Question 282 of 331

You are a ST1 doctor on a medical ward. It is 5:15pm and you were scheduled to finish your day 15 minutes ago. Today you're particularly keen to leave as it is your wife's birthday and you've arranged a night out. One of the staff nurses bleeps you as Mr Jones, one of your patients, has become drowsy. He was admitted two days ago to your ward with an exacerbation of COPD. What is the most appropriate course of action?

- A. Bleep the on-call doctor yourself and ask him to review
- B. Tell her to try decreasing his oxygen to 24% and see how he is in 30 minutes
- C. Tell the nurse to bleep the on-call doctor
- D. Tell the nurse to bleep the on-call doctor + fill in a clinical incident form as you bleeped after hours
- E. Go and assess the patient yourself

Question 282 of 331

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- D. Tell the nurse to bleep the on-call doctor + fill in a clinical incident form as you bleeped after hours
- ✓ E. Go and assess the patient yourself

This question is mainly about professionalism and 'putting the patient first'.

The most appropriate response is to go and assess the patient yourself. You are most likely to know their history and it is possible that the on-call doctor will be delayed in reaching the ward due to other patients. The next best option is to bleep the on-call doctor yourself. This allows for a proper hand-over, which would not happen if you asked the nurse to bleep the on-call doctor.

Filling in a clinical incident form as you were bleeped after hours is not appropriate.

The worst response would be to ask the nurse to instigate medical treatment without first assessing the patient. This is clearly dangerous.

Question 283 of 331

Where is B-type natriuretic peptide mainly secreted from?

- A. Atrial myocardium
- B. Juxtaglomerular cells
- C. Zona glomerulosa
- D. Ventricular myocardium
- E. Hypothalamus

Question 283 of 331

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B-type natriuretic peptide is mainly secreted by the ventricular myocardium

B-type natriuretic peptide

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

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

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

Clinical uses of BNP

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

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

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

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 284 of 331

Looser’s zones x-ray are most characteristically associated with which one of the following conditions?

- A. Primary hyperparathyroidism
- B. Hypoparathyroidism
- C. Osteomalacia
- D. Paget's disease
- E. Osteoporosis

Question 284 of 331

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Osteomalacia

Basics
- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

Types
- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis

Features
- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

Investigation
- low Ca^{2+}, PO_4^{3-}, 25(OH) vitamin D
- raised ALP
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser's zones or pseudofractures)

Treatment
- calcium with vitamin D tablets

Question 285 of 331

Which one of the following statements regarding galactosaemia is incorrect?

- A. Autosomal recessive inheritance
- B. May cause cataracts
- C. Caused by the absence of galactose-1-phosphate uridyl transferase
- D. May cause jaundice
- E. May cause peripheral neuropathy

Question 285 of 331

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- D. May cause jaundice
- ✓ E. May cause peripheral neuropathy

Galactosaemia

Galactosaemia is a rare autosomal recessive condition caused by the absence of galactose-1-phosphate uridyl transferase. This results in intracellular accumulation of galactose-1-phosphate

Features
- jaundice
- failure to thrive
- hepatomegaly
- cataracts
- hypoglycaemia after exposure to galactose
- Fanconi syndrome

Diagnosis
- urine reducing substances

Management is with a galactose free diet

Question 286 of 331

Which one of the following statements regarding vitamin D-resistant rickets is false?

- A. Management includes the use of high-dose vitamin D supplements
- B. Is a X-linked dominant condition
- C. X-ray changes include cupped metaphyses
- D. Failure to thrive may be seen
- E. Decreased urinary phosphate is characteristic

Question 286 of 331

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- D. Failure to thrive may be seen
- ✓ E. Decreased urinary phosphate is characteristic

Vitamin D-resistant rickets

Vitamin D-resistant rickets is a X-linked dominant condition which usually presents in infancy with failure to thrive. It is caused by impaired phosphate reabsorption in the renal tubules

Features
- failure to thrive
- normal serum calcium, low phosphate, elevated alkaline phosphotase
- x-ray changes: cupped metaphyses with widening of the epiphyses

Diagnosis is made by demonstrating increased urinary phosphate

Management
- high-dose vitamin D supplements
- oral phosphate supplements

Question 287 of 331

Which one of the following statements is true regarding monoclonal antibodies?

- A. They are produced by the polymerase chain reaction
- B. Infliximab is useful in chronic lymphocytic leukaemia
- C. A hybridoma is a combination of human spleen cells and mouse B-cells
- D. The constant region of the antibody is human in origin
- E. Alemtuzumab is used in the prevention of ischaemic events in patients undergoing percutaneous coronary interventions

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Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from an human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

Question 288 of 331

A 52-year-old obese lady with type 2 diabetes mellitus is interested in changing her diet. Which one of the following foods has the highest glycaemic index?

- A. Baked potato
- B. Apple
- C. Peanut
- D. Digestive biscuit
- E. Brown rice

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Whilst white rice has a glycaemic index of 87 brown rice has a much lower value of 58

Glycaemic index

The glycaemic index (GI) describes the capacity of a food to raise blood glucose compared glucose in normal glucose-tolerant individuals. Foods with a high GI may be associated with an increased risk of obesity and the post-prandial hyperglycaemia associated with such foods may also increase the risk of type 2 diabetes mellitus

High GI	White rice (87), baked potato (85), white bread (70)
Medium GI	Couscous (65), boiled new potato (62), digestive biscuit (59), brown rice (58)
Low GI	Fruit and vegetables, peanuts

The glycaemic index is shown in brackets. Glucose, by definition, would have a glycaemic index of 100

Question 289 of 331

Patients with deficiencies of which one of the following complement protein(s) are predisposed to immune complex diseases?

- A. C1-INH
- B. C1q, C1rs, C2, C4
- C. C5-9
- D. C3
- E. C3bBb

Question 289 of 331

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- C. C5-9
- D. C3
- E. C3bBb

Complement deficiencies

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

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

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 290 of 331

Which one of the following is not a risk factor for the development of pre-eclampsia?

- A. Previous history of pre-eclampsia
- B. Body mass index of 34 kg/m^2
- C. Age of 42 years
- D. Multiple pregnancy
- E. Multiparity

Question 290 of 331

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- A. Previous history of pre-eclampsia
- B. Body mass index of 34 kg/m^2
- C. Age of 42 years
- D. Multiple pregnancy
- ✓ E. Multiparity

No previous pregnancies is a risk factor for pre-eclampsia. Questions on maternal health during pregnancy are now common in the MRCP

Pre-eclampsia

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

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

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

Risk factors

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

Features of severe pre-eclampsia

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

Management

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

Question 291 of 331

A study compares the sensitivity of two tests for colorectal cancer. The first test has a sensitivity of 85% whilst the second test has a sensitivity of 91%. What type of significance test should be used for comparing the two results?

- A. Wilcoxon matched-pairs
- B. Mann-Whitney test
- C. Student's t-test
- D. Chi-squared test
- E. Pearson's test

Question 291 of 331

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As percentages are being compared the chi-squared test should be used

Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

Parametric tests
- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

Non-parametric tests
- Mann-Whitney - unpaired data
- Wilcoxon matched-pairs - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Question 292 of 331

Which one of the following types of immunoglobulins are responsible for haemolytic blood transfusion reactions?

- A. IgD
- B. IgE
- C. IgM
- D. IgA
- E. IgG

Question 292 of 331

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Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

IgG	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
IgA	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
IgM	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
IgD	1%	Monomer	Involved in activation of B cells
IgE	0.1%	Monomer	Involved in allergic reactions

Question 293 of 331

Which of the following physiological effects would be expected following administration of atropine?

- A. Bradycardia + mydriasis
- B. Tachycardia + miosis
- C. Bradycardia + salivation
- D. Bradycardia + miosis
- E. Tachycardia + mydriasis

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Atropine

Atropine is an antagonist of the muscarinic acetylcholine receptor

Uses
- resuscitation
- treatment of organophosphate poisoning

Physiological effects
- tachycardia
- mydriasis

Question 294 of 331

A nurse who is known to have an allergy to latex develops a widespread urticarial rash and facial oedema shortly after eating lunch. Which food is she most likely to have consumed?

- A. Orange
- B. Apple
- C. Grapes
- D. Pear
- E. Banana

Question 294 of 331

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- C. Grapes
- D. Pear
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The nurse is likely to suffer from latex-fruit syndrome.

Latex allergy

Sensitivity to latex may cause a number of problems:

- type I hypersensitivity (anaphylaxis)
- type IV hypersensitivity (allergic contact dermatitis)
- irritant contact dermatitis

Latex allergy is more common in children with myelomeningocele spina bifida.

Latex-fruit syndrome

It is recognised that many people who are allergic to latex are also allergic to fruits, particularly banana, pineapple, avocado, chestnut, kiwi fruit, mango, passionfruit and strawberry.

Question 295 of 331

A study looks at whether a new oral treatment for patients with heart failure can prevent hospital admissions. When reviewing the data how should it be decided if the test was statistically significant?

- A. p-value < 2 standard deviates from mean
- B. p-value < (1 - type II error)
- C. p-value < significance level
- D. p-value < power
- E. p-value < 0.05

Question 295 of 331

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The significance level of a test is defined as the probability of rejecting the null hypothesis when the null hypothesis is actually true (a Type I error). It is often represented by the Greek symbol alpha.

A study is only statistically significant if the p-value reaches the significance level set before the study is started. Popular levels of significance are 5% (0.05), 1% (0.01) and 0.1% (0.001).

Significance tests

A null hypothesis states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct. The **p value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true.

For example

- there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not

The alternative hypothesis is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist (= significance level)
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Question 296 of 331

A 68-year-old woman presents with lethargy and generalised aches. As part of a blood screen the following results are obtained:

Calcium 2.83 mmol/l

Albumin 42 g/l

ESR 26 mm/hr

What is the most likely cause of these blood results?

- A. Multiple myeloma
- B. Sarcoidosis
- C. Normal
- D. Breast cancer metastases
- E. Primary hyperparathyroidism

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This question tests whether you have an understanding of the incidence of common disorders. All of the above may cause hypercalcaemia but cancer and primary hyperparathyroidism are the most common causes in this age group. A normal ESR (given her age) points towards a diagnosis of primary hyperparathyroidism.

Hypercalcaemia: causes

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

Other causes include

- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, Ca2+ containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

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

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

Question 297 of 331

Which one of the following techniques would be most suitable to detect and quantify a viral protein?

- A. Polymerase chain reaction
- B. Northern blotting
- C. Western blotting
- D. Southern blotting
- E. Eastern blotting

Question 297 of 331

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

Molecular biology techniques

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

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Question 298 of 331

Which one of the following immunoglobulins is involved in the activation of B-cells?

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- B. IgM
- C. IgE
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Question 298 of 331

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The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

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Question 299 of 331

Which one of the following statements is true regarding cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA)?

A. Targeted against myeloperoxidase

B. Associated with Wegener's granulomatosis

C. Can be used to monitor activity in autoimmune haemolytic anaemia

D. Is more commonly seen in ulcerative colitis than perinuclear ANCA

E. Positive in > 90% of hepatitis C associated vasculitis

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- E. Positive in > 90% of hepatitis C associated vasculitis

cANCA = Wegener's; pANCA = Churg-Strauss + others

ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:
- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

cANCA
- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

pANCA
- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)
- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

Question 300 of 331

The average weight loss of a patient following a new type of bariatric surgery is 18 kg. The standard deviation of weight loss is 3kg. Assuming the weight loss is normally distributed, what percentage of patients will loss between 9 and 27 kg?

- A. 97.4%
- B. 95%
- C. 95.4%
- D. 68.3%
- E. 99.7%

Question 300 of 331

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- B. 95%
- C. 95.4%
- D. 68.3%
- ✓ E. 99.7%

99.7% of values of a normally distributed variable lie within 3 standard deviations of the mean.

