous disease	Lack of NADPH oxidase reduces ability of phagocytes to produce reactive oxygen species	Causes recurrent pneumonias and abscesses, particularly due to catalase-positive bacteria (e.g. *Staphylococcus aureus* and fungi (e.g. *Aspergillus*)
Chediak-Higashi syndrome	Microtubule polymerization defect which leads to a decrease in phagocytosis	Affected children have 'partial albinism' and peripheral neuropathy. Recurrent bacterial infections are seen
Leukocyte adhesion deficiency	Defect of LFA-1 integrin (CD18) protein on neutrophils	Recurrent bacterial infections. Delay in umbilical cord sloughing may be seen

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Hypogammaglobulinemia is seen. May predispose to autoimmune disorders and lymphoma
Bruton's congenital agammaglobulinaemia	Defect in Bruton's tyrosine kinase (BTK) gene that leads to a severe block in B cell development	X-linked recessive. Recurrent bacterial infections are seen *Live vaccines should be avoided*
Selective Ig A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4^{th} pharyngeal pouches	Common features include congenital heart disease, learning difficulties, hypocalcaemia, recurrent viral/fungal diseases

Combined B- and T-cell disorders

Disorder	Underlying defect	Notes
Severe combined immunodeficiency	Many varying causes. 3) Most common (X-linked) due to defect in the common gamma chain, a protein used in the receptors for IL-2 and other interleukins. 4) Other causes include adenosine deaminase deficiency	Recurrent infections due to viruses, bacteria and fungi. TTT: Stem cell transplantation may be successful
Ataxia telangiectasia	Defect in DNA repair enzymes	Autosomal recessive. Features include cerebellar ataxia, telangiectasia, recurrent chest infections and 10% risk of developing malignancy, lymphoma or leukaemia
Wiskott-Aldrich syndrome	Defect in WASP gene	X-linked recessive. Features include recurrent bacterial infections, eczema, thrombocytopaenia, low IgM levels

A  25.7% **B**  6.9% **C**  45.2% **D**  9.6% **E**  12.6%

A 65-year-old man presents with bilateral leg pain that is brought on by walking. His past medical history includes peptic ulcer disease and osteoarthritis. He can typically walk for around 5 minutes before it develops. The pain subsides when he sits down. He has also noticed that leaning forwards or crouching improves the pain. Musculoskeletal and vascular examination of his lower limbs is unremarkable. What is the most likely diagnosis?

○	Inflammatory arachnoiditis
○	Peripheral arterial disease
○	Raised intracranial pressure
○	Spinal stenosis
○	Lumbar vertebral crush fracture

This is a classic presentation of spinal stenosis. Whilst peripheral arterial disease is an obvious differential the characteristic relieving factors of the pain and normal vascular examination point away from this diagnosis.

Lower back pain:

- Lower back pain (LBP) is one of the most common presentations seen in practice.
- Whilst the majority of presentations will be of a non-specific muscular nature it is worth keeping in mind possible causes which may need specific treatment. **Red flags for lower back pain:**
  - age < 20 years or > 50 years
  - history of previous malignancy
  - night pain
  - history of trauma
  - systemically unwell e.g. weight loss, fever

The table below indicates some specific causes of LBP:

Facet joint	➢ **May be acute or chronic** ➢ **Pain worse in the morning and on standing** ➢ **On examination there may be pain over the facets.** ➢ **The pain is typically worse on extension of the back**
Spinal stenosis	➢ Usually gradual onset ➢ Unilateral or bilateral leg pain (with or without back pain), numbness, and weakness which is worse on walking. ➢ Resolves when sits down. ➢ Pain may be described as 'aching', 'crawling'. ➢ Relieved by sitting down, leaning forwards and crouching down ➢ Clinical examination is often normal ➢ Requires MRI to confirm diagnosis
Ankylosing spondylitis	➢ Typically a young man who presents with lower back pain and stiffness ➢ Stiffness is usually worse in morning and improves with activity Peripheral arthritis (25%, more common if female)
Peripheral arterial disease	➢ Pain on walking, relieved by rest ➢ Absent or weak foot pulses and other signs of limb ischaemia ➢ Past history may include smoking and other vascular diseases

Answer D

In the Gell and Coombs classification of hypersensitivity reactions scabies is an example of a:

○	Type I reaction
○	Type II reaction
○	Type III reaction
○	Type IV reaction
○	Type V reaction

Next question

Scabies produces a delayed type IV hypersensitivity reaction approximately one month after infestation. This produces the characteristic intense itching

A		8.7%
B		11.7%
C		15.1%
D		56.5%
E		7.9%

56.5% of users answered this question correctly

January 2005 exam

Which one of the following electrolyte disturbances is most associated with the development of a prolonged QT interval on ECG?

○	Hyponatraemia
○	Hypocalcaemia
○	Hyperkalaemia
○	Hypercalcaemia
○	Hypophosphataemia

Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

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

Features

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

Management

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

*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels.
**a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time
***note sotalol may exacerbate long QT syndrome

Answer : B **January 2011 exam**

Which one of the following statements regarding mitochondrial inheritance is true?

○	Friedreich's ataxia is caused by defects in mitochondrial DNA
○	There is a 50% chance that the female offspring of an affected male will inherit the disease
○	Affected females cannot pass on the disease
○	Most cases of spinocerebellar ataxia are caused by defects in mitochondrial DNA
○	Poor genotype: phenotype correlation

Mitochondrial diseases:

- Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria.
- It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

1) inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote.
2) all children of affected males will not inherit the disease
3) all children of affected females will inherit it
4) generally encode rare neurological diseases
5) poor genotype: phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

Histology:

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:

- Leber's optic atrophy.
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes.
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres.
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

A 18.7% **B** 12.3% **C** 8.9% **D** 17% **E** 43%

Which one of the following statements regarding nitric oxide is incorrect?

○	Promotes platelet aggregation
○	Raises intracellular cGMP levels
○	An inducible form of NOS is present in macrophages
○	In sepsis increased levels of NO contribute to septic shock
○	Causes venodilation

Next question

Nitric oxide - vasodilation + inhibits platelet aggregation

Nitric oxide inhibits, rather than promotes, platelet aggregation

Nitric oxide:

- Previously known as endothelium derived relaxation factor,
- Nitric oxide (NO) has emerged as a molecule which is integral to many physiological and pathological processes.
- It is formed from L-arginine and oxygen by nitric oxide synthetase (NOS).
- An inducible form of NOS has been shown to be present in macrophages.
- Nitric oxide has a very short half-life (seconds), being inactivated by oxygen free radicals

Effects:

- acts on guanylate cyclase leading to raised intracellular cGMP levels and therefore decreasing Ca2+ levels
- vasodilation, mainly venodilation
- inhibits platelet aggregation

Clinical relevance:

- underproduction of NO is implicated in hypertrophic pyloric stenosis
- lack of NO is thought to promote atherosclerosis
- in sepsis increased levels of NO contribute to septic shock
- organic nitrates (metabolism produces NO) is widely used to treat cardiovascular disease (e.g. angina, heart failure)
- sildenafil is thought to potentiate the action of NO on penile smooth muscle and is used in the treatment of erectile dysfunctions

A  42.9% **B**  15.6% **C**  10.4% **D**  13.3% **E**  17.8%

Which of the following statements is true regarding hyponatraemia?

○	In a dehydrated patient with urinary sodium < 20mmol/L it may be due to the diuretic stage of renal failure
○	SIADH typically leads to urine osmolality of < 500 mmol/kg
○	Hyperlipidaemia may cause pseudohyponatraemia
○	Cardiac failure and liver cirrhosis may lead to primary hyperaldosteronism
○	It is known to cause a long QT interval

Hyponatraemia:

- Hyponatraemia may be caused by water excess or sodium depletion.
- Causes of pseudohyponatraemia include
    1) Hyperlipidaemia (increase in serum volume) or a
    2) taking blood from a drip arm
- Urinary sodium and osmolarity levels aid making a diagnosis

Urinary sodium > 20 mmol/l

- Sodium depletion, renal loss (patient often hypovolaemic)
    1) diuretics
    2) Addison's
    3) diuretic stage of renal failure

- Patient often euvolaemic:
    1) SIADH (urine osmolality > 500 mmol/kg)
    2) Hypothyroidism

Urinary sodium < 20 mmol/l

- Sodium depletion, extra-renal loss
    1) diarrhoea, vomiting,
    2) adenoma of rectum
    3) sweating, burns

Water excess:

(Patient often hypervolaemic and oedematous)

- secondary hyperaldosteronism: heart failure, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Hyponatraemia: correction

Central pontine myelinolysis

- demyelination syndrome caused by rapid correction of chronic hyponatraemia
- may lead to quadriparesis and bulbar palsy
- diagnosis: MRI brain

Answer C

Doxazosin is a:

○	Alpha-1 antagonist
○	Alpha-1 agonist
○	Non-selective alpha antagonist
○	Alpha-2 agonist
○	Alpha-2 antagonist

Next question

Doxazosin is an alpha-1 adrenoceptor antagonist used in the treatment of hypertension and benign prostatic hypertrophy

Adrenoceptor antagonists:

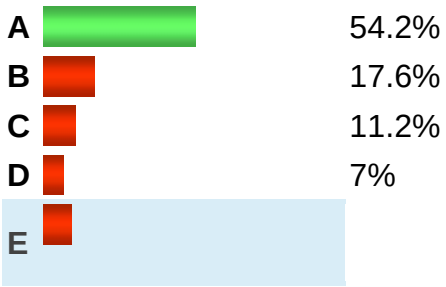
Alpha antagonists:

- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists

- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

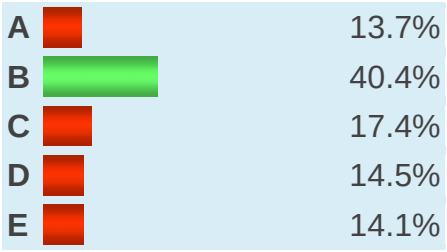


Which one of the following statements regarding glucagon-like peptide-1 (GLP-1) is incorrect?

○	Secreted in response to an oral glucose load
○	Increased levels are seen in type 2 diabetes mellitus
○	Slows gastric emptying
○	Secreted by the small intestine
○	Responsible for the incretin effect

Next question

Decreased levels of GLP-1 are seen in type 2 diabetes mellitus



Each one of the following may raise ESR, except:

○	Female sex
○	Systemic lupus erythematous
○	Polycythaemia
○	Myeloma
○	Increasing age

Next question

Erythrocyte sedimentation rate (ESR)

The ESR is a non-specific marker of inflammation and depends on both the size, shape and number of red blood cells and the concentration of plasma proteins such as fibrinogen, alpha2-globulins and gamma globulins

Causes of a high ESR

- temporal arteritis
- myeloma
- other connective tissue disorders e.g. systemic lupus erythematosus
- other malignancies
- infection
- other factors which raise ESR: increasing age, female sex, anaemia

Causes of a low ESR

- polycythaemia
- afibrinogenaemia/hypofibrinogenaemia

Answer C

You are speaking to a 24-year-old man who is known to have haemophilia A. His wife has had genetic testing and was found not to be a carrier of haemophilia. He asks you what the chances are of his future children developing haemophilia. What is the correct answer?

○	0%
○	25%
○	50%
○	50% if male, 0% if female
○	100%

Next question

X-linked recessive conditions - there is no male-to-male transmission. Affected males can only have unaffected sons and carrier daughters.

As we now know that mother is not a carrier of the disease there is no chance that any future children could develop haemophilia. You should of course also discuss with him that any daughters that he has will be carriers of the condition.

Answer : A

A patient is seen in clinic complaining of abdominal pain. Routine bloods show:

Na^+	142 mmol/l
K^+	4.0 mmol/l
Chloride	104 mmol/l
Bicarbonate	19 mmol/l
Urea	7.0 mmol/l
Creatinine	112 µmol/l

What is the anion gap?

○	4 mmol/L
○	14 mmol/L
○	20 mmol/L
○	21 mmol/L
○	23 mmol/L

Next question

The anion gap may be calculated by using (sodium + potassium) - (bicarbonate + chloride)

= (142 + 4.0) - (104 + 19) = 23 mmol/L

Answer : E

In the Gell and Coombs classification of hypersensitivity reactions Grave's disease is an example of a:

○	Type I reaction
○	Type II reaction
○	Type III reaction
○	Type IV reaction
○	Type V reaction

Next question

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy (e.g. asthma, eczema and hayfever)

Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's, pernicious anemia, acute hemolytic transfusion reactions, rheumatic fever, bullous pemphigoid, pemphigus vulgaris

Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase), multiple sclerosis, Guillain-Barre syndrome

In recent times a further category has been added:

Type V

- antibodies that recognise and bind to the cell surface receptors, either stimulating them or blocking ligand binding
- Graves' disease, myasthenia gravis

Answer :E

A 61-year-old woman is admitted to the Acute Medical Unit as she is generally unwell with muscle twitching. Blood pressure is recorded at 114/78 mmHg, pulse 84/min and she is apyrexial. Blood tests reveal the following:

Calcium	1.94 mmol/l
Albumin	38 g/l

Which one of the following tests is most useful in elucidating the cause of her symptoms?

○	Urea
○	Vitamin D
○	Phosphate
○	Parathyroid hormone
○	Magnesium

Next question

Parathyroid hormone is the single most useful test in determining the cause of hypocalcaemia

Answer : D

Which one of the following clotting factors is not affected by warfarin?

○	Factor II
○	Factor VII
○	Factor XII
○	Factor IX
○	Factor X

Next question

Warfarin - clotting factors affected mnemonic - 1972 (**1**0, **9**, **7**, **2**)

Factor XII is not affected by warfarin

Warfarin:

- Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the carboxylation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C.

Indications:

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

- Patients on warfarin are monitored using the INR (international normalised ration), the ratio of the prothrombin time for the patient over the normal prothrombin time.
- Warfarin has a long half-life and achieving a stable INR may take several days.
- There a variety of loading regimes and computer software is now often used to alter the dose.

Factors that may potentiate warfarin:

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

Side-effects:

- haemorrhage
- teratogenic, although can be used in breast-feeding mothers
- purple toes
- skin necrosis:
  - When warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration.
  - Thrombosis may occur in venules leading to skin necrosis

Answer : c

Which one of the following is involved in the degradation of polypeptides?

○	Peroxisome
○	Endoplasmic reticulum
○	Proteasome
○	Ribosome
○	Golgi apparatus

Answer: c

A 37-year-old man with a history of alcohol excess is admitted with alcohol-withdrawal seizures to the acute medical unit. Admission bloods show the following:

Na^+	137 mmol/l
K^+	3.0 mmol/l
Urea	2.0 mmol/l
Creatinine	78 µmol/l
Calcium	2.03 mmol/l

What other blood abnormality is he also most likely to have?

○	Hypomagnesaemia
○	Elevated ammonia levels
○	Hypophosphataemia
○	Partially compensated metabolic alkalosis
○	Raised bilirubin

Next question

Hypomagnesaemia

Cause of low magnesium

- diuretics
- diarrhoea
- total parenteral nutrition
- alcohol
- hypokalaemia, hypocalcaemia

Features:

- paraesthesia
- tetany
- seizures
- arrhythmias
- decreased PTH secretion → hypocalcaemia
- ECG features similar to those of hypokalaemia
- exacerbates digoxin toxicity

Answer : A

Immunoglobulin therapy may be indicated in each of the following except:

○	Dermatomyositis
○	Guillain-Barre syndrome
○	Kawasaki disease
○	Idiopathic thrombocytopenic purpura
○	Thrombotic thrombocytopenic purpura

Next question

The management of management thrombotic thrombocytopenic purpura involves steroids and immunosuppressants. Plasma exchange is also commonly used

Answer : E

A 64 year old woman who is reviewed due to multiple non-healing leg ulcers, She reports feeling generally unwell for many months. Examination findings include a blood pressure of 138/72 mmHg, pulse 90 bpm, pale conjunctivae and poor dentition associated with bleeding gums. What is the most likely underlying diagnosis?

○	Thyrotoxicosis
○	Vitamin B12 deficiency
○	Vitamin C deficiency
○	Diabetes mellitus
○	Sarcoidosis

Vitamin C (ascorbic acid)

Vitamin C is a water soluble vitamin.

Functions:

- antioxidant
- collagen synthesis: acts as a cofactor for enzymes that are required for the hydroxylation proline and lysine in the synthesis of collagen
- facilitates iron absorption
- cofactor for norepinephrine synthesis

Vitamin C deficiency (scurvy) leads to defective synthesis of collagen resulting in capillary fragility (bleeding tendency) and poor wound healing

Features vitamin C deficiency:

- gingivitis, loose teeth
- poor wound healing
- bleeding from gums, haematuria, epistaxis
- general malaise

Answer : C

A 14-year-old girl is admitted to the Emergency Department. Over the past hour she has developed a painless, non-pruritic erythematous rash associated with severe angioedema. She has a past medical history of recurrent abdominal pain. Her symptoms fail to respond to adrenaline and she is therefore intubated to protect the airway. She is discharged from ITU after three days. During outpatient follow-up two weeks later a diagnosis of hereditary angioedema is suspected. What is the most appropriate screening test to perform?

○	Serum IgE levels
○	Serum C3 levels
○	Serum tryptase levels
○	Serum C4 levels
○	Serum C1-INH levels

Next question

Hereditary angioedema - C4 is the best screening test inbetween attacks

Answer : D

A scientist is investigated potential targets for anti-HIV drugs. What is the role of reverse transcriptase in HIV infection?

○	Inhibits topoisomeras II (DNA gyrase) and topoisomerase IV
○	Prevents supercoiling during replication
○	Unwinds the DNA double helix at the replication fork
○	Transcribes viral RNA to host DNA
○	Produces viral RNA in host cells from DNA template

Answer : D

A 43-year-old man has a routine medical for insurance purposes. The following result is obtained:

Uric acid	622 µmol/l (210 - 480)

He is well with no significant past medical history. What is the most appropriate test to perform next?

- Lipid profile
- Thyroid function test
- Calcium
- Parathyroid hormone
- Pyrophosphate levels

Next question

Hyperuricaemia may be associated with both hyperlipidaemia and hypertension. It may also be seen in conjunction with the metabolic syndrome

Answer : A

A 27-year-old man is reviewed in a fertility clinic. Semen analysis has revealed azoospermia. On examination at the previous appointment he was noted to be 1.83 metres tall with a body mass index of 25 kg / m^2. A degree of gynaecomastia is noted, testicular volume is around 10ml bilaterally and his visual fields were normal. Which investigation is likely to be diagnostic?

○	FISH analysis of DNA
○	Prolactin level
○	Karyotype
○	MRI pituitary
○	PCR analysis of DNA

Next question

Klinefelter's? - do a karyotype

Answer : c

A 65-year-old woman is investigated for a 6 week history of worsening shortness of breath, lethargy and weight loss. Her past medical history includes chronic obstructive pulmonary disease, hypertension and she is an ex-smoker. Clinical examination is unremarkable. Investigation results are as follows:

Chest x-ray

Hyperinflated lung fields, normal heart size

Bloods

Sodium	131 mmol/l
Potassium	3.4 mmol/l
Urea	7.2 mmol/l
Creatinine	101 µmol/l
Hb	10.4 g/dl
MCV	91 fl
Plt	452 * 10^9/l
WBC	3.7 * 10^9/l

What is the most appropriate management?

○	Screen for depression
○	Short synacthen test
○	Urgent referral to the chest clinic
○	Stop bendroflumethiazide
○	Urgent gastroscopy

Next question

Despite a normal chest x-ray an ex-smoker with shortness of breath, weight loss and hyponatraemia should be investigated on an urgent basis for lung cancer. This approach is supported by current NICE guidelines. Whilst gastrointestinal cancer is a possibility the normal MCV is not entirely consistent with chronic blood loss

Answer : c

Which one of the following molecules acts as the co-receptor for cells expressing antigens combined with MHC class I molecules?