Normal distribution

The normal distribution is also normal as Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. if a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) represents the average difference each observation in a sample lies from the sample mean
- SD = square root (variance)

Question 301 of 331

Which cell organelle is involved in the synthesis of lipids?

- A. Golgi apparatus
- B. Smooth endoplasmic reticulum
- C. Ribosome
- D. Rough endoplasmic reticulum
- E. Nucleolus

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Cell organelles

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

Organelle/macromolecule	**Main function**
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Energy production. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide

Question 302 of 331

Where is somatostatin secreted from?

- A. D cells in the pancreas
- B. I cells in upper small intestine
- C. K cells in upper small intestine
- D. S cells in upper small intestine
- E. G cells in stomach

Question 302 of 331

Where is somatostatin secreted from?

- ✓ A. D cells in the pancreas
- B. I cells in upper small intestine
- C. K cells in upper small intestine
- D. S cells in upper small intestine
- E. G cells in stomach

D cells are also found in the stomach and intestine

Gastrointestinal hormones

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

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

Question 303 of 331

Pellagra is caused by a deficiency in:

- A. Vitamin B12
- B. Thiamine
- C. Nicotinic acid
- D. Vitamin B2
- E. Vitamin B6

Question 303 of 331

Pellagra is caused by a deficiency in:

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- B. Thiamine
- ✓ C. Nicotinic acid
- D. Vitamin B2
- E. Vitamin B6

Pellagra

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

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin)

Features

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

Question 304 of 331

A 25-year-old woman presents with a symmetrical arthropathy affecting her hands. On examination she has synovitis of the 2nd and 2rd metacarpophalangeal joints. What type of HLA allele is most associated with this condition?

- A. HLA DR3
- B. HLA A3
- C. HLA DR4
- D. HLA DR2
- E. HLA B27

Question 304 of 331

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- A. HLA DR3
- B. HLA A3
- ✓ C. HLA DR4
- D. HLA DR2
- E. HLA B27

Rheumatoid arthritis - HLA DR4

This patient has rheumatoid arthritis.

HLA associations

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

HLA-A3
- haemochromatosis

HLA-B5
- Behcet's disease

HLA-B27
- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

HLA-DR2
- narcolepsy
- Goodpasture's

HLA-DR3
- coeliac disease
- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

HLA-DR4
- type 1 diabetes mellitus*
- rheumatoid arthritis

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

Question 305 of 331

Which foramen does the oculomotor nerve go through?

- A. Superior orbital fissure
- B. Foramen ovale
- C. Foramen rotundum
- D. Optic canal
- E. Inferior orbital fissure

Question 305 of 331

Which foramen does the oculomotor nerve go through?

- ✓ A. Superior orbital fissure
- B. Foramen ovale
- C. Foramen rotundum
- D. Optic canal
- E. Inferior orbital fissure

Foramina of the skull

Questions asking about foramina of the skull have come up in the exam in previous years. Below is a brief summary of the major foramina, please see the Wikipedia link for a full list.

Foramen	Bone	Vessels	Nerves
Optic canal	Sphenoid	Ophthalmic artery	Optic nerve (II)
Superior orbital fissure	Sphenoid	Superior ophthalmic vein Inferior ophthalmic vein	Oculomotor nerve (III) Trochlear nerve (IV) lacrimal, frontal and nasociliary branches of ophthalmic nerve (V1) Abducent nerve (VI)
Inferior orbital fissure	Sphenoid and maxilla	Inferior ophthalmic veins Infraorbital artery Infraorbital vein	Zygomatic nerve and infraorbital nerve of maxillary nerve (V2) Orbital branches of pterygopalatine ganglion
Foramen rotundum	Sphenoid	-	Maxillary nerve (V2)
Foramen ovale	Sphenoid	Accessory meningeal artery	Mandibular nerve (V3)
Jugular foramen	Occipital and temporal	Posterior meningeal artery Ascending pharyngeal artery Inferior petrosal sinus Sigmoid sinus Internal jugular vein	Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI)

Question 306 of 331

A 23-year-old man is admitted with sepsis. Blood cultures are reported as follows:
Neisseria gonorrhoeae

Which of the following complement proteins is the patient most likely to deficient in?

- A. C1q, C1rs, C2, C4
- B. C3a + C5a
- C. C5-9
- D. C4
- E. C2

Question 306 of 331

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Which of the following complement proteins is the patient most likely to deficient in?

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- ✓ C. C5-9
- D. C4
- E. C2

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection and other Gram negative diplococcal infections

Complement deficiencies

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

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

C1q, C1rs, C2, C4 deficiency (classical pathway components)
- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency
- causes recurrent bacterial infections

C5 deficiency
- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency
- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Question 307 of 331

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

- A. Gallbladder
- B. Liver
- C. Stomach
- D. Distal part of small intestine
- E. Duodenum

Question 307 of 331

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- C. Stomach
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Renal anatomy

The tables below show the anatomical relations of the kidneys:

Right kidney

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

Left kidney

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

Question 308 of 331

A small study looks at the weight of patients diagnosed with type 2 diabetes mellitus. Overall 64 patients were reviewed. The average weight was 81 kg, with a standard deviation of 12 kg. What is the standard error of the mean?

- A. Square root (64 / 12)
- B. Square root (81 / 12)
- C. 12 / 9
- D. 9 / 12
- E. 1.5

Question 308 of 331

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- D. 9 / 12
- ✓ E. 1.5

Standard error of the mean = standard deviation / square root (number of patients)

The standard error of the mean is calculated by the standard deviation / square root (number of patients)= 12 / square root (64) = 12 / 8 = 1.5

Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- SEM = SD / square root (n)
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation i.e. the 95% confidence interval = mean - (1.96 *SEM) to the mean + (1.96 * SEM)

Question 309 of 331

Which one of the following is most commonly secreted by T-helper cells subset 2 (Th2 cells) ?

- A. Interleukin 2
- B. Tumour necrosis factor
- C. Interferon gamma
- D. Interleukin 4
- E. Interleukin 3

Question 309 of 331

Which one of the following is most commonly secreted by T-helper cells subset 2 (Th2 cells) ?

- A. Interleukin 2
- B. Tumour necrosis factor
- C. Interferon gamma
- ✓ D. Interleukin 4
- E. Interleukin 3

T-Helper cells

There are two major subsets of T-Helper cells:

Th1
- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2
- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Question 310 of 331

Which one of the following features is least associated with zinc deficiency?

- A. Acrodermatitis
- B. Alopecia
- C. Short stature
- D. Perioral dermatitis
- E. Gingivitis

Question 310 of 331

Which one of the following features is least associated with zinc deficiency?

- A. Acrodermatitis
- B. Alopecia
- C. Short stature
- D. Perioral dermatitis
- ✓ E. Gingivitis

Gingivitis is more commonly seen in vitamin C deficiency

Zinc deficiency

Features
- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Question 311 of 331

Which layer of the epidermis is immediately next to the dermis?

- A. Stratum granulosum
- B. Stratum lucidum
- C. Stratum corneum
- D. Stratum germinativum
- E. Stratum spinosum

Question 311 of 331

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- B. Stratum lucidum
- C. Stratum corneum
- ✓ D. Stratum germinativum
- E. Stratum spinosum

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

Epidermis

The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina

It may be divided in to five layers:

Layer	**Description**
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

Question 312 of 331

A 62-year-old man is admitted to resus with a low GCS. Blood gases taken on admission show the following:

pH 7.23

pCO2 2.2 kPa

pO2 13.8 kPa

IV access is obtained and bloods are taken. He is given supportive care with oxygen and fluids. Renal function results show:

Na^+	143 mmol/l
K^+	4.2 mmol/l
Chloride	109 mmol/l
Bicarbonate	12 mmol/l
Urea	2.1 mmol/l
Creatinine	79 µmol/l
Glucose	7.1 mmol/l

Which one of the following diagnoses would be most consistent with these results?

- A. Massive pulmonary embolism
- B. Methanol poisoning
- C. Paraquat poisoning
- D. Diabetic ketoacidosis
- E. Addisonian crisis

Question 312 of 331

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- E. Addisonian crisis

This patient has a raised anion gap metabolic acidosis which may be caused by methanol poisoning. Massive pulmonary embolism is unlikely given the pO2 as is diabetic ketoacidosis given the blood glucose.

Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by: $(Na^+ + K^+) - (Cl^- + HCO_3^-)$. If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap (= hyperchloraemic metabolic acidosis)

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

Raised anion gap

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:

- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Question 313 of 331

Which one of the following syndromes is associated with an increased risk of Crohn's disease?

- A. Turner's syndrome
- B. Down's syndrome
- C. Fragile X syndrome
- D. Patau syndrome
- E. Edward's syndrome

Question 313 of 331

Which one of the following syndromes is associated with an increased risk of Crohn's disease?

- ✓ A. Turner's syndrome
- B. Down's syndrome
- C. Fragile X syndrome
- D. Patau syndrome
- E. Edward's syndrome

Turner's syndrome

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

Features

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

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

Question 314 of 331

A study is performed to assess the correlation between age and systolic blood pressure. Which one of the following statements regarding the calculation of the correlation coefficient, r, is incorrect?

- A. A value of r greater than 0 implies a positive correlation between age and systolic blood pressure
- B. If r = 0 then there is no correlation between systolic blood pressure and age
- C. r may lie anywhere between -1 and 1
- D. May be used to predict systolic blood pressure for a given age
- E. Do not provide evidence of cause and effect

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- C. r may lie anywhere between -1 and 1
- ✓ D. May be used to predict systolic blood pressure for a given age
- E. Do not provide evidence of cause and effect

Linear regression is needed to predict systolic blood pressure in this scenario

Correlation and linear regression

Two measurements, or variables, may be plotted on a scatter plot. For example, age may be marked along the x axis and systolic blood pressure along the y axis

Correlation

The correlation coefficient (sometimes referred to as Pearson's product-moment coefficient) indicates how closely the points lie to a line drawn through the plotted data. It is denoted by the value r which may lie anywhere between -1 and 1.

For example

- r = 1 - strong positive correlation (e.g. systolic blood pressure always increases with age)
- r = 0 - no correlation (e.g. there is no correlation between systolic blood pressure and age)
- r = - 1 - strong negative correlation (e.g. systolic blood pressure always decreases with age)

Whilst correlation coefficients give information about how one variable may increase or decrease as another variable increases they do not give information about how much the variable will change. They also do not provide information on cause and effect

Linear regression

In contrast to the correlation coefficient, linear regression may be used to predict how much one variable changes when a second variable is changed. A regression equation may be formed, y = a + bx, where

- y = the variable being calculated
- a = the intercept value, when x = 0
- b = the slope of the line or regression coefficient. Simply put, how much y changes for a given change in x
- x = the second variable

Question 315 of 331

A study is performed comparing two chemotherapy regimes for patients with small cell lung cancer. The end point of the study is survival time. Which one of the following types statistical measures is it most appropriate to compare survival time with?

- A. Odds ratio
- B. Pearson's product-moment coefficient
- C. Relative risk
- D. Hazard ratio
- E. Absolute risk reduction

Question 315 of 331

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- B. Pearson's product-moment coefficient
- C. Relative risk
- ✓ D. Hazard ratio
- E. Absolute risk reduction

Hazard ratio

The hazard ratio (HR) is similar to relative risk but is used when risk is not constant to time. It is typically used when analysing survival over time

Question 316 of 331

A couple present for genetic counselling. The male partner has haemophilia whilst the female partner has been screened and shown to be a carrier of the gene causing haemophilia. What is the chance that a child would have haemophilia?