○	CD4
○	CD2b
○	CD1
○	CD8
○	CD2

Clusters of differentiation:

The table below lists the major clusters of differentiation (CD) molecules

Cluster of differentiation	Function
CD1	MHC molecule that presents lipid molecules
CD2	Found on thymocytes, T cells, and some natural killer cells that acts as a ligand for CD58 and CD59 and is involved in signal transduction and cell adhesion
CD3	The signalling component of the T cell receptor (TCR) complex
CD4	Found on helper T cells. Co-receptor for MHC class II Used by HIV to enter T cells
CD5	Found in the majority of mantle cell lymphomas
CD8	Found on cytotoxic T cells. Co-receptor for MHC class I Found on a subset of myeloid dendritic cells
CD14	Cell surface marker for macrophages
CD15	Expressed on Reed-Sternberg cells (along with CD30)
CD28	Interacts with B7 on antigen presenting cell as costimulation signal
CD95	Acts as the FAS receptor, involved in apoptosis

Answer : D

You are asked to review some arterial blood gases (ABGs) done on a patient who has recently been admitted to the Emergency Department. The ABGs shown below were taken on air:

pH	7.53
pCO2	5.1 kPa
pO2	13.9 kPa

Which one of the following is the most likely cause?

○	Chronic obstructive pulmonary disease
○	Renal tubular acidosis
○	Mesenteric ischaemia
○	Anxiety
○	Vomiting

The blood gases show a metabolic alkalosis

Metabolic alkalosis:

- Metabolic alkalosis may be caused by a loss of hydrogen ions or a gain of bicarbonate.
- It is due mainly to problems of the kidney or gastrointestinal tract

Causes:

- vomiting / aspiration (e.g. peptic ulcer leading to pyloric stenos, nasogastric suction)
- diuretics
- liquorice, carbenoxolone
- hypokalaemia
- primary hyperaldosteronism
- Cushing's syndrome
- Bartter's syndrome
- congenital adrenal hyperplasia

Mechanism of metabolic alkalosis:

- activation of renin-angiotensin II-aldosterone (RAA) system is a key factor
- aldosterone causes reabsorption of Na^+ in exchange for H+ in the distal convoluted tubule
- ECF depletion (vomiting, diuretics) → Na^+ and Cl- loss → activation of RAA system → raised aldosterone levels
- in hypokalaemia, K^+ shift from cells → ECF, alkalosis is caused by shift of H+ into cells to maintain neutrality

Answer : E

Which of the following conditions is inherited in an autosomal dominant fashion?

○	Noonan syndrome
○	Homocystinuria
○	Cystinuria
○	Congenital adrenal hyperplasia
○	Fanconi anaemia

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Answer : A

A 14-year-old girl presents with a swollen left knee. Her parents state she suffers from haemophilia and has been treated for a right-sided haemarthrosis previously. What other condition is she most likely to have?

○	Turner's syndrome
○	Down's syndrome
○	Ataxia telangiectasia
○	Hunter's syndrome
○	Coeliac disease

Next question

Haemophilia is a X-linked recessive disorder and would hence be expected only to occur in males. As patients with Turner's syndrome only have one X chromosome however, they may develop X-linked recessive conditions

Answer : A

Which one of the following statements regarding interleukin 1 (IL-1) is true?

○	It is released mainly by macrophages/monocytes
○	It causes vasoconstriction
○	It reduces expression of selectin molecules on the endothelium
○	IL-1 antagonists are currently licensed for use in colorectal cancer
○	It inhibits the release of nitric oxide by the endothelium

IL-1:

- Interleukin 1 (IL-1) is a key mediator of the immune response.
- It is secreted mainly by macrophages and monocytes and acts as a costimulator of T cell and B cell proliferation.
- Other effects include increasing the expression of adhesion molecules on the endothelium.
- By stimulating the release by the endothelium of vasoactive factors such as PAF, nitric oxide and prostacyclin it also causes vasodilation and increases vascular permeability. It is therefore one of the mediators of shock in sepsis.
- Along with IL-6 and TNF, it acts on the hypothalamus causing pyrexia.

ANSWER : A

Which one of the following is not associated with hypocalcaemia combined with a raised phosphate level?

○	Chronic renal failure
○	Pseudohypoparathyroidism
○	Hypoparathyroidism
○	Osteomalacia
○	Acute rhabdomyolysis

Next question

Osteomalacia causes hypocalcaemia associated with a low serum phosphate, rather than a raised phosphate level.

Hypocalcaemia: causes and management:

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

Causes:

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)
- massive blood transfusion
- Acute pancreatitis may also cause hypocalcaemia.
- Contamination of blood samples with EDTA may also give falsely low calcium levels

Management:

- Acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Answer : D

A 40-year-old man presents with pain in his lower back and 'sciatica' for the past three days. He describes bending down to pick up a washing machine when he felt 'something go'. He now has severe pain radiating from his back down the right leg. On examination he describes paraesthesia over the anterior aspect of the right knee and the medial aspect of his calf. Power is intact and the right knee reflex is diminished. The femoral stretch test is positive on the right side. Which nerve root is most likely to be affected?

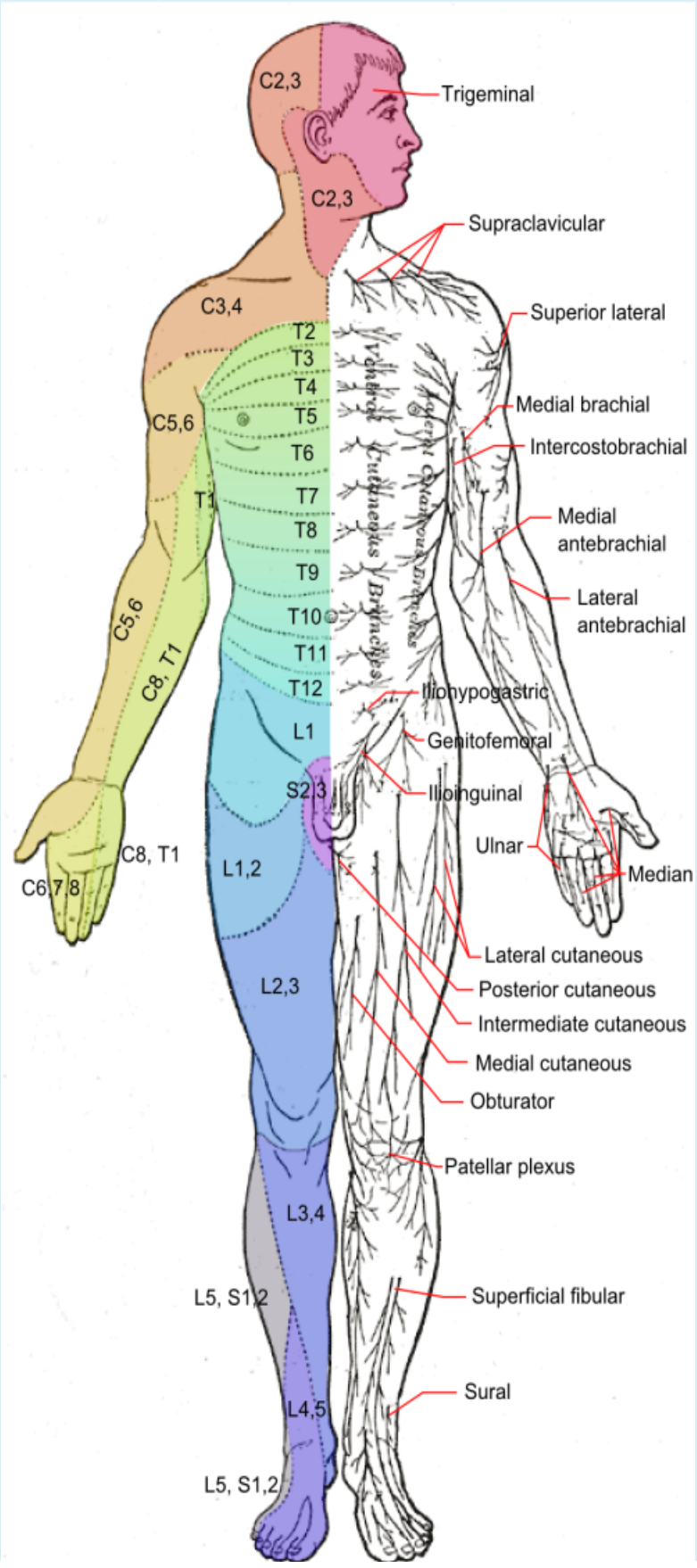
○	Common peroneal nerve
○	Lateral cutaneous nerve of the thigh
○	L5
○	L3
○	L4

Answer : E

Dermatomes:

The table below lists the major dermatome landmarks:

Nerve root	Landmark
C2	Posterior half of the skull (cap)
C3	High turtleneck shirt
C4	Low-collar shirt
C5, C6	Thumb + index finger Make a 6 with your left hand by touching the tip of the thumb & index finger together - C6
C7	Middle finger + palm of hand
C8	Ring + little finger
T4	Nipples T4 at the Teat Pore
T5	Inframammary fold
T7	Xiphoid process
T10	Umbilicus BellybuT-TEN
L1	Inguinal ligament L for ligament, 1 for 1nguinal
L4	Knee caps Down on aLL fours - L4
L5	Big toe, dorsum of foot (except lateral aspect) L5 = Largest of the 5 toes
S1	Lateral foot, small toe S1 = the smallest one
S2, S3	Genitalia



The muscarinic acetylcholine receptor is an example of a:

○	Ligand-gated ion channel
○	Tyrosine kinase receptor
○	Guanylate cyclase receptor
○	G protein-coupled receptor
○	Intracellular receptor

Answer : d

Membrane receptors:

- There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

3) Ligand-gated ion channel receptors:

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

4) Tyrosine kinase receptors:

- intrinsic tyrosine kinase: insulin, insulin-like growth factor (IGF), epidermal growth factor (EGF)
- receptor-associated tyrosine kinase: growth hormone, prolactin, interferon, interleukin

3) Guanylate cyclase receptors:

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor, brain natriuretic peptide

4) G protein-coupled receptors:

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- 7-helix membrane-spanning domains
- consist of 3 main subunits: alpha, beta and gamma
- the alpha subunit is linked to GDP.Ligand binding causes conformational changes to receptor, GDP is phosphorylated to GTP,and the alpha subunit is activated
- G proteins are named according to the alpha subunit (G_s, G_i, G_q)

	G_s	G_i	G_q
Mechanism	Activates adenylate cyclase → increases cAMP → activates protein kinase A	Inhibits adenylate cyclase → decreases cAMP → inhibits protein kinase A	Activates phospholipase C → splits PIP_2 to IP_3 & DAG → activates protein kinase C
Examples	➢ Beta-1 receptors (epinephrine, norepinephrine, dobutamine) ➢ Beta-2 receptors (epinephrine, salbuterol) ➢ H2 receptors (histamine) ➢ D1 receptors (dopamine) ➢ V2 receptors (vasopressin) ➢ Receptors for ACTH, LH, FSH, glucagon, PTH, calcitonin, prostaglandins	1) M2 receptors (acetylcholine) 2) Alpha-2 receptors (epinephrine, norephinephrine) 3) D2 receptors (dopamine) 4) GABA-B receptor	1) Alpha-1 receptors (epinephrine, norepinephrine) 2) H1 receptors (histamine) 3) V1 receptors (vasopressin) 4) M1, M3 receptors (acetylcholine)

During which of the following stages of mitosis does chromatin condense to form chromosomes?

○	Telophase
○	Metaphase
○	Prophase
○	Interphase
○	Anaphase

Answer : C

Cell cycle

Phase	Notes
G_0	• 'resting' phase • quiescent cells such as hepatocytes and more permanently resting cells such as neurons
G_1	• **G**ap 1, cells increase in size • determines length of cell cycle • under influence of p53
S	• **S**ynthesis of DNA, RNA and histone • centrosome duplication
G_2	• **G**ap 2, cells continue to increase in size
M	• **M**itosis - cell division

Cell division

There are two types of cell division; mitosis and meiosis.
The table below demonstrates the key differences:

Mitosis	Meiosis
Occurs in somatic cells	Occurs in gametes
Results in 2 diploid daughter cells	Results in 4 haploid daughter cells
Daughter cells are genetically identical to parent cell	Daughter cells contain one homologue of each chromosome pair and are therefore genetically different

Remember:

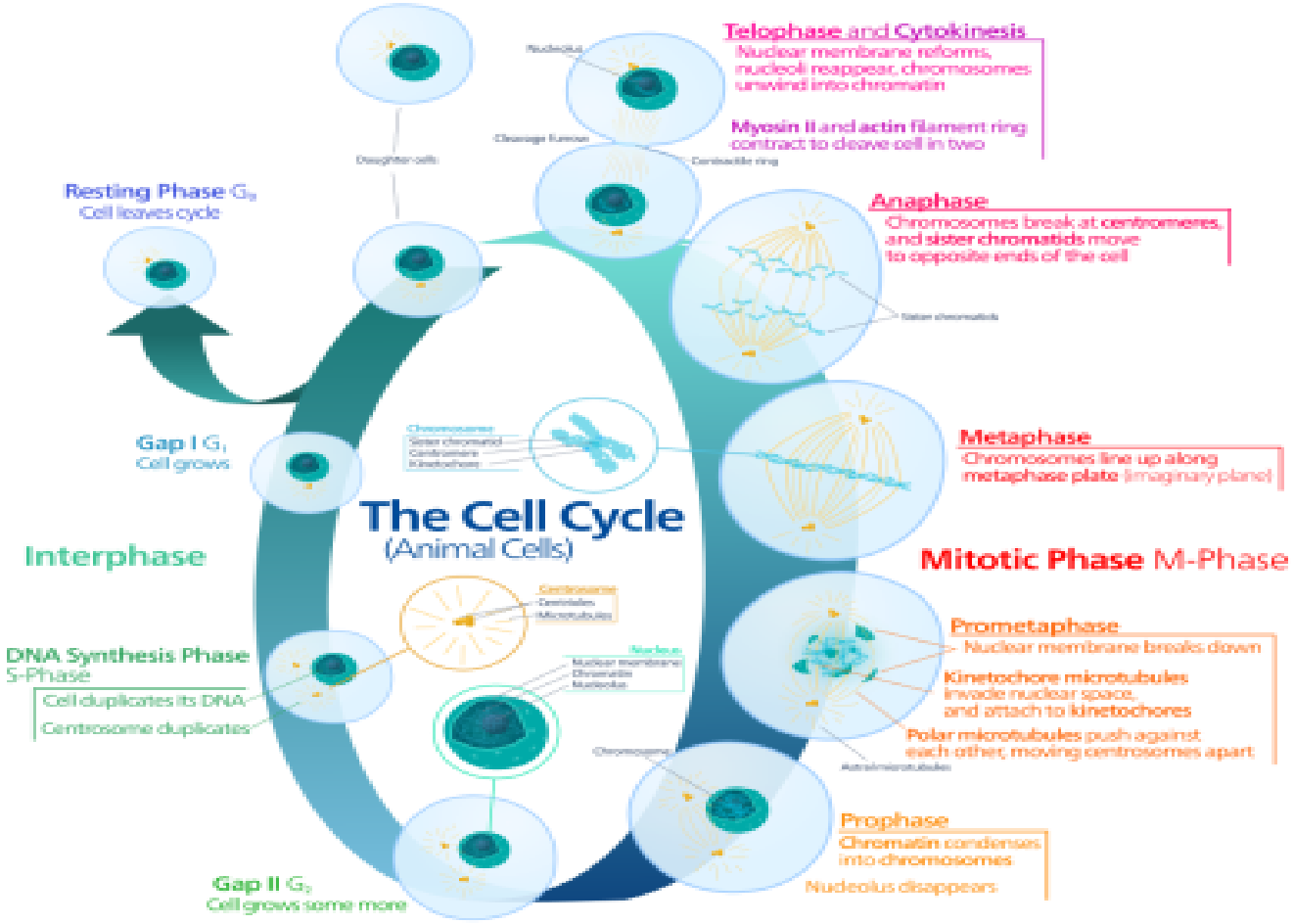
- somatic cells have 22 pairs of autosomes and 1 pair of sex chromosomes, i.e. 46XY or 46XX
- cells with a normal chromosome complement are known as diploid cells
- gametes (ova or spermatozoa) have a single copy of each chromosome and are known as haploid cells

https://www.youtube.com/watch?v=JcZQkmooyPk

Mitosis

- Mitosis occurs during the M phase of the cell cycle.
- It describes the process in which somatic cells divide and replicate producing genetically identical diploid daughter cells.
- This allows tissue to grow and renew itself.
- During the S phase of the cell cycle the cell prepares itself for division by duplicating the chromosomes.
- The table below shows the phases of mitosis itself:

Prophase	Chromatin in the nucleus condenses
Prometaphase	Nuclear membrane breaks down allowing the microtubules to attach to the chromosomes
Metaphase	Chromosomes aligned at middle of cell
Anaphase	The paired chromosomes separate at the kinetochores and move to opposite sides of the cell
Telophase	Chromatids arrive at opposite poles of cell
Cytokinesis	Actin-myosin complex in the centre of the cell contracts resulting in it being 'pinched' into two daughter cells



Which one of the following karyotypes is associated with short stature?

○	45,XO
○	46,YO
○	46,XO
○	47,XYY
○	47,XXY

Answer: A

T-Helper cells of the Th2 subset typically secrete:

○	IL-4, IL-5, IL-6, IL-10, IL-13
○	IFN-gamma, IL-2, IL-3
○	IL-1, IL-6, TNF-alpha
○	IFN-beta, IL-4, IL-8
○	IL-1

Next question

T-Helper cells

There are two major subsets of T-Helper cells:

Th1

- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2

- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Answer : A

A patient with lung cancer has a Positron Emission Tomography (PET) scan to evaluate possible metastatic disease. What does this type of scan demonstrate?

○	Cellular proliferation
○	Apoptotic activity
○	Glucose uptake
○	Vascular supply
○	Tyrosine kinase activity

Next question

Positron Emission Tomography (PET)

- Positron Emission Tomography (PET) is a form of nuclear imaging which uses fluorodeoxyglucose (FDG) as the radiotracer.
- This allows a 3D image of metabolic activity to be generated using glucose uptake as a proxy marker.
- The images obtained are then combined with a conventional imaging technique such as CT to decide whether lesions are metabolically active.

Uses:

- evaluating primary and possible metastatic disease
- cardiac PET: not used mainstream currently

Answer : c

How is the left ventricular ejection fraction calculated?

○	End systolic LV volume / end diastolic LV volume
○	End diastolic LV volume / end systolic LV volume
○	End diastolic LV volume / stroke volume
○	End systolic LV volume - end diastolic LV volume
○	Stroke volume / end diastolic LV volume

Next question

Cardiovascular physiology

Left ventricular ejection fraction:

- Left ventricular ejection fraction = (stroke volume / end diastolic LV volume) * 100%
- Stroke volume = end diastolic LV volume - end systolic LV volume

Pulse pressure:

- Pulse pressure = Systolic Pressure - Diastolic Pressure

Factors which increase pulse pressure

1) a less compliant aorta (this tends to occur with advancing age)
2) increased stroke volume

Answer : E

Which one of the following is associated with increased lung compliance?

○	Kyphosis
○	Pulmonary oedema
○	Emphysema
○	Pulmonary fibrosis
○	Pneumonectomy

Next question

Respiratory physiology: lung compliance

Lung compliance is defined as change in lung volume per unit change in airway pressure

Causes of increased compliance

- age
- emphysema - this is due to loss alveolar walls and associated elastic tissue

Causes of decreased compliance

- pulmonary oedema
- pulmonary fibrosis
- pneumonectomy
- kyphosis

Answer : C

Which cell organelle is involved in the breakdown of oligopeptides?

○	Golgi apparatus
○	Rough endoplasmic reticulum
○	Peroxisome
○	Lysosome
○	Smooth endoplasmic reticulum

Next question

Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	**Main function**
Endoplasmic reticulum	Rough endoplasmic reticulum 1) translation and folding of new proteins 2) manufacture of lysosomal enzymes 3) site of N-linked glycosylation examples of cells with extensive RER include pancreatic cells, goblet cells, plasma cells Smooth endoplasmic reticulum • steroid, lipid synthesis examples of cells with extensive SER include those of the adrenal cortex, hepatocytes, testes, ovaries
Golgi apparatus	Modifies, sorts, and packages these molecules that are destined for cell secretion Site of O-linked glycosylation
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Proteasome	Along with the lysosome pathway involved in degradation of protein molecules that have been tagged with ubiquitin
Peroxisome	• Catabolism of very long chain fatty acids and amino acids • Results in the formation of hydrogen peroxide

Protein degradation in eukaryotes is also carried out by protein complexes called proteasomes.