- A. 25% if male child, 0% if female child
- B. 50%
- C. 100% if male child, 0% if female child
- D. 50% if male child, 0% if female child
- E. 25%

Question 316 of 331

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- ✓ B. 50%
- C. 100% if male child, 0% if female child
- D. 50% if male child, 0% if female child
- E. 25%

This question asks about the unusual situation of an affected male having children with a heterozygous (carrier) female. In this situation 50% of all children will be affected

X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen

Question 317 of 331

A new adjuvant treatment for women with breast cancer is investigated. The study looks at the recurrence rate after 5 years. The following data is obtained:

	Number of patients	**Number who had a recurrence within a 5 year period**
New drug	200	40
Placebo	400	100

What is the relative risk reduction?

- A. 50%
- B. 20%
- C. 4
- D. 0.8
- E. 5%

Question 317 of 331

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What is the relative risk reduction?

- A. 50%
- ✓ B. 20%
- C. 4
- D. 0.8
- E. 5%

Relative risk reduction = (EER - CER) / CER

Experimental event rate, EER = 40 / 200 = 0.2
Control event rate, CER = 100 / 400 = 0.25
Relative risk reduction = (EER - CER) / CER = (0.2 - 0.25) / 0.25 = -0.2 or a 20% reduction

Relative risk

Relative risk (RR) is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER)

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate, EER = 60 / 100 = 0.6
Control event rate, CER = 20 / 80 = 0.25
Therefore the relative risk = EER / CER = 0.6 / 0.25 = 2.4

If the risk ratio is > 1 then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is < 1 then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

Relative risk reduction (RRR) or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate
Using the above data, RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140%

Question 318 of 331

In terms of the cell cycle, which one of the following phases determine the length of the cell cycle:

- A. M
- B. M0
- C. G1
- D. S
- E. G2

Question 318 of 331

In terms of the cell cycle, which one of the following phases determine the length of the cell cycle:

- A. M
- B. M0
- ✓ C. G1
- D. S
- E. G2

Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

Question 319 of 331

A 45-year-old man who is known to have Marfan's syndrome presents with lower back pain. This has been present for a few months now and is associated with headaches, leg pain and intemittent episodes of urinary incontinence. What is the most likely diagnosis?

- A. Depression
- B. Spinal stenosis
- C. Leaking aortic abdominal aneurysm
- D. Multiple sclerosis
- E. Dural ectasia

Question 319 of 331

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- C. Leaking aortic abdominal aneurysm
- D. Multiple sclerosis
- ✓ E. Dural ectasia

Dural ectasia affects around 60% of patients with Marfan's syndrome. It may cause lower back pain associated with neurological problems such as bladder and bowel dysfunction.

Marfan's syndrome

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

Features

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

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

Question 320 of 331

You are caring for a local cardiology consultant's father who has been admitted following a myocardial infarction. He bleeps you from the switchboard and asks how his father is doing. You recognise his voice on the phone. What is the most appropriate response?

- A. Decline to give any details over the phone but offer to meet the consultant face-to-face for a chat
- B. As a matter of professional courtesy ask for his advice on post-myocardial infarction care
- C. Ask permission from his father then give relevant details
- D. Give full details include the troponin I value and offer to fax the ECG
- E. Say he is 'doing fine'

Question 320 of 331

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- ✓ C. Ask permission from his father then give relevant details
- D. Give full details include the troponin I value and offer to fax the ECG
- E. Say he is 'doing fine'

The main nub of this question relates to confidentiality. You cannot give details over the phone to anyone, even his son, without the patient's express permission. Whilst it may be presumed that this is what the patient would want it is impossible to be sure of the family dynamics.

If the patient has given permission and you are sure you are speaking to the son then giving relevant details is the best option. Asking the consultant to come in as an option but may not be necessary if the previous conditions are met. Saying he is 'doing fine' is unlikely to satisfy a consultant cardiologist.

Giving details without first getting permission from the patient is breaking confidentiality, however well intentioned. Involving a relative in the management of a patient is inappropriate and the worst option.

Question 321 of 331

Potential complications of Paget's disease include each of the following except:

- A. Deafness
- B. Cerebral calcification
- C. Skull thickening
- D. Bone sarcoma
- E. Fractures

Question 321 of 331

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Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors
- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic
- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's
- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications
- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

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

Question 322 of 331

Which of the following is not true regarding B-type natriuretic peptide?

- A. Secreted mainly by the ventricles
- B. Acts as a diuretic
- C. Acts as a vasoconstrictor
- D. Levels rise in left ventricular failure
- E. Reduces sympathetic tone

Question 322 of 331

Which of the following is not true regarding B-type natriuretic peptide?

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- B. Acts as a diuretic
- ✓ C. Acts as a vasoconstrictor
- D. Levels rise in left ventricular failure
- E. Reduces sympathetic tone

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

B-type natriuretic peptide

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

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

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

Clinical uses of BNP

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

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

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

Screening for cardiac dysfunction
- not currently recommended for population screening

Question 323 of 331

A 16-year-old male is reviewed in the endocrinology clinic due to lack of pubertal development. On examination his testes are undescended and there is only scanty pubic hair. What is the most likely diagnosis?

- A. Down's syndrome
- B. Kallman's syndrome
- C. Dubin-Johnson syndrome
- D. Turner's syndrome
- E. Klinefelter's syndrome

Question 323 of 331

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- A. Down's syndrome
- ✓ B. Kallman's syndrome
- C. Dubin-Johnson syndrome
- D. Turner's syndrome
- E. Klinefelter's syndrome

Cryptorchidism is more suggestive of Kallman's than Klinefelter's syndrome

Kallman's syndrome

Kallman's syndrome is a recognised cause of delayed puberty secondary to hypogonadotrophic hypogonadism. It is usually inherited as an X-linked recessive trait. Kallman's syndrome is thought to be caused by failure of GnRH-secreting neurons to migrate to the hypothalamus.

The clue given in many questions is lack of smell (anosmia) in a boy with delayed puberty

Features
- 'delayed puberty'
- hypogonadism, cryptorchidism
- anosmia
- sex hormone levels are low
- LH, FSH levels are inappropriately low/normal
- patients are typically of normal or above average height

Cleft lip/palate and visual/hearing defects are also seen in some patients

Question 324 of 331

You are a ST1 doctor in medicine doing a nightshift. An elderly patient with colorectal cancer has been admitted to the Emergency Department with suspected bowel obstruction. The Emergency Department F2 doctor has tried to refer the patient to the surgeons but was told that as no surgical intervention is likely the patient should be admitted to the medics. The F2 doctor therefore phones yourself and asks you to accept the patient. What is the most appropriate response?

- A. Accept the patient and ask the staff to transfer her to the medical assessment unit
- B. Simply refuse in order to avoid the patient being admitted under an inappropriate specialty
- C. Tell the surgical registrar that you will contact the on-call surgical consultant if he refuses to accept the patient
- D. Go down to the emergency department and review the patient
- E. Phone the surgical team yourself to discuss the matter

Question 324 of 331

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- C. Tell the surgical registrar that you will contact the on-call surgical consultant if he refuses to accept the patient
- ✓ D. Go down to the emergency department and review the patient
- E. Phone the surgical team yourself to discuss the matter

Scenarios similar to this occur on an almost daily basis for admitting medical teams. The priority in all of this has to be the patient. It may be the case if the patient is end-stage then medical admission is more appropriate. If they are Duke's A and awaiting an operation then clearly they are surgical. Until you review the patient yourself you will not have all the facts and this is therefore the best option.

Discussing the matter with the surgical team will help to clarify their opinion about the patient and is the next best option. Accepting the patient without review risks placing a patient with an acute surgical problem on a medical ward. This may delay or compromise care.

Getting into an argument with the surgical registrar is not constructive and is a poor choice, as is simply refusing to see the patient as this indicates a disregard for the patient.

Question 325 of 331

The adrenergic receptor is an example of a:

- A. Intracellular receptor
- B. Tyrosine kinase receptor
- C. Guanylate cyclase receptor
- D. G protein-coupled receptor
- E. Ligand-gated ion channel

Question 325 of 331

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- ✓ D. G protein-coupled receptor
- E. Ligand-gated ion channel

Membrane receptors

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

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

Tyrosine kinase receptors
- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors
- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors
- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Question 326 of 331

Which one of the following conditions is NOT an autosomal dominant condition?

- A. Retinoblastoma
- B. Tuberose sclerosis
- C. Achondroplasia
- D. Myotonic dystrophy
- E. Albinism

Question 326 of 331

Which one of the following conditions is NOT an autosomal dominant condition?

- A. Retinoblastoma
- B. Tuberose sclerosis
- C. Achondroplasia
- D. Myotonic dystrophy
- ✓ E. Albinism

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

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

Autosomal dominant conditions

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

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

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes
- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease*

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 327 of 331

What is the correct formula to calculate the negative predictive value of a screening test? TP = true positive; FP = false positive; TN = true negative; FN = false negative

- A. TN / (TN + FN)
- B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. Sensitivity / (1 - specificity)
- E. TP / (TP + FN)

Question 327 of 331

What is the correct formula to calculate the negative predictive value of a screening test?

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- B. TP / (TP + FP)
- C. TN / (TN + FP)
- D. Sensitivity / (1 - specificity)
- E. TP / (TP + FN)

Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	**Disease absent**
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	TP / (TP + FN)	Proportion of true positives that are correctly identified by the test
Specificity	TN / (TN + FP)	Proportion of true negatives that are correctly identified by the test
Positive predictive value	TP / (TP + FP)	Proportion of patients with positive test results who are correctly diagnosed
Negative predictive value	TN / (TN + FN)	Proportion of patients with negative test results who are correctly diagnosed
Likelihood ratio for a positive test result	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
Likelihood ratio for a negative test result	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Question 328 of 331

Which of the following is most likely to cause hypokalaemia associated with alkalosis?

- A. Acetazolamide
- B. Partially treated diabetic ketoacidosis
- C. Diarrhoea
- D. Cushing's syndrome
- E. Renal tubular acidosis

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Hypokalaemia and acid-base balance

Potassium and hydrogen can be thought of as competitors. Hyperkalaemia tends to be associated with acidosis because as potassium levels rise fewer hydrogen ions can enter the cells

Hypokalaemia with alkalosis
- vomiting
- diuretics
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)

Hypokalaemia with acidosis
- diarrhoea
- renal tubular acidosis
- acetazolamide
- partially treated diabetic ketoacidosis

Question 329 of 331

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

- A. Di George syndrome
- B. Chediak-Higashi syndrome
- C. Common variable immunodeficiency
- D. Chronic granulomatous disease
- E. Wiskott-Aldrich syndrome

Question 329 of 331

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- B. Chediak-Higashi syndrome
- ✓ C. Common variable immunodeficiency
- D. Chronic granulomatous disease
- E. Wiskott-Aldrich syndrome

Primary immunodeficiency

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

Neutrophil disorders
- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders
- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders
- DiGeorge syndrome

Combined B- and T-cell disorders
- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Question 330 of 331

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

- A. Mucosal oedema and mucus plugging
- B. Destruction of alveolar walls secondary to proteinases
- C. Airway hypersensitivity
- D. Smooth muscle contraction
- E. Hypertrophy of mucous secreting glands

Question 330 of 331

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

COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

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

Question 331 of 331

Which one of the following defines the standard error of the mean?

- A. Square root (Standard deviation / number of patients)
- B. Number of patients / square root (mean)
- C. Number of patients / square root (standard deviation)
- D. Standard deviation / square root (number of patients)
- E. Standard deviation / square root (mean)

Question 331 of 331

Which of the following conditions is not caused by a trinucleotide repeat expansion?

- A. Fragile X syndrome
- B. Huntington's
- C. Ataxia telangiectasia
- D. Myotonic dystrophy
- E. Friedreich's ataxia

Question 1 of 116

A 56-year-old man with metastatic prostate cancer comes for review. He is known to have spinal metastases but until now has not had any significant problems with pain control. Unfortunately he is now getting regular back pain despite taking paracetamol 1g qds. Neurological examination is unremarkable. What is the most appropriate next step?