Answer: D

Where is CCK secreted from?

○	I cells in upper small intestine
○	G cells in stomach
○	K cells in upper small intestine
○	D cells in the pancreas
○	S cells in upper small intestine

Answer A

Aldosterone is secreted by the:

○	Juxtaglomerular apparatus
○	Zona glomerulosa
○	Posterior pituitary
○	Zona reticularis
○	Zona fasciculata

Next question

Adrenal cortex mnemonic: GFR - ACD

Renin-angiotensin-aldosterone system

Adrenal cortex (mnemonic **GFR - ACD**)

- zona **g**lomerulosa (on outside): mineralocorticoids, mainly **a**ldosterone
- zona **f**asciculata (middle): glucocorticoids, mainly **c**ortisol
- zona **r**eticularis (on inside): androgens, mainly **d**ehydroepiandrosterone (DHEA)

Answer B

Where are G protein-coupled receptors located?

○	Nucleus
○	Golgi apparatus
○	Ribosome
○	Cell membrane
○	Mitochondria

Next question

G protein-coupled receptors span the cell membrane

Answer D

A 54-year-old woman is treated with rituximab for non-Hodgkin's lymphoma. What is the target of rituximab?

○	CD20
○	CD52
○	Epidermal growth factor receptor
○	CD22
○	Vascular endothelial growth factor receptor

Next question

Rituximab - monoclonal antibody against CD20

Answer A

A 25-year-old man who has been morbidly obese for the past five years is reviewed in the endocrinology clinic. In this patient, which one of the following hormones would increase appetite as levels increase?

○	Leptin
○	Thyroxine
○	Adiponectin
○	Ghrelin
○	Serotonin

Next question

Obesity hormones

- **L**eptin **L**owers appetite
- **G**hrelin **G**ains appetite

Whilst thyroxine can increase appetite it does not fit with the clinical picture being described

Answer D

A 50-year-old man is reviewed in the neurology clinic. For the past four months he has been experiencing problems with his right shoulder. On examination he has weakness of shoulder abduction and to a lesser extent weak elbow flexion. A small patch of numbness is noted over the deltoid muscle but otherwise sensation is normal. Where is the neurological lesion?

○	C4
○	C5
○	C6
○	C7
○	C8

Next question

This man has weakness of both the deltoid (C5, C6) and the biceps muscle (C5, C6, C7). The location of the sensory loss points to a C5 lesion however

Answer B

A 30-year-old man with a history of mitral valve prolapse, recurrent pneumothorax, lower back pain secondary to scoliosis and pectus excavatum is considering starting a family. Given the likely diagnosis, what is the mode of inheritance of this condition?

○	X-linked recessive
○	Mitochondrial
○	Autosomal codominant
○	Autosomal recessive
○	Autosomal dominant

Marfan's syndrome:

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

Features:

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

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

Which one of the following is in direct anatomical contact with the left kidney?

○	Stomach
○	Distal part of small intestine
○	Spleen
○	Pancreas
○	Duodenum

Renal anatomy:

The tables below show the anatomical relations of the kidneys:

Right kidney

Direct contact	Layer of peritoneum in-between
Right suprarenal gland Duodenum Colon	Liver Distal part of small intestine

Left kidney

Direct contact	Layer of peritoneum in-between
Left suprarenal gland Pancreas Colon	Stomach Spleen Distal part of small intestine

Answer D

The parents of a 3-year-old boy with cystic fibrosis ask for advice. They are considering having more children. What is the chance that their next child will be a carrier of the cystic fibrosis gene?

○	50%
○	100%
○	1 in 25
○	25%
○	66.6%

Next question

As cystic fibrosis is an autosomal recessive condition there is a 50% chance that their next child will be a **carrier** of cystic fibrosis (i.e. be heterozygous for the genetic defect) and a 25% chance that the child will actually have the disease (be homozygous).

Answer A

What does troponin T bind to?

○	Tropomyosin
○	Actin in thin myofilaments
○	Protein kinase C inhibitors
○	Calcium ions
○	T-tubule membrane wall

Next question

Tropomyosin is a protein which regulates actin. It associates with actin in muscle fibres and regulates muscle contraction by regulating the binding of myosin.

Answer A

Acute intermittent porphyria is due to a defect in:

○	ALA synthetase
○	PPG oxidase
○	Uroporphyrinogen decarboxylase
○	Ferrochelatase
○	Porphobilinogen deaminase

Next question

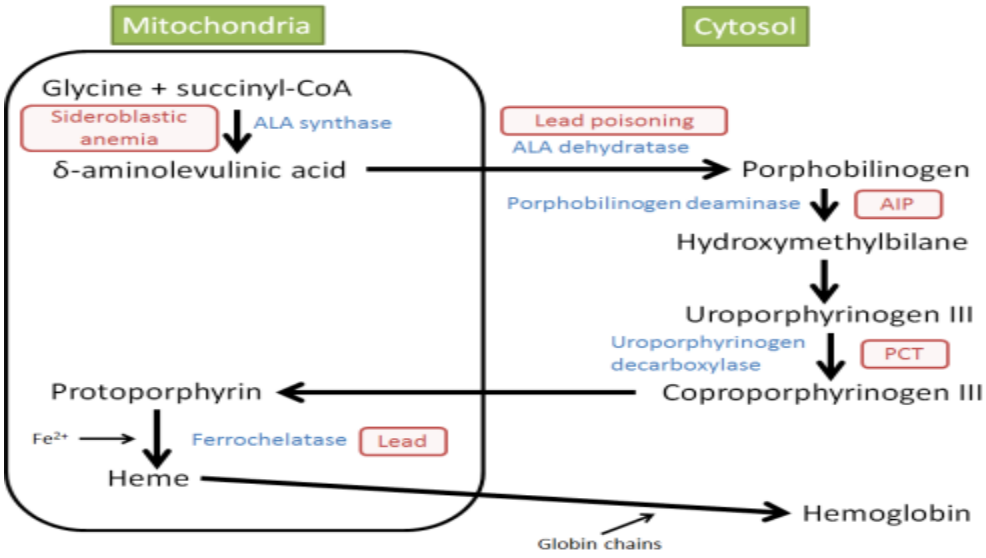
AIP - porphobilinogen de**A**minase; P**C**T - uroporphyrinogen de**C**arboxylase

Answer E

Porphyrias

Overview

- abnormality in enzymes responsible for the biosynthesis of haem
- results in overproduction of intermediate compounds (porphyrins)
- may be acute or non-acute



Acute intermittent porphyria:

- a rare autosomal dominant condition
- caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem.
- This results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen.
- It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds.
- AIP is more common in females (5:1)

Features:

1) abdominal: abdominal pain, vomiting
2) neurological: motor neuropathy
3) psychiatric: e.g. depression
4) hypertension and tachycardia common

Diagnosis:

1) classically urine turns deep red on standing
2) raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
3) assay of red cells for porphobilinogen deaminase
4) raised serum levels of delta aminolaevulinic acid and porphobilinogen

Drugs which may precipitate attack

1) barbiturates
2) benzodiazepines
3) halothane
4) alcohol
5) oral contraceptive pill
6) sulphonamides

Drugs considered safe to use

1) paracetamol
2) aspirin
3) codeine
4) morphine
5) chlorpromazine
6) beta-blockers
7) penicillin
8) metformin

Porphyria cutanea tarda (PCT):

- most common hepatic porphyria
- defect in uroporphyrinogen decarboxylase
- may be caused by hepatocyte damage e.g. alcohol, oestrogens
- classically photosensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp
- manage with chloroquine

Variegate porphyria:

- autosomal dominant
- defect in protoporphyrinogen oxidase
- photosensitive blistering rash
- abdominal and neurological symptoms
- more common in South Africans

Which one of the following pathophysiological changes is most responsible for emphysema?

○	Mucosal oedema and mucus plugging
○	Destruction of alveolar walls secondary to proteinases
○	Airway hypersensitivity
○	Smooth muscle contraction
○	Hypertrophy of mucous secreting glands

Next question

Proteinases such as elastase cause irreversible damage to the supporting connective tissue of the alveolar septa. Smoking accelerates this process.

COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

Other causes

- cadmium (used in smelting)
- coal
- cotton
- cement
- grain

Answer B

A 17-year-old man is investigated for recurrent infections and easy bruising. In the past year he has had four episodes of pneumonia. Other than the bruising he is noted to have severe eczema on his trunk and arms. A full blood count is ordered and reported as follows:

Hb	14.1 g/dl
Plt	82 * 10^9/l
WBC	5.9 * 10^9/l
Neuts	4.4 * 10^9/l

Further bloods show low immunoglobulin M levels. What is the most likely diagnosis?

○	Bruton's congenital agammaglobulinaemia
○	Wiskott-Aldrich syndrome
○	Ataxic telangiectasia
○	Chediak-Higashi syndrome
○	DiGeorge syndrome

Next question

Wiskott-Aldrich syndrome
- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia

Wiskott-Aldrich syndrome

- Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction.
- It is inherited in a X-linked recessive fashion
- thought to be caused by mutation in the WASP gene

Features

- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia
- low IgM levels

Answer B

Which of the following may be used in the treatment of hereditary angioedema?

○	Anabolic steroids
○	Oral contraceptive pill
○	ACE inhibitors
○	Beta-blockers
○	Aspirin

Next question

Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

Symptoms

- attacks may be proceeded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

Management

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help

Answer A

Which of the following conditions is inherited in a X-linked recessive fashion?

○	Androgen insensitivity syndrome
○	Myotonic dystrophy
○	von Willebrand's disease
○	Ehlers-Danlos syndrome
○	Huntington's disease

Next question

X-linked conditions: Duchenne/Becker, haemophilia, G6PD

X-linked recessive:

- In X-linked recessive inheritance only males are affected.
- An exception to this seen in examinations is patients with Turner's syndrome, who are affected due to only having one X chromosome.
- X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen.
- Affected males can only have unaffected sons and carrier daughters.
- Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.
- The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

X-linked recessive conditions:

1) Androgen insensitivity syndrome
2) Duchenne muscular dystrophy
3) Becker muscular dystrophy
4) Fabry's disease
5) G6PD deficiency
6) Haemophilia A,B
7) Hunter's disease
8) Lesch-Nyhan syndrome
9) Nephrogenic diabetes insipidus
10) Colour blindness
11) Ocular albinism
12) Retinitis pigmentosa
13) Wiskott-Aldrich syndrome

The following diseases have varying patterns of inheritance, with the majority being in an X-linked recessive fashion:

Chronic granulomatous disease (in > 70%)

Answer A

Which one of the following statements regarding hypersensitivity reactions is false?

○	Delayed hypersensitivity is responsible for graft versus host disease
○	Anaphylaxis is a type I reaction
○	Type II reactions are caused by circulating antibodies reacting with antigen on cell surface
○	Type IV reactions are T cell mediated
○	Goodpasture's syndrome is an example of a type III reaction

Next question

Goodpasture's syndrome is actually an example of a type II reaction. The other statements are true

Answer E

You are discussing conception with two parents who both have achondroplasia. They ask you what the chances are that a child of theirs would be of normal height. What is the correct response?

○	0%
○	25%
○	50% independent of gender
○	50% if male
○	75%

Next question

Many questions relating to autosomal dominant conditions are based around one of the parents being affected. With achondroplasia both parents are often affected which can make the interpretation slightly trickier.

As an autosomal dominant condition, two affected parents can expect:

- 1 in 4 chance of an unaffected child
- 1 in 2 chance of an affected heterozygous child
- 1 in 4 chance of an affected homozygous child. With achondroplasia children unfortunately don't live past the first few months of life

The answer of having a child of normal height is therefore 1 in 4 or 25%.

Achondroplasia

- Achondroplasia is an autosomal dominant disorder associated with short stature.
- It is caused by a mutation in the fibroblast growth factor receptor 3 (FGFR-3) gene.
- This results in abnormal cartilage giving rise to:

    - short limbs (rhizomelia) with shortened fingers (brachydactyly)
    - large head with frontal bossing
    - midface hypoplasia with a flattened nasal bridge
    - 'trident' hands
    - lumbar lordosis

Answer B

Which one of the following best describes the Bohr effect?

○	Increase in pO2 means CO2 binds less well to Hb
○	Decreasing acidity (or pCO2) means oxygen binds less well to Hb
○	Decrease in pO2 means CO2 binds less well to Hb
○	Raised 2,3-DPG enhances oxygen delivery to the tissues
○	Increasing acidity (or pCO2) means oxygen binds less well to Hb

Respiratory physiology

Chloride shift

- CO2 diffuses into RBCs
- CO2 + H20 ---- carbonic anhydrase -→ HCO3- + H+
- H+ combines with Hb
- HCO3- diffuses out of cell,- Cl- replaces it

Bohr effect:

- increasing acidity (or pCO2) means O2 binds less well to Hb

Haldane effect:

- increase pO2 means CO2 binds less well to Hb

Answer E

A 34-year-old man is climbing Mount Kilimanjaro. For the past two days he has complained of nausea and a headache. The climbing team is now at an altitude of 4,500m when he develops shortness of breath and a pink frothy cough. Examination reveals bibasal crackles. What is the most appropriate treatment, other than descent?

○	Nifedipine
○	Frusemide
○	Mannitol
○	Hydralazine
○	Third-generation cephalosporin

Next question

This man has developed high altitude pulmonary oedema (HAPE) and should to be treated with prompt descent, oxygen and nifedipine if it is available. Other options for treating HAPE include dexamethasone, acetazolamide and phosphodiesterase type V inhibitors.

Answer A

What is the main mechanism by which vitamin B12 is absorbed?

○	Passive absorption in the terminal ileum
○	Active absorption in the middle to terminal part of jejunum
○	Active absorption by the parietal cells of the stomach
○	Active absorption in the terminal ileum
○	Passive absorption in the proximal ileum

Next question

Vitamin B12 is actively absorbed in the terminal ileum

A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Answer D

For a patient undergoing an elective splenectomy, when is the optimal time to give the pneumococcal vaccine?

○	Four weeks before surgery
○	One week before surgery
○	Immediately following surgery
○	Two weeks after surgery
○	At least one month after surgery

Next question

The current British National Formulary recommends giving the vaccine at least 2 weeks before elective splenectomy. Therefore 4 weeks is the best response from the given options.

Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus* infections

Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

Antibiotic prophylaxis

- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

*usually from dog bites

Answer A

A 20-year-old man is admitted to the Emergency Department with chest pain. He confides that he has snorted 'a large amount' of cocaine in the previous hours. Which one of the following features is his cocaine use most likely to cause?

○	Hypokalaemia
○	Hyperthermia
○	Decreased deep tendon reflexes
○	Hypotension
○	Metabolic alkalosis

Answer B

Cocaine:

- Cocaine is an alkaloid derived from the coca plant.
- It is widely used as a recreational stimulant.
- The price of cocaine has fallen sharply in the past decade resulting in cocaine toxicity becoming a much more frequent clinical problem.
- This increase has made cocaine a favourite topic of question writers.

Mechanism of action

- cocaine blocks the uptake of dopamine, noradrenaline and serotonin

The use of cocaine is associated with a wide variety of adverse effects:
Cardiovascular effects:

- myocardial infarction
- both tachycardia and bradycardia may occur
- hypertension
- QRS widening and QT prolongation
- aortic dissection

Neurological effects:

- seizures
- mydriasis
- hypertonia
- hyperreflexia

Psychiatric effects

- agitation
- psychosis
- hallucinations

Others

- hyperthermia
- metabolic acidosis
- rhabdomyolysis

Management of cocaine toxicity

- in general benzodiazipines are generally first-line for most cocaine related problems
- chest pain: benzodiazipines + glyceryl trinitrate.
- If myocardial infarction develops then primary percutaneous coronary intervention
- hypertension: benzodiazipines + sodium nitroprusside
- the use of beta-blockers in cocaine-induced cardiovascular problems is a controversial issue. The American Heart Association issued a statement in 2008 warning against the use of beta-blockers (due to the risk of unopposed alpha-mediated coronary vasospasm) but many cardiologists since have questioned whether this is valid. If a reasonable alternative is given in an exam it is probably wise to choose it

Which one of the following types of thyroid cancer is associated with the RET oncogene?

○	Anaplastic
○	Lymphoma
○	Follicular
○	Medullary
○	All types of thyroid cancer

Next question

The RET oncogene encodes a receptor tyrosine kinase and is associated with MEN type 2.

Papillary thyroid cancer also appears to be associated with the RET oncogene

Answer D

Which of the following statements is true regarding the p53 gene?

○	It is an oncogene
○	Mutation results in a gain of function
○	50% of families with a strong history of breast cancer have a p53 mutation
○	Li-Fraumeni syndrome predisposes to the development of sarcomas
○	It is located on chromosome 13

Next question

p53

p53 is a tumour suppressor gene located on chromosome 17p. It is the most commonly mutated gene in breast, colon and lung cancer

p53 is thought to play a crucial role in the cell cycle, preventing entry into the S phase until DNA has been checked and repaired. It may also be a key regulator of apoptosis

Li-Fraumeni syndrome is a rare autosomal dominant disorder characterised by the early onset of a variety of cancers such as sarcomas and breast cancer. It is caused by mutation in the p53 gene

Answer D

A 38-year-old woman comes for review. Six months ago she fractured her left wrist whilst skiing. The fracture was treated using a cast and repeat x-rays showed that the bone had healed well. Unfortunately for the past few weeks she has been plagued with ongoing 'shooting pains' in her left hand associated with swelling. On examination the left hand is extremely tender to even light touch. Her left hand is also slightly swollen compared to the right. What is the most likely diagnosis?

○	Depression
○	Conversion disorder
○	Complex regional pain syndrome
○	Ulnar nerve injury
○	Osteomyelitis

Complex regional pain syndrome:

- Complex regional pain syndrome (CRPS) is the modern, umbrella term for a number of conditions such as reflex sympathetic dystrophy and causalgia.
- It describes a number of neurological and related symptoms which typically occur following surgery or a minor injury.
- CRPS is 3 times more common in women.
- There are two types of CRPS:
    - type I (most common): there is no demonstrable lesion to a major nerve
    - type II: there is a lesion to a major nerve

Features:

- progressive, disproportionate symptoms to the original injury/surgery
- allodynia
- temperature and skin colour changes
- oedema and sweating
- motor dysfunction
- the Budapest Diagnostic Criteria are commonly used in the UK

Management:

- early physiotherapy is important
- neuropathic analgesia in-line with NICE guidelines
- specialist management (e.g. Pain team) is required

Answer c

Which one of the following is the most common cause of recurrent first trimester spontaneous miscarriage?

○	Factor V Leiden gene mutation
○	Polycystic ovarian syndrome
○	Hyperprolactinaemia
○	Antithrombin III deficiency
○	Antiphospholipid syndrome

Next question

Antiphospholipid antibodies (aPL) are present in 15% of women with recurrent miscarriage, but in comparison, the prevalence of aPL in women with a low risk obstetric history is less than 2%

Which one of the following foods is the best source of folic acid?

○	Cheese
○	Red meat
○	Liver
○	Fish
○	Milk

Next question

Folic acid is also present in green vegetables and nuts

Folate metabolism

Drugs which interfere with metabolism

- trimethoprim
- methotrexate
- pyrimethamine

Drugs which can reduce absorption

- phenytoin

Answer C

A 24-year-old man is investigated for visual loss and is diagnosed as having Leber's optic atrophy. Given the mitochondrial inheritance of this condition, which one of the following relatives is most likely to be also affected?

○	Daughter
○	Sister
○	Son
○	Paternal uncle
○	Father

Next question

Mitochondrial diseases follow a maternal inheritance pattern

All the children of an affected mother will inherit a mitochondrial condition. His sister will therefore also be affected.

Mitochondrial diseases:

- Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria.
- It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

6) inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote.
7) all children of affected males will not inherit the disease
8) all children of affected females will inherit it
9) generally encode rare neurological diseases
10) poor genotype: phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

Histology:

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:

- Leber's optic atrophy.
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes.
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres.
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

Answer B

You review a patient in the respiratory clinic who has a history of recurrent pulmonary embolism despite anticoagulation with warfarin. Which one of the following physiological changes would be expected?