- A. Switch to co-codamol 30/500
- B. Refer for radiotherapy
- C. Add oral bisphosphonate
- D. Add diclofenac
- E. Add dexamethasone

Question 1 of 116

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- A. Switch to co-codamol 30/500
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- D. Add diclofenac
- E. Add dexamethasone

Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Bone pain often responds well to NSAIDs. Both radiotherapy and bisphosphonates have a role in managing bony pain but these are not first-line treatments

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 2 of 116

A 4-year-old boy is admitted after developing a haemarthrosis in his right knee whilst playing in the garden. The following blood results are obtained:

Platelets	220 * 10^9/l
PT	12 secs
APTT	78 secs
Factor VIIIc activity	Normal

What is the most likely diagnosis?

- A. Antithrombin III deficiency
- B. Von Willebrand's disease
- C. Antiphospholipid syndrome
- D. Haemophilia A
- E. Haemophilia B

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A grossly elevated APTT may be caused by heparin therapy, haemophilia or antiphospholipid syndrome. A normal factor VIIIc activity points to a diagnosis of haemophilia B (lack of factor IX). Antiphospholipid syndrome is a prothrombotic condition

Haemophilia

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

Features

- haemoarthroses, haematomas
- prolonged bleeding after surgery or trauma

Blood tests

- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

Question 3 of 116

Which one of the following cytotoxic agents acts by inhibiting dihydrofolate reductase and thymidylate synthesis?

- A. Methotrexate
- B. Vincristine
- C. Bleomycin
- D. Cyclophosphamide
- E. Doxorubicin

Question 3 of 116

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 4 of 116

A 52-year-old man with a history of anaemia and abdominal discomfort is diagnosed as having chronic myeloid leukaemia. What is the mechanism of action of imatinib?

- A. EGF receptor antagonist
- B. Tyrosine kinase inhibitor
- C. Anti-CD52 monoclonal antibody
- D. Anti-CD23 monoclonal antibody
- E. p53 inhibitor

Question 4 of 116

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Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor

Imatinib is an inhibitor of the tyrosine kinase associated with the BCR-ABL defect

Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)
- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management
- hydroxyurea
- interferon-alpha
- imatinib
- allogenic bone marrow transplant

Imatinib
- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Question 5 of 116

A 12-year-old boy is noted to bleed excessively during an elective dental extraction. Following the procedure, examination reveals petechial skin haemorrhages. Blood results show:

Hb	12.3 g/dl
Plt	255 * 10^9/l
WBC	7.9 * 10^9/l
PT	13.3 secs
APTT	39 secs
Factor VIII activity	87%

What is the most likely diagnosis?

- A. Disseminated intravascular coagulation
- B. Idiopathic thrombocytopenic purpura
- C. Von Willebrand's disease
- D. Haemophilia A
- E. Haemophilia B

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- C. Von Willebrand's disease
- D. Haemophilia A
- E. Haemophilia B

The combination of a petechial skin rash combined with a slightly elevated APTT and reduced factor VIII activity make Von Willebrand's disease the most likely diagnosis

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 6 of 116

A 52-year-old woman with a history of hypothyroidism presents with lethargy and a sore tongue. Blood tests are reported as follows:

Hb 10.7 g/dl

MCV 121 fl

Plt 177 * 10^9/l

WBC 5.4 * 10^9/l

Further tests are ordered:

Vitamin B12 64 ng/l (200-900 ng/l)

Folic acid 7.2 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- A. 1 mg of IM hydroxocobalamin once every 3 months
- B. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- C. 1 mg of IM hydroxocobalamin once every 2 months + folic acid 5mg od
- D. Give folic acid 5mg od one week then recheck bloods
- E. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months + folic acid 5mg od

Question 6 of 116

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- D. Give folic acid 5mg od one week then recheck bloods
- E. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months + folic acid 5mg od

If the patient was deficient in folic acid it would important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord.

Vitamin B12 deficiency

Vitamin B12 is mainly used in the body for red blood cell development and also maintenance of the nervous system. It is absorbed after binding to intrinsic factor (secreted from parietal cells in the stomach) and is actively absorbed in the terminal ileum. A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Causes of vitamin B12 deficiency

- pernicious anaemia
- post gastrectomy
- poor diet
- disorders of terminal ileum (site of absorption): Crohn's, blind-loop etc

Features of vitamin B12 deficiency

- macrocytic anaemia
- sore tongue and mouth
- neurological symptoms: e.g. Ataxia
- neuropsychiatric symptoms: e.g. Mood disturbances

Management

- if no neurological involvement 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- if a patient is also deficient in folic acid then it is important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

Question 7 of 116

A 72-year-old women is found to have a marked lymphocytosis associated with smudge cells on the blood film. A diagnosis of chronic lymphocytic leukaemia is suspected. Which one of the following is the investigation of choice?

- A. Immunophenotyping
- B. Bone marrow aspiration
- C. Protein electrophoresis
- D. White cell scan
- E. Bone marrow trephine

Question 7 of 116

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- B. Bone marrow aspiration
- C. Protein electrophoresis
- D. White cell scan
- E. Bone marrow trephine

CLL - immunophenotyping is investigation of choice

Immunophenotyping will demonstrate the cells to be B-cells (CD19 positive). CD5 and CD23 are also characteristically positive in chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 8 of 116

A 50-year-old man with a history of ulcerative colitis comes for review. Six years ago he had an ileostomy formed which has been functioning well until now. Unfortunately he is currently suffering significant pain around the stoma site. On examination a deep erythematous ulcer is noted with a ragged edge. The surrounding skin is erythematous and swollen. What is the most likely diagnosis?

- A. Munchausen's syndrome
- B. Irritant contact dermatitis
- C. Pyoderma gangrenosum
- D. Dermatitis artefacta
- E. Stomal granuloma

Question 8 of 116

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- B. Irritant contact dermatitis
- C. Pyoderma gangrenosum
- D. Dermatitis artefacta
- E. Stomal granuloma

Pyoderma gangrenosum is associated with inflammatory bowel disease and may be seen around the stoma site. Treatment is usually with immunosuppressants as surgery may worsen the problem

A differential diagnosis would be malignancy and hence lesions should be referred for specialist opinion to evaluate the need for a biopsy. Irritant contact dermatitis is common but would not be expected to cause such a deep ulcer.

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic systems e.g. fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 9 of 116

Which one of the following may be used to monitor patients with colorectal cancer?

- A. CA-125
- B. Carcinoembryonic antigen
- C. Alpha-fetoprotein
- D. CA 19-9
- E. CA 15-3

Question 9 of 116

Which one of the following may be used to monitor patients with colorectal cancer?

- A. CA-125
- B. Carcinoembryonic antigen
- C. Alpha-fetoprotein
- D. CA 19-9
- E. CA 15-3

Carcinoembryonic antigen may be used to monitor for recurrence in patients post-operatively or to assess response to treatment in patients with metastatic disease

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Question 10 of 116

A 33-year-old male patient with a history of recurrent nose bleeds, iron-deficiency anaemia and dyspnoea is found to have a pulmonary AV malformation on pulmonary angiography. What is the likely underlying diagnosis?

- A. Haemophilia A
- B. Hereditary haemorrhagic telangiectasia
- C. Mantle cell lymphoma
- D. Wegener's granulomatosis
- E. Down's syndrome

Question 10 of 116

A 33-year-old male patient with a history of recurrent nose bleeds, iron-deficiency anaemia and dyspnoea is found to have a pulmonary AV malformation on pulmonary angiography. What is the likely underlying diagnosis?

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- B. Hereditary haemorrhagic telangiectasia
- C. Mantle cell lymphoma
- D. Wegener's granulomatosis
- E. Down's syndrome

Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history

Features

- epistaxis
- telangiectasia develop is skin, mucous membranes and internal organs
- associated with pulmonary AV malformations and other AV malformations in 10%
- may present as iron-deficiency anaemia secondary to bleeding in the GI tract or nasal mucosa

Question 11 of 116

Which one of the following is least likely to cause a warm autoimmune haemolytic anaemia?

- A. Mycoplasma infection
- B. Methyldopa
- C. Chronic lymphocytic leukaemia
- D. Lymphoma
- E. Systemic lupus erythematous

Question 11 of 116

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- B. Methyldopa
- C. Chronic lymphocytic leukaemia
- D. Lymphoma
- E. Systemic lupus erythematous

Mycoplasma infection causes a cold autoimmune haemolytic anaemia. Systemic lupus erythematous can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia (AIHA) may be divided in to 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

Warm AIHA

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyldopa

Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Question 12 of 116

Which one of the following is a marker of a bad prognosis in acute lymphoblastic leukaemia?

- A. Pre-B phenotype
- B. Presentation in childhood
- C. Initial white cell count of 18 * 10^9/l
- D. Female sex
- E. Philadelphia chromosome positive

Question 12 of 116

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- D. Female sex
- E. Philadelphia chromosome positive

Philadelphia translocation, t(9;22) - good prognosis in CML, poor prognosis in AML + ALL

Acute lymphoblastic leukaemia: prognostic features

Good prognostic factors
- FAB L1 type
- common ALL
- pre-B phenotype
- low initial WBC

Poor prognostic factors
- FAB L3 type
- T or B cell surface markers
- Philadelphia translocation, t(9;22)
- age < 2 years or > 10 years
- male sex
- CNS involvement
- high initial WBC (e.g. > 100 * 10^9/l)
- non-Caucasian

Question 13 of 116

A 42-year-old female is noted to have a Hb of 17.8 g/dL. Which one of the following is least likely to be the cause?

- A. Polycythaemia rubra vera
- B. Chronic obstructive pulmonary disease
- C. Hypernephroma
- D. Haemochromatosis
- E. Dehydration

Question 13 of 116

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- C. Hypernephroma
- D. Haemochromatosis
- E. Dehydration

Haemochromatosis is not associated with polycythaemia. Blood tests typically reveal a raised ferritin and iron, associated with a transferrin saturation of greater than 60% and a low total iron binding capacity

Polycythaemia

Polycythaemia may be relative, primary (polycythaemia rubra vera) or secondary

Relative causes
- dehydration
- stress: Gaisbock syndrome

Primary
- polycythaemia rubra vera

Secondary causes
- COPD
- altitude
- obstructive sleep apnoea
- excessive erythropoietin: cerebellar haemangioma, hypernephroma, hepatoma, uterine fibroids*

To differentiate between true (primary or secondary) polycythaemia and relative polycythaemia red cell mass studies are sometimes used. In true polycythaemia the total red cell mass in males > 35 ml/kg and in women > 32 ml/kg

*uterine fibroids may cause menorrhagia which in turn leads to blood loss - polycythaemia is rarely a clinical problem

Question 14 of 116

A 49-year-old female is admitted to hospital due to shortness of breath and pleuritic chest pain. She also complains of a marked decrease in appetite for the past 4 months. An admission chest x-ray shows a right-sided pleural effusion. An underlying malignancy is suspected and a series of tumour markers are requested:

CA 19-9 55 u/ml (< 40)

CA 125 654 u/ml (< 30)

CA 15-3 9 u/ml (<40)

What is the most likely underlying diagnosis?

- A. Ovarian fibroma
- B. Small cell lung cancer
- C. Pancreatic carcinoma
- D. Hepatocellular cancer
- E. Breast carcinoma

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- D. Hepatocellular cancer
- E. Breast carcinoma

This patient has Meig's syndrome - an ovarian fibroma associated with a pleural effusion and ascites

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 15 of 116

A 21-year-old man comes for review. He recently had an abdominal ultrasound for episodic right upper quadrant pain which demonstrated gallstones. A full blood count was also ordered which was reported as follows:

Hb 9.8 g/dl

MCV 91 fl

Plt 177 * 10^9/l

WBC 5.3 * 10^9/l

The patient also mentions that his father had a splenectomy at the age of 30 years. Which one of the following tests is most likely to be diagnostic?