○	Increased lung compliance
○	Reduced TLCO
○	Reduced forced vital capacity
○	Reduced FEV1
○	Increased FEV1 / FVC ration

Answer B

Transfer factor:

- The transfer factor describes the rate at which a gas will diffuse from alveoli into blood.
- Carbon monoxide is used to test the rate of diffusion.
- Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	**Causes of a lower TLCO**
• **asthma** • **pulmonary haemorrhage (Wegener's, Goodpasture's)** • **left-to-right cardiac shunts** • **polycythaemia** • **hyperkinetic states** • **male gender, exercise**	• **pulmonary fibrosis** • **pneumonia** • **pulmonary emboli** • **pulmonary oedema** • **emphysema** • **anaemia** • **low cardiac output**

- KCO also tends to increase with age.
- Some conditions may cause an increased KCO with a normal or reduced TLCO
  - pneumonectomy/lobectomy
  - scoliosis/kyphosis
  - neuromuscular weakness
  - ankylosis of costovertebral joints e.g. ankylosing spondylitis

One of your colleagues confides in you that he has just been diagnosed with hepatitis B. He has not told anyone else as he is worried he may lose his job. He is currently working as a general surgeon in the local hospital. You try to persuade him to inform occupational health but he refuses. What is the most appropriate action?

○	Keep confidentiality but ask him to stop taking blood
○	Send an anonymous letter to his employer
○	Keep confidentiality
○	Inform your colleague's employing body
○	Contact the police

Answer D

What level of evidence does a randomised control trial offer?

○	Ia
○	Ib
○	IIa
○	IIb
○	IV

Answer B

A 67-year-old woman presents with lethargy, depression and constipation. A set of screening blood tests reveals the following:

Calcium	3.05 mmol/l
Albumin	41 g/l

What is the single most useful test for determining the cause of her hypercalcaemia?

○	ESR
○	Phosphate
○	Vitamin D level
○	Parathyroid hormone
○	ACE level

Next question

Parathyroid hormone levels are useful as malignancy and primary hyperparathyroidism are the two most common causes of hypercalcaemia. A parathyroid hormone that is normal or raised suggests primary hyperparathyroidism.

Answer D

Which one of the following is only secreted by the adrenal medulla?

○	Noradrenaline
○	Aldosterone
○	Metadrenaline
○	Cortisol
○	Adrenaline

Answer E

At which point in the menstrual cycle do progesterone levels peak?

○	Luteal phase
○	Ovulation
○	Follicular phase
○	Levels remain constant throughout cycle
○	Menstruation

Next question

Progesterone is secreted by the corpus luteum following ovulation.

Answer A

A 23-year-old female with Down's syndrome is reviewed in clinic. Which one of the following features is least associated with her condition?

○	Infertility
○	Hypothyroidism
○	Alzheimer's disease
○	Short stature
○	Ventricular septal defect

Next question

As this patient is female she is likely to be subfertile rather than infertile - please see the notes below

Answer A

Down's syndrome: epidemiology and genetics

Risk of Down's syndrome with increasing maternal age

- risk at 30 years = 1/1000
- 35 years = 1/350
- 40 years = 1/100
- 45 years = 1/30

One way of remembering this is by starting at 1/1,000 at 30 years and then dividing the denominator by 3 (i.e. 3 times more common) for every extra 5 years of age

Cytogenetics

Mode	% of cases	Risk of recurrence
Non-disjunction	94%	1 in 100 if under mother < 35 years
Robertsonian translocation (usually onto 14)	5%	10-15% if mother is translocation carrier 2.5% if father is translocation carrier
Mosaicism	1%	

The chance of a further child with Down's syndrome is approximately 1 in 100 if the mother is less than 35 years old. If the trisomy 21 is a result of a translocation the risk is much higher

Down syndrome: features

Clinical features

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

Cardiac complications

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

Later complications

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

How many protein-coding genes does a haploid human genome contain?

○	50,000
○	25,000
○	275.000
○	10,000
○	3 billion

Next question

Human genome - 25,000 protein-coding genes

Human genome

The human genome is stored on 23 chromosome pairs.
The haploid human genome has a total of 3 billion DNA base pairs, making up an estimated 20,000-25,000 protein-coding genes

Answer B

Which of the following conditions is inherited in an autosomal dominant fashion?

○	Familial Mediterranean Fever
○	Homocystinuria
○	Tuberose sclerosis
○	Ataxia telangiectasia
○	Friedreich's ataxia

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Answer C

A 72-year-old woman is admitted for investigation of hyponatraemia. Which one of the following features is most consistent with the syndrome of inappropriate ADH secretion?

○	Peripheral oedema
○	Recent lisinopril therapy
○	Urine osmolality of 325 mmol/kg
○	Serum sodium of 115 mmol/l
○	Urinary sodium of 40 mmol/l

Answer E

Which one of the following features is least likely to be seen in a patient with pellagra?

○	Diarrhoea
○	Depression
○	Dysphagia
○	Dermatitis
○	Dementia

Next question

Depression is quite a common early finding in patients with pellagra

Pellagra

Pellagra is a caused by nicotinic acid (niacin) deficiency.
The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin) and it is more common in alcoholics.

Features

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

Answer C

Which of the following conditions is inherited in an autosomal recessive fashion?

○	Familial adenomatous polyposis
○	Noonan syndrome
○	Malignant hyperthermia
○	Antithrombin III deficiency
○	Congenital adrenal hyperplasia

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Answer E

Southern blotting is used to:

○	Amplify RNA
○	Detect DNA
○	Detect RNA
○	Detect and quantify proteins
○	Amplify DNA

Next question

Molecular biology techniques

- SNOW (**S**outh - **NO**rth - **W**est)
- DROP (**D**NA - **R**NA - **P**rotein)

Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Technique	**Description**
Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects proteins Uses gel electrophoresis to separate native proteins by 3-D structure Examples include the **confirmatory** HIV test

Enzyme-linked immunosorbent assay (ELISA)

- a type of biochemical assay used to detect antigens and antibodies
- a colour changing enzyme is attached to the antibody if looking for an antigen and to an antigen if looking for an antibody
- the sample therefore changes colour if the antigen or antibody is detected
- an example includes the **initial** HIV test

Answer B

Which of the following is not a tumour suppressor gene?

○	p53
○	APC
○	NF-1
○	Rb
○	Myc

Next question

myc is an oncogene which encodes a transcription factor

Tumour suppressor genes

Basics

- genes which normally control the cell cycle
- loss of function results in an increased risk of cancer
- both alleles must be mutated before cancer occurs

Examples

Gene	Associated cancers
p53	Common to many cancers, Li-Fraumeni syndrome
APC	Colorectal cancer
BRCA1	Breast and ovarian cancer
BRCA2	Breast and ovarian cancer
NF1	Neurofibromatosis
Rb	Retinoblastoma
WT1	Wilm's tumour
Multiple tumor suppressor 1 (MTS-1, p16)	Melanoma

Tumour suppressor genes - loss of function results in an increased risk of cancer

Oncogenes - gain of function results in an increased risk of cancer

Answer E

Which one of the following best describes the main action of the polymerase chain reaction?

○	DNA identification using RNA
○	DNA amplification
○	RNA translation to protein
○	RNA amplification
○	DNA to RNA conversion

Answer B

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

○	Acute asthma
○	Wegener's granulomatosis
○	Polycythaemia
○	Exercise
○	Emphysema

Next question

Transfer factor

- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

Answer E

In which one of the following conditions is intravenous immunoglobulin therapy most likely to be beneficial?

○	Graves' ophthalmopathy
○	Kawasaki disease
○	Inclusion body myositis
○	Multiple sclerosis
○	Rheumatoid arthritis

Answer B

A 37-year-old woman who has a BMI of 44 kg/m^2 undergoes a Roux-en-Y gastric bypass. Of which vitamin/mineral is she most likely to require supplementation?

○	Vitamin C
○	Iron
○	Folic acid
○	Zinc
○	Vitamin B6

Next question

The duodenum is the primary site of absorption for both iron and calcium. All gastric bypass operations bypass the duodenum. Nearly all menstruating women will therefore require iron supplementation.

Answer B

A 67-year-old man presents with shortness-of-breath. He has a past history of aortic stenosis but is otherwise well. On examination he has a systolic murmur and a clear chest. Routine bloods are as follows:

Hb	8.7 g/dl
MCV	71 fl
Plt	277 * 10^9/l
WBC	6.4 * 10^9/l

Which one of the following investigations is most likely to explain his anaemia?

○	Colonoscopy
○	Renal biopsy
○	Duodenal biopsy
○	Gastroscopy
○	Echocardiogram

Next question

This patient most likely has angiodysplasia which has a known association with aortic stenosis.

Angiodysplasia

Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia. There is thought to be an association with aortic stenosis, although this is debated. Angiodysplasia is generally seen in elderly patients

Diagnosis

- colonoscopy
- mesenteric angiography if acutely bleeding

Management

- endoscopic cautery or argon plasma coagulation
- antifibrinolytics e.g. Tranexamic acid
- oestrogens may also be used

Answer A

Which one of the following hormones is under continuous inhibition?

○	Growth hormone
○	Prolactin
○	Gonadotropin releasing hormone
○	Thyroid releasing hormone
○	Adrenocorticotrophic hormone

Next question

Prolactin - under continuous inhibition

Prolactin is unique amongst the pituitary hormones in being tonically inhibited by the hypothalamus

Answer B

What is the main constituent of pulmonary surfactant?

○	Apolipoprotein SP-B
○	Phosphatidylglycerol
○	Pulmonary elastase
○	Apolipoprotein SP-A
○	Dipalmitoyl phosphatidylcholine

Next question

Pulmonary surfactant - main constituent is **dipalmitoyl phosphatidylcholine (DPPC)**

Answer E

Whilst reviewing a patient's drug card you notice that you prescribed the wrong dose of atenolol when the patient was initially clerked. Instead of 25mg atenolol od you prescribed 50mg atenolol od. She has received the incorrect dose on two occasions. On examining Mrs Smith you note her blood pressure and pulse are normal. Mrs Smith has a past history of anxiety and describes herself as a 'worrier'. What is the most appropriate action?

○	Complete an entry in your e-portfolio
○	Apologise to the patient + complete a clinical incident form
○	Complete a clinical incident form + avoid telling patient to prevent unnecessary anxiety
○	Fill out a 'yellow card'
○	Keep her on the higher dose as she is suffering no ill effects

Next question

In this scenario the patient appears to have come to no harm following the error. This should not however change your approach to the situation. The patient should be informed of what has happened, an apology should be made and reassurance give that there appears to be no ill effects. By completing a clinical incident form you add to a body of data which may in the long term change to practice.

An entry to your e-portfolio at least shows that you both acknowledge and are willing to learn from the error. The yellow card system is intended to report side-effects from drugs rather than prescription errors and hence is fairly pointless.

The dose of a drug a patient takes should be based on clinical need rather than a reluctance to acknowledge an error.

Answer B

A 25-year-old man is counselled regarding the genetics of Huntington's disease. Which one of the following best describes the concept of anticipation?

○	The psychological effect of a patient knowing they will develop an incurable condition
○	Earlier age of onset in successive generations
○	More severe disease in successive generations
○	Where there is a known history of inherited conditions, patients may attribute symptoms to the onset of the disease
○	Screening at risk families to allow early intervention and improve outcomes

Next question

Anticipation in trinucleotide repeat disorders = **earlier onset** in successive generations

Difficult question. In the exam both B and C were given as choices. The 'classic' definition of anticipation is earlier onset in successive generations. However, in most cases, an increase in the severity of symptoms is also noted. If both options are presented then B should be chosen, as this represents the more accepted definition of anticipation. What do you think?

Trinucleotide repeat disorders:

- Trinucleotide repeat disorders are genetic conditions caused by an abnormal number of repeats (expansions) of a repetitive sequence of three nucleotides.
- These expansions are unstable and may enlarge which may lead to an earlier age of onset in successive generations - a phenomenon known as anticipation*. In most cases, an increase in the severity of symptoms is also noted
  Examples - note dominance of neurological disorders

  - Fragile X (CGG)
  - Huntington's (CAG)
  - myotonic dystrophy (CTG)
  - Friedreich's ataxia* (GAA)
  - spinocerebellar ataxia
  - spinobulbar muscular atrophy
  - dentatorubral pallidoluysian atrophy

*Friedreich's ataxia is unusual in not demonstrating anticipation

Answer B

Tamsulosin is a:

○	Alpha-1b agonist
○	Alpha-1a agonist
○	Non-selective alpha antagonist
○	Alpha-1a antagonist
○	Alpha-1b antagonist

Answer D

A 30-year-old man is referred to ophthalmology due to deteriorating visual acuity. Both his brother and uncle on his mother's side have developed similar problems. What is the most likely mode of inheritance of his condition?

○	Autosomal dominant
○	Autosomal recessive
○	X-linked recessive
○	X-linked dominant
○	Polygenic

Next question

This first clue is the nature of the disease - many of the inherited eye disorders such as retinitis pigmentosa and ocular albinism are inherited in an x-linked recessive pattern.

For this disorder to be autosomal recessive both the patient's parents would need to be carriers (heterozygous) as well as both his maternal aunt and uncle. Even for common autosomal recessive disorders such as cystic fibrosis the carrier rate is around 1 in 25 making this statistically less likely.

Answer C

Which one of the following best describes rheumatoid factor?

○	IgG against the Fc portion of IgM
○	IgM against the Fc portion of IgA
○	IgM against the Fc portion of IgM
○	IgM against the Fc portion of IgG
○	IgG against the Fc portion of IgA

Next question

Rheumatoid factor is an IgM antibody against IgG

Answer D

A 24-year-old man presents to the Emergency Department with palpitations. He is diagnosed with a supraventricular tachycardia and given intravenous adenosine. Which type of membrane receptor will adenosine interact with?

○	Ligand-gated ion channel
○	Tyrosine kinase receptor
○	Guanylate cyclase receptor
○	Histidine kinase
○	G protein-coupled receptor

Answer E

Membrane receptors:

- There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

5) Ligand-gated ion channel receptors:

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

6) Tyrosine kinase receptors:

- intrinsic tyrosine kinase: insulin, insulin-like growth factor (IGF), epidermal growth factor (EGF)
- receptor-associated tyrosine kinase: growth hormone, prolactin, interferon, interleukin

3) Guanylate cyclase receptors:

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor, brain natriuretic peptide

4) G protein-coupled receptors:

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- 7-helix membrane-spanning domains
- consist of 3 main subunits: alpha, beta and gamma
- the alpha subunit is linked to GDP.Ligand binding causes conformational changes to receptor, GDP is phosphorylated to GTP,and the alpha subunit is activated
- G proteins are named according to the alpha subunit (G_s, G_i, G_q)

	G_s	G_i	G_q
Mechanism	Activates adenylate cyclase → increases cAMP → activates protein kinase A	Inhibits adenylate cyclase → decreases cAMP → inhibits protein kinase A	Activates phospholipase C → splits PIP_2 to IP_3 & DAG → activates protein kinase C
Examples	➢ Beta-1 receptors (epinephrine, norepinephrine, dobutamine) ➢ Beta-2 receptors (epinephrine, salbuterol) ➢ H2 receptors (histamine) ➢ D1 receptors (dopamine) ➢ V2 receptors (vasopressin) ➢ Receptors for ACTH, LH, FSH, glucagon, PTH, calcitonin, prostaglandins	5) M2 receptors (acetylcholine) 6) Alpha-2 receptors (epinephrine, norephinephrine) 7) D2 receptors (dopamine) 8) GABA-B receptor	5) Alpha-1 receptors (epinephrine, norepinephrine) 6) H1 receptors (histamine) 7) V1 receptors (vasopressin) 8) M1, M3 receptors (acetylcholine)

Which one of the following stimulates the release of gastrin from G-cells?

○	Histamine
○	Somatostatin
○	Gastric acid
○	Cholecystokinin
○	Luminal peptides

Answer E

A 67-year-old woman who is taking long-term prednisolone for polymyalgia rheumatica presents with progressive pain in her right hip joint. A diagnosis of avascular necrosis is suspected. Which investigation is most likely to be diagnostic?

○	Radionuclide bone scan
○	MRI
○	Plain x-ray
○	CT
○	DEXA scan

Next question

In early avascular necrosis a radionuclide bone scan is less sensitive than MRI and the findings may be nonspecific. MRI is therefore the investigation of choice.

Answer B

What is the underlying problem in methaemoglobinaemia?

○	The oxidation of Fe2+ in haemoglobin to Fe3+
○	The reduction of Fe2+ in haemoglobin to Fe+
○	The oxidation of Fe3+ in haemoglobin to Fe2+
○	The reduction of Fe2+ in haemoglobin to Fe3+
○	The reduction of Fe3+ in haemoglobin to Fe2+

Next question

Methaemoglobinaemia = oxidation of Fe2+ in haemoglobin to Fe3+

Answer A

A 65-year-old Asian female presents with generalised bone pain and muscle weakness. Investigations show:

Calcium	2.07 mmol/l
Phosphate	0.66 mmol/l
ALP	256 U/l

What is the most likely diagnosis?

○	Bone tuberculosis
○	Hypoparathyroidism
○	Myeloma
○	Osteomalacia
○	Paget's disease

Next question

Osteomalacia

- low: calcium, phosphate
- raised: alkaline phosphatase

The low calcium and phosphate combined with the raised alkaline phosphatase point towards osteomalacia

Answer D

Which one of the following statements is not correct regarding hypertension in pregnancy?

○	An increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic suggests hypertension
○	Pre-eclampsia occurs in around 5% of pregnancies
○	Urine dipstick showing protein + is consistent with gestational hypertension
○	A rise in blood pressure before 20 weeks suggests pre-existing hypertension
○	With gestational hypertension the blood pressure rises in the second half of pregnancy

Next question

Proteinuria suggests pre-eclampsia
Answer c

Which one of the following cardiac tissue types has the highest conduction velocity?

○	Atrial myocardial tissue
○	Ventricular myocardial tissue
○	Purkinje fibres
○	Atrioventricular node
○	Sinoatrial node

Answer C

The commonest chromosomal defect in Down's syndrome is:

○	Trinucleotide repeat disorder
○	Autosomal dominant
○	Translocation
○	Mosaicism
○	Non-dysjunction

Answer E

What is the site of action of antidiuretic hormone?

○	Descending loop of Henle
○	Distal convoluted tubule
○	Ascending loop of Henle
○	Proximal convoluted tubule
○	Collecting ducts

Next question

Antidiuretic hormone (ADH) - site of action = collecting ducts

Answer E

A 24-year-old man is planning an expedition to the Andes. He asks for advice on preventing acute mountain sickness (AMS), other than gradual ascent. What is the most appropriate advice?

○	Carbonic anhydrase inhibitor
○	Non-steroid anti-inflammatories
○	Ensure maximal physical fitness prior to trip
○	Dexamethasone starting 2 days prior to arrival
○	There is no evidence of any effective intervention to prevent AMS

Next question

Acetazolamide, a carbonic anhydrase inhibitor, has an evidence to support its use in preventing AMS. Interestingly, there actually appears to be a positive correlation between physical fitness and the risk of developing AMS

Answer A

Which one of the following causes of primary immunodeficiency is due to a defect in neutrophil function?

○	Wiskott-Aldrich syndrome
○	Common variable immunodeficiency
○	Bruton's congenital agammaglobulinaemia
○	Di George syndrome
○	Chronic granulomatous disease

Answer E

A 55-year-old man with a history of type 2 diabetes mellitus, bipolar disorder and chronic obstructive pulmonary disease has bloods taken as part of his annual diabetic review:

Na^+	129 mmol/l
K^+	3.8 mmol/l
Bicarbonate	24 mmol/l
Urea	3.7 mmol/l
Creatinine	92 µmol/l

Due to his smoking history a chest x-ray is ordered which is reported as normal. Which one of the following medications is most likely to be responsible?

○	Metformin
○	Lithium
○	Carbamazepine
○	Sodium valproate
○	Exenatide

Next question

SIADH - drug causes: carbamazepine, sulfonylureas, SSRIs, tricyclics

Lithium can cause diabetes insipidus but this is generally associated with a high sodium. Lithium only tends to cause raised antidiuretic hormone levels following a severe overdosage. Please see the BNF for more details.

Answer c