- A. Ham's test
- B. PAS staining of erythrocytes
- C. Glucose-6-phoshate dehydrogenase levels
- D. Osmotic fragility test
- E. Direct Coombs' test

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- D. Osmotic fragility test
- E. Direct Coombs' test

This patient has hereditary spherocytosis as evidenced by the normocytic anaemia, gallstones and family history.

Hereditary spherocytosis

Basics
- most common hereditary haemolytic anaemia in northern Europeans
- autosomal dominant defect of RBC cytoskeleton
- biconcave disc --> spherocyte
- red cell survival reduced, destroyed by spleen

Presentation
- e.g. failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

Diagnosis
- osmotic fragility test

Management
- folate replacement
- splenectomy

Question 16 of 116

Which one of the following is not a feature of paroxysmal nocturnal haemoglobinuria?

- A. Haemolytic anaemia
- B. Positive Ham test
- C. Haemoglobinuria
- D. Aplastic anaemia
- E. Haemarthrosis

Question 16 of 116

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- C. Haemoglobinuria
- D. Aplastic anaemia
- E. Haemarthrosis

Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology
- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features
- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopaenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis
- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management
- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation

Question 17 of 116

A 22-year-old man with sickle cell anaemia presents with vomiting, abdominal pain and a rash. Blood results are as follows:

Hb	4.6 g/dl
Reticulocytes	3%

Infection with a parvovirus is suspected. What is the likely diagnosis?

- A. Thrombotic crisis
- B. Sequestration crisis
- C. Transformation to myelodysplasia
- D. Haemolytic crisis
- E. Aplastic crisis

Question 17 of 116

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- B. Sequestration crisis
- C. Transformation to myelodysplasia
- D. Haemolytic crisis
- E. Aplastic crisis

The sudden fall in haemoglobin without an appropriate reticulocytosis (3% is just above the normal range) is typical of an aplastic crisis, usually secondary to parvovirus infection

Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:
- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

Thrombotic crises
- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain

Sequestration crises
- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO2 - the most common cause of death after childhood

Aplastic crises
- caused by infection with parvovirus
- sudden fall in haemoglobin

Haemolytic crises
- rare
- fall in haemoglobin due an increased rate of haemolysis

Question 18 of 116

Which one of the following factors is most associated with an increased risk of developing bladder cancer?

- A. Strongyloides stercoralis infection
- B. Beryllium salt exposure
- C. Aniline dye exposure
- D. Aflatoxin exposure
- E. Long term phenytoin use

Question 18 of 116

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- C. Aniline dye exposure
- D. Aflatoxin exposure
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Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

Question 19 of 116

A 34-year-old man who is HIV positive is starting treatment for Burkitt's lymphoma. His chemotherapy regime includes cyclophosphamide, vincristine, methotrexate and prednisolone. Around 24 hours after starting chemotherapy he becomes confused and complains of muscle cramps in his legs. Which one of the following is most likely to have occurred?

- A. Prednisolone-induced psychosis
- B. Hypercalcaemia
- C. Methotrexate pneumonitis leading to hypoxia
- D. Haemorrhagic cystitis leading to acute renal failure
- E. Tumour lysis syndrome

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- E. Tumour lysis syndrome

Burkitt's lymphoma is a common cause of tumour lysis syndrome

Burkitt's lymphoma

Burkitt's lymphoma is a high-grade B-cell neoplasm. There are two major forms:

- endemic (African) form: typically involves maxilla or mandible
- sporadic form: abdominal (e.g. ileo-caecal) tumours are the most common form. More common in patients with HIV

Burkitt's lymphoma is associated with the c-myc gene translocation, usually t(8:14). The Epstein-Barr virus (EBV) is strongly implicated in the development of the African form but the link to sporadic Burkitt's is less clear

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Complications of tumour lysis syndrome include:

- hyperkalaemia
- hyperphosphataemia
- hypocalcaemia
- hyperuricaemia
- acute renal failure

Question 20 of 116

A 67-year-old man with a 10-year history of gastro-oesophageal reflux disease is investigated for dysphagia. An endoscopy shows an obstructive lesion highly suspicious of oesophageal cancer. What is the biopsy most likely to show?

- A. Squamous cell carcinoma
- B. Normal squamous epithelium
- C. Adenocarcinoma
- D. Leiomyoma
- E. Metaplastic columnar epithelium

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- B. Normal squamous epithelium
- C. Adenocarcinoma
- D. Leiomyoma
- E. Metaplastic columnar epithelium

Oesophageal cancer
- squamous cell carcinoma is more common overall
- adenocarcinoma is more common in patients with GORD or Barrett's

Metaplastic columnar epithelium would be seen with Barrett's but this is not consistent with the obstructive lesion seen on endoscopy.

Oesophageal cancer

Oesophageal cancer is most commonly due to a squamous carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is the most common type of cancer to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

Risk factors
- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

Question 21 of 116

Which one of the following viruses is associated with nasopharyngeal carcinoma?

- A. Adenovirus
- B. Rhinovirus
- C. Herpes simplex virus
- D. Epstein-Barr virus
- E. Picornavirus

Question 21 of 116

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- A. Adenovirus
- B. Rhinovirus
- C. Herpes simplex virus
- D. Epstein-Barr virus
- E. Picornavirus

EBV: associated malignancies:
- Burkitt's lymphoma
- Hodgkin's lymphoma
- nasopharyngeal carcinoma

Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection
- Burkitt's lymphoma*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also assocaiated with EBV infection.

*EBV is currently thought to be associated with both African and sporadic Burkitt's

Question 22 of 116

Which one of the following features is least recognised in thrombotic thrombocytopenic purpura?

- A. Fever
- B. Microangiopathic haemolytic anaemia
- C. Renal failure
- D. Thrombocytopenia
- E. Livedo reticularis

Question 22 of 116

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- A. Fever
- B. Microangiopathic haemolytic anaemia
- C. Renal failure
- D. Thrombocytopenia
- E. Livedo reticularis

Livedo reticularis is not commonly seen in thrombotic thrombocytopenic purpura. It occurs more commonly in conditions such as antiphospholipid syndrome and cholesterol embolism

Thrombotic thrombocytopenic purpura

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia
- renal failure

Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV

Question 23 of 116

Which one of the following would most suggest a leukaemoid reaction rather than chronic myeloid leukaemia?

- A. Raised packed cell volume
- B. Right shift of neutrophils
- C. A low leucocyte alkaline phosphatase score
- D. Dohle bodies in the white cells
- E. Positive osmotic fragility test

Question 23 of 116

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Leukaemoid reaction

The leukaemoid reaction describes the presence of immature cells such as myeloblasts, promyelocytes and nucleated red cells in the peripheral blood. This may be due to infiltration of the bone marrow causing the immature cells to be 'pushed out' or sudden demand for new cells

Causes
- severe infection
- severe haemolysis
- massive haemorrhage
- metastatic cancer with bone marrow infiltration

A relatively common clinical problem is differentiating chronic myeloid leukaemia from a leukaemoid reaction. The following differences may help:

Leukaemoid reaction
- high leucocyte alkaline phosphatase score
- toxic granulation (Dohle bodies) in the white cells
- 'left shift' of neutrophils i.e. three or less segments of the nucleus

Chronic myeloid leukaemia
- low leucocyte alkaline phosphatase score

Question 24 of 116

A 49-year-old women is referred to the haematology clinic with easy bruising and recurrent epistaxis. She is otherwise well. Blood tests reveal the following:

Hb 12.9 g/dl

Platelets 19 * 10^9/l

WCC 6.6 * 10^9/l

The patient refuses consent for a bone marrow examination. What is the most appropriate initial management?

- A. Platelet transfusion
- B. Oral prednisolone
- C. No treatment
- D. ABVD chemotherapy
- E. Splenectomy

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ITP - give oral prednisolone

The likely diagnosis in this patient is idiopathic thrombocytopenic purpura. The first line treatment in such patients is high-dose prednisolone. Bone marrow examination would demonstrate increased megakaryocytes

ITP: investigation and management

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

Investigations

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

Management

- oral prednisolone (80% of patients respond)
- splenectomy if platelets < 30 after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide

Question 25 of 116

A 65-year-old woman is reviewed. She is on the waiting list for a varicose vein operation but during the preoperative assessment was noted to have a raised lymphocyte count. She reports feeling well currently and clinical examination is normal. Her bloods were as follows:

Hb 11.8 g/dl

Plt 184 * 10^9/l

WBC 21.2 * 10^9/l

There are no previous bloods to compare these results with. Following referral to haematology a diagnosis of chronic lymphocytic leukaemia was made. What is the most appropriate management?

- A. No treatment + cancel operation
- B. No treatment + go ahead with operation
- C. Chlorambucil + cancel operation
- D. Fludarabine + go ahead with operation but with quinolone prophylaxis
- E. Alemtuzumab + cancel operation

Question 25 of 116

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- E. Alemtuzumab + cancel operation

There is no indication for treating this patient at the current time or not going ahead with surgery

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 26 of 116

A patient with a history of recurrent thromboembolic events develops a deep vein thrombosis despite full anticoagulation with heparin. Which one of the following causes of thrombophilia is associated with resistance to heparin?

- A. Protein S deficiency
- B. Antithrombin III deficiency
- C. Protein C deficiency
- D. Lupus anticoagulant
- E. Activated protein C resistance

Question 26 of 116

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Heparin works by binding to antithrombin III, enhancing its anticoagulant effect by inhibiting the formation of thrombin and other clotting factors. Patients with antithrombin III deficiency may therefore by resistant to heparin treatment

Antithrombin III deficiency

Antithrombin III deficiency is an inherited cause of thrombophilia occurring in approximately 1:2,000 of the population. Inheritance is autosomal dominant

Antithrombin III inhibits several clotting factors, primarily thrombin, factor X and factor IX. It mediates the effects of heparin

Antithrombin III deficiency comprises a heterogeneous group of disorders, with some patients having a deficiency of normal antithrombin III whilst others produce abnormal antithrombin III

Features
- recurrent venous thromboses
- arterial thromboses do occur but is uncommon

Management
- thromboembolic events are treated with lifelong warfarinisation
- heparinisation during pregnancy*
- antithrombin III concentrates (often using during surgery or childbirth)

*as patients with antithrombin III deficiency have a degree of resistance to heparin anti-Xa levels should be monitored carefully to ensure adequate anticoagulation

Question 27 of 116

Which of the following is most associated with thymomas?

- A. Myelodysplasia
- B. Thrombocytopenia
- C. Acute myeloid leukaemia
- D. Acute lymphoblastic leukaemia
- E. Red cell aplasia

Question 27 of 116

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- C. Acute myeloid leukaemia
- D. Acute lymphoblastic leukaemia
- E. Red cell aplasia

Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with
- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death
- compression of airway
- cardiac tamponade

Question 28 of 116

A 24-year-old nulliparous female with a history of recurrent deep vein thrombosis presents with shortness of breath. The full blood count and clotting screen reveals the following results:

Hb 12.4 g/dl

Plt 137

WBC 7.5 * 10^9/l

PT 14 secs

APTT 46 secs

What is the most likely underlying diagnosis?

- A. Third generation oral contraceptive pill use
- B. Protein C deficiency
- C. Antithrombin III deficiency
- D. Antiphospholipid syndrome
- E. Activated protein C resistance

Question 28 of 116

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Antiphospholipid syndrome: (paradoxically) prolonged APTT + low platelets

The combination of a prolonged APTT and thrombocytopenia make antiphospholipid syndrome the most likely diagnosis

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Question 29 of 116

A 72-year-old man is admitted with a deep vein thrombosis. He is normally fit and well but has recently lost weight. Blood tests reveal the following:

IgG 889 mg/dl (range 600-1300 mg/dl)

IgM 1674 mg/dl (range 50-330 mg/dl)

IgA 131 mg/dl (range 60-300 mg/dl)

What is the most likely diagnosis?

- A. Monoclonal gammopathy of undetermined significance
- B. Acute promyelocytic leukaemia
- C. Waldenstrom's macroglobulinaemia
- D. Antiphospholipid syndrome
- E. Multiple myeloma

Question 29 of 116

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IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is more likely than monoclonal gammopathy of undetermined significance given the weight loss and deep vein thrombosis (evidence of hyperviscosity).

IgG and IgA and the most common type of immunoglobulins produced in myeloma.

Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Question 30 of 116

Each one of the following may cause eosinophilia, except:

- A. Allergic bronchopulmonary aspergillosis
- B. Extrinsic allergic alveolitis
- C. Churg-Strauss syndrome
- D. Psoriasis
- E. Toxocara infection

Question 30 of 116

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- C. Churg-Strauss syndrome
- D. Psoriasis
- E. Toxocara infection

Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes
- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Loffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes
- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes
- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

Question 31 of 116

A 73-year-old woman presents with lethargy for the past two weeks. Clinical examination is unremarkable. Her past medical history includes polymyalgia rheumatica and ischaemic heart disease. Screening blood tests are ordered and the full blood count is reported as follows:

Hb 12.9 g/dl

Plt 158 * 10^9/l

WBC 19.0 * 10^9/l

Neuts 4.2 * 10^9/l

Lymphs 14.1 * 10^9/l

What is the most likely diagnosis?

- A. Lymphoma
- B. Nicorandil-related lymphocytosis
- C. Transient viral illness
- D. Chronic lymphocytic leukaemia
- E. Secondary to steroid use

Question 31 of 116

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- E. Secondary to steroid use

Such a lymphocytosis is an elderly patient is very likely to be caused by chronic lymphocytic leukaemia. Steroids tend to cause a neutrophilia. It would be unusual for a viral illness to cause such a marked lymphocytosis in an elderly person.

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 32 of 116

A 67-year-old man is diagnosed with myelofibrosis. What is the most common presenting symptom of myelofibrosis?

- A. Lethargy
- B. Anorexia and weight loss
- C. Night sweats
- D. Easy bruising
- E. Splenomegaly

Question 32 of 116

A 67-year-old man is diagnosed with myelofibrosis. What is the most common presenting symptom of myelofibrosis?

- A. Lethargy
- B. Anorexia and weight loss
- C. Night sweats
- D. Easy bruising
- E. Splenomegaly

Myelofibrosis - most common presenting symptom - lethargy

Whilst all the above may be seen in myelofibrosis lethargy is the most common

Myelofibrosis

Overview
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

Features
- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

Laboratory findings
- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)

Question 33 of 116

Which one of the following translocations is associated with acute promyelocytic leukaemia?

- A. t(15;17)
- B. t(9;17)
- C. t(9;22)
- D. t(15;22)
- E. t(17;22)

Question 33 of 116

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- A. t(15;17)
- B. t(9;17)
- C. t(9;22)
- D. t(15;22)
- E. t(17;22)

Acute promyelocytic leukaemia - t(15;17)

Acute promyelocytic leukaemia

You are not normally expected to be able to differentiate the different subtypes of acute myeloid leukaemia (AML) for the MRCP. An exception to this is acute promyelocytic leukaemia (APML, the M3 subtype of AML). The importance of identifying APML lies in both the presentation (classically disseminated intravascular coagulation) and management

APML is associated with the t(15;17) translocation which causes fusion of the PML and RAR-alpha genes.

Features

- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Question 34 of 116

A 51-year-old female is referred to the haematology clinic with a haemoglobin of 19.2 g/dl. She is a non-smoker. Her oxygen saturations on room air are 98% and she is noted to have mass in the left upper quadrant. What is the most useful test to establish whether she has polycythaemia rubra vera?

- A. Bone marrow aspiration
- B. Blood film
- C. Red cell mass
- D. Transferrin saturation
- E. JAK2 mutation screen

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Polycythaemia rubra vera - JAK2 mutation

The discovery of the JAK2 mutation has made red cell mass a second-line investigation for patients with suspected JAK2-negative polycythaemia rubra vera

Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

Features
- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed
- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:
- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphotase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count >450 * 10^9/l)
B2	Neutrophil leucocytosis (neutrophil count > 10 * 10^9/l in non-smokers; > 12.5*10^9/l in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Question 35 of 116

Which one of the following malignancies may be associated with HTLV-1?

- A. Adult T-cell leukaemia
- B. Colorectal cancer
- C. Burkitt's lymphoma
- D. Medullary thyroid cancer
- E. Breast cancer

Question 35 of 116

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- B. Colorectal cancer
- C. Burkitt's lymphoma
- D. Medullary thyroid cancer
- E. Breast cancer

Haematological malignancies: infections

Viruses
- EBV: Hodgkin's and Burkitt's lymphoma, nasopharyngeal carcinoma
- HTLV-1: Adult T-cell leukaemia/lymphoma
- HIV-1: High-grade B-cell lymphoma

Bacteria
- *Helicobacter pylori*: gastric lymphoma (MALT)

Protozoa
- malaria: Burkitt's lymphoma

Question 36 of 116

Which one of the following ethnic groups have an increased incidence of prostate cancer?

- A. Afro-Caribbean
- B. Ashkenazi Jews
- C. Chinese
- D. Indian subcontinent
- E. White

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- D. Indian subcontinent
- E. White

Prostate cancer: features

Prostate cancer is the second most common cancer in adult males in the UK and is the most common malignant condition in men over 65 years.

Risk factors
- increasing age
- Afro-Caribbean ethnicity

Features
- bladder outlet obstruction: hesitancy, urinary retention
- haematuria, haematospermia
- pain: back, perineal or testicular
- digital rectal examination: asymmetrical, hard, nodular enlargement with loss of median sulcus

Question 37 of 116

A 71-year-old woman who is known to have multiple myeloma is admitted with confusion. Blood tests show the following:

Corrected calcium 2.91 mmol/l

Which one of the following is the most significant cause of the raised calcium level?

- A. Adverse effects of standard treatment
- B. Increased osteoclastic activation
- C. Impaired renal function
- D. Increased renal tubular calcium reabsorption
- E. Elevated PTH-rP levels

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Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 38 of 116

What is the mechanism of action of DDAVP in von Willebrand's disease?

- A. Prevents renal excretion of von Willebrand's factor
- B. Promotes breakdown of large multimers
- C. Induces release of von Willebrand's factor from endothelial cells
- D. Inhibits breakdown of von Willebrand's factor
- E. Acts as substitute carrier molecule for factor VIII

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Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 39 of 116

A 62-year-old man presents with lethargy. A full blood count is taken and is reported as follows:

Hb 10.2 g/dl

Platelets 330 * 10^9/l

WBC 15.2 * 10^9/l

Film Leucoerythroblastic picture. Tear-drop poikilocytes seen

What is the most likely diagnosis?

- A. Aplastic anaemia
- B. Chronic lymphocytic leukaemia
- C. Myelofibrosis
- D. Chronic myeloid leukaemia
- E. Post-splenectomy

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Tear-drop poikilocytes = myelofibrosis

Thrombocytopenia and leucopenia are seen in progressive disease

Blood films: typical pictures

Hyposplenism e.g. post-splenectomy
- target cells
- Howell-Jolly bodies
- Cabot's rings
- siderotic granules
- acanthocytes
- schizocytes

Iron-deficiency anaemia
- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

Myelofibrosis
- 'tear-drop' poikilocytes

Intravascular haemolysis
- schistocytes

Megaloblastic anaemia
- hypersegmented neutrophils

Question 40 of 116

What is the mechanism of action of cisplatin?

- A. Stabilises DNA-topoisomerase II complex
- B. Causes cross-linking in DNA
- C. Inhibits ribonucleotide reductase
- D. Inhibits purine synthesis
- E. Inhibits formation of microtubules

Question 40 of 116

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Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 41 of 116

Which of the following is a cause of extravascular haemolysis?

- A. Hereditary spherocytosis
- B. G6PD deficiency
- C. Disseminated intravascular coagulation
- D. Mismatched blood transfusion
- E. Haemolytic uraemic syndrome

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Haemolytic anaemias: by site

In intravascular haemolysis free haemoglobin is released which binds to haptoglobin. As haptoglobin becomes saturated haemoglobin binds to albumin forming methaemalbumin (detected by Schumm's test). Free haemoglobin is excreted in the urine as haemoglobinuria, haemosiderinuria

Intravascular haemolysis: causes

- mismatched blood transfusion
- G6PD deficiency
- red cell fragmentation: heart valves, TTP, DIC, HUS
- paroxysmal nocturnal haemoglobinuria
- cold autoimmune haemolytic anaemia

Extravascular haemolysis: causes

- haemoglobinopathies: sickle cell, thalassaemia
- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

Question 42 of 116

Which one of the following features is least recognised in myeloma?

- A. Bone pain
- B. Amyloidosis
- C. Lethargy
- D. Night sweats
- E. Pathological fractures

Question 42 of 116

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Night sweats are a feature of non-Hodgkin's lymphoma

Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 43 of 116

A 31-year-old woman who is 25-weeks pregnant is brought to the Emergency Department by her husband. Over the past two days she has become increasingly confused. Her temperature is 37.8ºC and blood pressure is 104/62 mmHg. Blood tests show:

Hb	8.3 g/dl
Platelets	88 * 10^9/l
WBC	15.1 * 10^9/l
Blood film	Fragmented red blood cells
Sodium	139 mmol/l
Potassium	5.2 mmol/l
Urea	19.4 mmol/l
Creatinine	296 µmol/l

What is the most appropriate treatment?

- A. Rituximab
- B. Intravenous immunoglobulin
- C. Methylprednisolone
- D. Ceftriaxone + vancomycin
- E. Plasma exchange

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TTP - plasma exchange is first-line

This patient has thrombotic thrombocytopenic purpura, a condition associated with pregnancy

Thrombotic thrombocytopenic purpura: management

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine

Question 44 of 116

A 26-year-old man with a history of hereditary haemorrhagic telangiectasia is planning to start a family. What is the mode of inheritance?

- A. Autosomal dominant with incomplete penetrance
- B. Autosomal codominant
- C. Autosomal recessive with incomplete penetrance
- D. Autosomal dominant
- E. Autosomal recessive

Question 44 of 116

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- D. Autosomal dominant
- E. Autosomal recessive

Hereditary haemorrhagic telangiectasia - autosomal dominant

Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history

Features

- epistaxis
- telangiectasia develop is skin, mucous membranes and internal organs
- associated with pulmonary AV malformations and other AV malformations in 10%
- may present as iron-deficiency anaemia secondary to bleeding in the GI tract or nasal mucosa

Question 45 of 116

Which of the following is a cause of intravascular haemolysis?

- A. Hereditary spherocytosis
- B. Sickle cell anaemia
- C. Paroxysmal nocturnal haemoglobinuria
- D. Haemolytic disease of the newborn
- E. Warm autoimmune haemolytic anaemia

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- warm autoimmune haemolytic anaemia

Question 46 of 116

A 64-year-old man is reviewed in the haematology clinic. Which one of the following features would suggest that a diagnosis monoclonal gammopathy of undetermined significance is more likely than myeloma?

- A. Bone pain
- B. IgG paraprotein band = 18g/l
- C. Creatinine = 160 µmol/l
- D. Raised beta-2 microglobulin
- E. Lytic lesions on x-ray

Question 46 of 116

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- E. Lytic lesions on x-ray

Paraproteinaemia is seen in both myeloma and monoclonal gammopathy of undetermined significance (MGUS) - at this level a diagnosis of MGUS is more likely. The other features indicate myeloma

MGUS

Monoclonal gammopathy of undetermined significance (MGUS, also known as benign paraproteinaemia and monoclonal gammopathy) is a common condition that causes a paraproteinaemia and is often mistaken for myeloma. Differentiating features are listed below. Around 10% of patients eventually develop myeloma at 5 years, with 50% at 15 years

Features

- usually asymptomatic
- no bone pain or increased risk of infections
- around 10-30% of patients have a demyelinating neuropathy

Differentiating features from myeloma

- normal immune function
- normal beta-2 microglobulin levels
- lower level of paraproteinaemia than myeloma (e.g. < 30g/l IgG, or < 20g/l IgA)
- stable level of paraproteinaemia
- no clinical features of myeloma (e.g. lytic lesions on x-rays or renal disease)

Question 47 of 116

A 54-year-old female is receiving a course of chemotherapy for breast cancer. She is experiencing troublesome vomiting which has not been helped by domperidone. What is the most appropriate next management step?

- A. Add an antihistamine
- B. Add a 5HT2 antagonist
- C. Add a phenothiazine
- D. Add a dopamine receptor antagonist
- E. Add a 5HT3 antagonist

Question 47 of 116

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- E. Add a 5HT3 antagonist

Chemotherapy side-effects: nausea and vomiting

Nausea and vomiting are common side-effects of chemotherapy. Risk factors for the development of symptoms include:

- anxiety
- age less than 50 years old
- concurrent use of opioids
- the type of chemotherapy used

For patients at low-risk of symptoms then drugs such as metoclopramide may be used first-line. For high-risk patients then 5HT3 receptor antagonists such as ondansetron are often effective, especially if combined with dexamethasone

Question 48 of 116

Which of the following is a good prognostic factor in chronic lymphocytic leukaemia?

- A. Female sex
- B. Lymphocyte doubling time < 12 months
- C. CD38 expression positive
- D. Age > 70 years
- E. Raised LDH

Question 48 of 116

Which of the following is a good prognostic factor in chronic lymphocytic leukaemia?

- A. Female sex
- B. Lymphocyte doubling time < 12 months
- C. CD38 expression positive
- D. Age > 70 years
- E. Raised LDH

Chronic lymphocytic leukaemia: prognostic factors

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive

Question 49 of 116

What is the most common complication seen in patients with polycythaemia rubra vera?

- A. Chronic myeloid leukaemia
- B. Osteosarcoma
- C. Myelodysplasia
- D. Myelofibrosis
- E. Acute myeloid leukaemia

Question 49 of 116

What is the most common complication seen in patients with polycythaemia rubra vera?

- A. Chronic myeloid leukaemia
- B. Osteosarcoma
- C. Myelodysplasia
- D. Myelofibrosis
- E. Acute myeloid leukaemia

Polycythaemia rubra vera - around 30% progress to myelofibrosis

Whilst a significant percentage of patients (around 5-15%) develop an acute leukaemia, myelofibrosis is a more common transformation

Polycythaemia rubra vera: management

Polycythaemia rubra vera is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets.. It has peak incidence in the sixth decade, with typical features including hyperviscosity, pruritus and splenomegaly

Management
- venesection - first line treatment
- hydroxyurea -slight increased risk of secondary leukaemia
- phosphorus-32 therapy

Prognosis
- thrombotic events are a significant cause of morbidity and mortality
- 30% of patients progress to myelofibrosis
- 5-15% of patients progress to acute leukaemia

Question 50 of 116

Which one of the following is the most common type of Hodgkin's lymphoma?

- A. Lymphocyte predominant
- B. Nodular sclerosing
- C. Lymphocyte depleted
- D. Mixed cellularity
- E. Hairy cell

Question 50 of 116

Which one of the following is the most common type of Hodgkin's lymphoma?

- A. Lymphocyte predominant
- B. Nodular sclerosing
- C. Lymphocyte depleted
- D. Mixed cellularity
- E. Hairy cell

Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Histological classification
- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis
- weight loss > 10% in last 6 months
- fever > 38ºC
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:
- age = 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/µl or < 8%
- male
- albumin < 40 g/l
- white blood count = 15,000/µl

Question 51 of 116

A 45-year-old man known to have haemochromatosis attends for blood test to assess when he next needs venesection. Of the options given, which one of the following blood tests should be used to assess the adequacy of venesection?

- A. Ferritin
- B. Serum iron
- C. Haemoglobin
- D. Total iron binding capacity
- E. Haematocrit

Question 51 of 116

A 45-year-old man known to have haemochromatosis attends for blood test to assess when he next needs venesection. Of the options given, which one of the following blood tests should be used to assess the adequacy of venesection?

- A. Ferritin
- B. Serum iron
- C. Haemoglobin
- D. Total iron binding capacity
- E. Haematocrit

The British Committee for Standards in Haematology recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:

- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

Diagnostic tests

- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection

- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 52 of 116

A man is investigated for anaemia. A blood film is ordered and reported as follows:
Ring sideroblasts

Which one of the following is least likely to give this picture?

- A. Anti-tuberculosis medication
- B. Alcohol
- C. Pyridoxine
- D. Lead
- E. Myelodysplasia

Question 52 of 116

A man is investigated for anaemia. A blood film is ordered and reported as follows:
Ring sideroblasts

Which one of the following is least likely to give this picture?

- A. Anti-tuberculosis medication
- B. Alcohol
- C. Pyridoxine
- D. Lead
- E. Myelodysplasia

Pyridoxine is actually a treatment for sideroblastic anaemia. Rarely pyridoxine deficiency may be the cause

Sideroblastic anaemia

Sideroblastic anaemia is a condition where red cells fail to completely form haem, whose biosynthesis takes place partly in the mitochondrion. This leads to deposits of iron in the mitochondria that form a ring around the nucleus called a ring sideroblast. It may be congenital or acquired

Congenital cause: delta-aminolevulinate synthase-2 deficiency

Acquired causes
- myelodysplasia
- alcohol
- lead
- anti-TB medications

Investigations
- hypochromic microcytic anaemia (more so in congenital)
- bone marrow: sideroblasts and increased iron stores

Management
- supportive
- treat any underlying cause
- pyridoxine may help

Question 53 of 116

In idiopathic thrombocytopenic purpura what are the autoantibodies most commonly directed at?

- A. Platelet activating factor
- B. Glycoprotein IIb/IIIa complex
- C. ATP receptor
- D. Anti-thrombin III receptor
- E. ADP receptor

Question 53 of 116

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ITP

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex.

ITP can be divided into acute and chronic forms:

Acute ITP
- more commonly seen in children
- equal sex incidence
- may follow an infection or vaccination
- usually runs a self-limiting course over 1-2 weeks

Chronic ITP
- more common in young/middle-aged women
- tends to run a relapsing-remitting course

Evan's syndrome
- ITP in association with autoimmune haemolytic anaemia (AIHA)

Question 54 of 116

Burkitt's lymphoma is associated with a mutation in which one of the following genes?

- A. Cyclin D1 gene
- B. PML gene
- C. BCR-ABL gene
- D. RAR-alpha gene
- E. MYC gene

Question 54 of 116

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- B. PML gene
- C. BCR-ABL gene
- D. RAR-alpha gene
- E. MYC gene

Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome
- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)
- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)
- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)
- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

Question 55 of 116

Regarding the Ann-Arbor classification of Hodgkin's lymphoma, which one of the following would be staged as IIIB?

- A. Nodes on both sides of diaphragm with pruritus
- B. Two or more lymph nodes on the same side of the diaphragm with pruritus
- C. Nodes on both sides of diaphragm with night sweats
- D. Two or more lymph nodes on the same side of the diaphragm with night sweats
- E. Two or more lymph nodes on the same side of the diaphragm with no systemic symptoms

Question 55 of 116

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Hodgkin's lymphoma: staging

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Ann-Arbor staging of Hodgkin's lymphoma

- I: single lymph node
- II: 2 or more lymph nodes/regions on same side of diaphragm
- III: nodes on both sides of diaphragm
- IV: spread beyond lymph nodes

Each stage may be subdivided into A or B

- A = no systemic symptoms other than pruritus
- B = weight loss > 10% in last 6 months, fever > 38c, night sweats (poor prognosis)

Question 56 of 116

Which one of the following is not an indication for treatment in chronic lymphocytic leukaemia?

- A. Massive splenomegaly
- B. Platelet count of 77 * 10^9/l
- C. Night sweats
- D. Lymphocyte count of 65 * 10^9/l
- E. Extreme fatigue

Question 56 of 116

Which one of the following is not an indication for treatment in chronic lymphocytic leukaemia?

- A. Massive splenomegaly
- B. Platelet count of 77 * 10^9/l
- C. Night sweats
- D. Lymphocyte count of 65 * 10^9/l
- E. Extreme fatigue

The absolute lymphocyte count is not an indication for treatment, rather than the rate of increase (see guidelines below)

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 57 of 116

Each one of the following is associated with iron-deficiency anaemia, except:

- A. Atrophic glossitis
- B. Onycholysis
- C. Post-cricoid webs
- D. Koilonychia
- E. Angular stomatitis

Question 57 of 116

Each one of the following is associated with iron-deficiency anaemia, except:

- A. Atrophic glossitis
- B. Onycholysis
- C. Post-cricoid webs
- D. Koilonychia
- E. Angular stomatitis

Iron deficiency anaemia

Features
- koilonychia
- atrophic glossitis
- post-cricoid webs
- angular stomatitis

Blood film
- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

Question 58 of 116

A 35-year-old female who is 34 weeks pregnant presents with a swollen, painful right calf. A deep vein thrombosis is confirmed on Doppler scan. What is the preferred anticoagulant?

- A. Clopidogrel
- B. Aspirin
- C. Intravenous heparin
- D. Warfarin
- E. Subcutaneous low molecular weight heparin

Question 58 of 116

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- A. Clopidogrel
- B. Aspirin
- C. Intravenous heparin
- D. Warfarin
- E. Subcutaneous low molecular weight heparin

Although teratogenic effects of warfarin are greater in the first trimester most clinicians would use low molecular weight heparin in this situation. Another factor to consider is the risk of peripartum haemorrhage and potential problems reversing the effects of warfarin if this occurred

Pregnancy: DVT/PE

Overview
- pregnancy is a hypercoagulable state
- majority occur in last trimester

Pathophysiology
- increase in factors VII, VIII, X and fibrinogen
- decrease in protein S
- uterus presses on IVC causing venous stasis in legs

Management
- warfarin contraindicated
- S/C low-molecular weight heparin preferred to IV heparin (less bleeding and thrombocytopenia)

Question 59 of 116

What is the most common inherited bleeding disorder?

- A. Haemophilia A
- B. Activated protein C resistance
- C. Haemophilia B
- D. Antithrombin III deficiency
- E. von Willebrand's disease

Question 59 of 116

What is the most common inherited bleeding disorder?

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- B. Activated protein C resistance
- C. Haemophilia B
- D. Antithrombin III deficiency
- E. von Willebrand's disease

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor
- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types
- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation
- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management
- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 60 of 116

A 31-year-old man is referred to the acute medical unit with a painful swollen left leg. The patient reports that he has the 'Factor V Leiden mutation'. Which one of the following best describes the pathophysiology of his condition?

- A. Protein S deficiency
- B. Activated protein C excess
- C. Antithrombin deficiency
- D. Resistance to action of protein C
- E. Activated protein C deficiency

Question 60 of 116

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- C. Antithrombin deficiency
- D. Resistance to action of protein C
- E. Activated protein C deficiency

Factor V Leiden mutation results in activated protein C resistance

Activated protein C resistance

Activated protein C resistance is the most common inherited thrombophilia. It is due to a mutation in the Factor V Leiden gene. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Question 61 of 116

A 52-year-old is found to have chronic myeloid leukaemia following investigation for splenomegaly. Which one of the following best describes the function of the BCR-ABL fusion protein?

- A. Epidermal growth factor receptor
- B. Phospholipase C
- C. CD52 co-receptor
- D. Tyrosine kinase
- E. Fibroblast growth factor receptor

Question 61 of 116

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- C. CD52 co-receptor
- D. Tyrosine kinase
- E. Fibroblast growth factor receptor

Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)
- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management
- hydroxyurea
- interferon-alpha
- imatinib
- allogenic bone marrow transplant

Imatinib
- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Question 62 of 116

A 73-year-old man is prescribed cetuximab after being diagnosed with metastatic colorectal cancer. What target is this monoclonal antibody directed against?

- A. Vascular endothelial growth factor receptor
- B. Angiopoietin-2 receptors
- C. CD20 protein complex
- D. Epidermal growth factor receptor
- E. Fibroblast growth factor receptor

Question 62 of 116

A 73-year-old man is prescribed cetuximab after being diagnosed with metastatic colorectal cancer. What target is this monoclonal antibody directed against?

- A. Vascular endothelial growth factor receptor
- B. Angiopoietin-2 receptors
- C. CD20 protein complex
- D. Epidermal growth factor receptor
- E. Fibroblast growth factor receptor

Cetuximab - monoclonal antibody against the epidermal growth factor receptor

Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from an human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

Question 63 of 116

A 18-year-old man who is known to have hereditary spherocytosis is admitted to hospital with lethargy. Admission bloods show the following:

Hb 4.7 g/dl

Retics 0.3%

What is the most likely explanation for these findings?

- A. Haemolytic crisis
- B. Recent ciprofloxacin therapy
- C. Parvovirus infection
- D. Sequestration crises
- E. Angiodysplastic bowel lesions

Question 63 of 116

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What is the most likely explanation for these findings?

- A. Haemolytic crisis
- B. Recent ciprofloxacin therapy
- C. Parvovirus infection
- D. Sequestration crises
- E. Angiodysplastic bowel lesions

This man has had an aplastic crisis secondary to parvovirus infection.

Hereditary spherocytosis

Basics
- most common hereditary haemolytic anaemia in northern Europeans
- autosomal dominant defect of RBC cytoskeleton
- biconcave disc --> spherocyte
- red cell survival reduced, destroyed by spleen

Presentation
- e.g. failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

Diagnosis
- osmotic fragility test

Management
- folate replacement
- splenectomy

Question 64 of 116

A 62-year-old man is called for review after a positive faecal occult blood test done as part of the national screening programme. During counselling for colonoscopy he asks what percentage of patients with a positive faecal occult blood test have colorectal cancer. What is the most accurate answer?

- A. 0.5 - 2%
- B. 5 - 15%
- C. 20 - 30%
- D. 30 - 50%
- E. 55 - 75%

Question 64 of 116

A 62-year-old man is called for review after a positive faecal occult blood test done as part of the national screening programme. During counselling for colonoscopy he asks what percentage of patients with a positive faecal occult blood test have colorectal cancer. What is the most accurate answer?

- A. 0.5 - 2%
- B. 5 - 15%
- C. 20 - 30%
- D. 30 - 50%
- E. 55 - 75%

Colorectal cancer screening - PPV of FOB = 5 - 15%

There is also a 30-45% chance of having an adenoma with a positive faecal occult blood test

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cance

Question 65 of 116

A 27-year-old male is receiving cyclophosphamide as part of his chemotherapy for non-Hodgkin' lymphoma. What is the most appropriate management to reduce the likelihood of haemorrhagic cystitis?

- A. Hydration + tranexamic acid
- B. Hydration + twice-daily bladder washouts
- C. Hydration + prophylactic antibiotics
- D. Hydration + twice-daily bladder washouts + prophylactic antibiotics
- E. Hydration + mesna

Question 65 of 116

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- C. Hydration + prophylactic antibiotics
- D. Hydration + twice-daily bladder washouts + prophylactic antibiotics
- E. Hydration + mesna

Cyclophosphamide - haemorrhagic cystitis - prevent with mesna

Cyclophosphamide may be converted to urotoxic metabolites such as acrolein. Mesna binds to these metabolites through its sulfhydryl-moieties and reduces the incidence of haemorrhagic cystitis

Cyclophosphamide

Cyclophosphamide is an alkylating agent used in the management of cancer and autoimmune conditions. It works by causing cross-linking of DNA

Adverse effects

- haemorrhagic cystitis: incidence reduced by the use of hydration and mesna
- myelosuppression
- transitional cell carcinoma

Question 66 of 116

A 35-year-old woman presents with menorrhagia and a persistent sore throat. A full blood count shows her to be pancytopenic. Which one of the following medications is most likely to account for this finding?

- A. Trimethoprim
- B. Rifampicin
- C. Olanzapine
- D. Montelukast
- E. Clomifene

Question 66 of 116

A 35-year-old woman presents with menorrhagia and a persistent sore throat. A full blood count shows her to be pancytopenic. Which one of the following medications is most likely to account for this finding?

- A. Trimethoprim
- B. Rifampicin
- C. Olanzapine
- D. Montelukast
- E. Clomifene

Drug-induced pancytopaenia

Drug causes of pancytopaenia

- cytotoxics
- antibiotics: trimethoprim, chloramphenicol
- anti-rheumatoid: gold, penicillamine
- carbimazole*
- anti-epileptics: carbamazepine
- sulphonylureas: tolbutamide

*causes both agranulocytosis and pancytopaenia

Question 67 of 116

A 74-year-old woman with a past history of chronic lymphocytic leukaemia presents with lethargy. The following blood results are obtained:

Hb	7.9 g/dl
Plt	158 * 10^9/l
WCC	24.0 * 10^9/l

Blood film: normochromic, normocytic anaemia

What complication has most likely occurred?

- A. Paroxysmal nocturnal haemoglobinuria
- B. Microangiopathic haemolytic anaemia
- C. Sideroblastic anaemia
- D. Warm autoimmune haemolytic anaemia
- E. Cold autoimmune haemolytic anaemia

Question 67 of 116

A 74-year-old woman with a past history of chronic lymphocytic leukaemia presents with lethargy. The following blood results are obtained:

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Blood film: normochromic, normocytic anaemia

What complication has most likely occurred?

- A. Paroxysmal nocturnal haemoglobinuria
- B. Microangiopathic haemolytic anaemia
- C. Sideroblastic anaemia
- D. Warm autoimmune haemolytic anaemia
- E. Cold autoimmune haemolytic anaemia

Warm autoimmune haemolytic anaemia occurs in around 10-15% of patients with chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 68 of 116

A 54-year-old woman presents to the Emergency Department with a five day history of back pain. Her past medical history includes breast cancer and osteoarthritis. The back pain is located in the lower thoracic region and is made worse by coughing and sneezing. There has been no change in bowel habit or urinary symptoms. On examination there is diffuse tenderness in the lower thoracic region. Peri-anal sensation is normal and lower limb reflexes are brisk. Which one of the following is the most appropriate management plan?

- A. Organise outpatient MRI
- B. Oral paracetamol + urgent MRI
- C. Oral paracetamol + urgent thoracic/lumbar spine x-ray
- D. Oral dexamethasone + urgent thoracic/lumbar spine x-ray
- E. Oral dexamethasone + urgent MRI

Question 68 of 116

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- B. Oral paracetamol + urgent MRI
- C. Oral paracetamol + urgent thoracic/lumbar spine x-ray
- D. Oral dexamethasone + urgent thoracic/lumbar spine x-ray
- E. Oral dexamethasone + urgent MRI

This woman has spinal cord compression until proven otherwise and should have urgent assessment.

Recent NICE guidelines suggest contacting the local metastatic spinal cord compression coordinator in this situation. This should hopefully prevent delays in treatment by ensuring the patient is admitted to the most appropriate place

Spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. It is more common in patients with lung, breast and prostate cancer

Features

- back pain: may be worse on lying down and coughing
- neurological signs depend on the level of the lesion. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

Management

- high-dose oral dexamethasone
- urgent oncological assessment for consideration of radiotherapy or surgery

Question 69 of 116

What is the most useful marker of prognosis in myeloma?

- A. Calcium level
- B. Urine Bence-Jones protein levels
- C. Alkaline phosphotase
- D. ESR
- E. B2-microglobulin

Question 69 of 116

What is the most useful marker of prognosis in myeloma?

- A. Calcium level
- B. Urine Bence-Jones protein levels
- C. Alkaline phosphotase
- D. ESR
- E. B2-microglobulin

Myeloma: prognosis

B2-microglobulin is a useful marker of prognosis - raised levels imply poor prognosis. Low levels of albumin are also associated with a poor prognosis

International prognostic index

Stage	Criteria	Median survival (months)
I	B2 microglobulin < 3.5 mg/l Albumin > 35 g/l	62
II	Not I or III	45
III	B2 microglobulin > 5.5 mg/l	29

Question 70 of 116

A 61-year-old presents for review. She has been having atypical lower back pain for the past two months. An x-ray of her lumbar spine reported raised the possibility of spinal metastases but there is no current evidence of a primary tumour. A series of tumour markers were sent. Which one of the following is most associated with raised levels of CA 15-3?

- A. Pancreatic cancer
- B. Colorectal cancer
- C. Breast cancer
- D. Ovarian cancer
- E. Hepatocellular carcinoma

Question 70 of 116

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Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 71 of 116

A woman is prescribed docetaxel as part of her chemotherapy for breast cancer. What is the mechanism of action of docetaxel?

- A. Inhibits RNA synthesis
- B. Stabilizes DNA-topoisomerase II complex
- C. Prevents microtubule disassembly
- D. Inhibits formation of microtubules
- E. Causes cross-linking in DNA

Question 71 of 116

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Taxanes (e.g. Docetaxel) prevent microtubule disassembly

Like other taxanes the principal mechanism of action is the prevention of microtubule disassembly.

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 72 of 116

Which one of the following haematological malignancies is most commonly associated with the t(11;14) translocation?

- A. Acute promyelocytic leukaemia
- B. Burkitt's lymphoma
- C. Acute lymphoblastic leukaemia
- D. Mantle cell lymphoma
- E. Chronic myeloid leukaemia

Question 72 of 116

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- D. Mantle cell lymphoma
- E. Chronic myeloid leukaemia

Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome
- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)
- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)
- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)
- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

Question 73 of 116

A 30-year-old man enquires about screening for haemochromatosis as his brother was diagnosed with the condition 2 years ago. The patient is currently well with no features suggestive of haemochromatosis. What is the most appropriate investigation?

- A. Serum total iron-binding capacity
- B. HFE gene analysis
- C. Serum transferrin saturation
- D. Serum ferritin
- E. Serum iron

Question 73 of 116

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- D. Serum ferritin
- E. Serum iron

Screening for haemochromatosis
- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

Serum transferrin saturation is currently the preferred investigation for population screening. However, the patient has a sibling with haemochromatosis and therefore HFE gene analysis is the most suitable investigation. In clinical practice this would be combined with iron studies as well

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:
- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive
Diagnostic tests
- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis
- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection
- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 74 of 116

A patient presents as she has a strong family history of cancer. Which one of the following cancers is least likely to be inherited?

- A. Colorectal cancer
- B. Breast cancer
- C. Gastric cancer
- D. Endometrial cancer
- E. Ovarian cancer

Question 74 of 116

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Between 5 and 10% of all breast cancers are thought to be hereditary. Mutation in the BRCA1 and BRCA2 genes also increase the risk of ovarian cancer. For colorectal cancer around 5% of cases are caused by hereditary non-polyposis colorectal carcinoma (HNPCC) and 1% are due to familial adenomatous polyposis. Women who have HNPCC also have a markedly increased risk for developing endometrial cancer - around 5% of endometrial cancers occur in women with this risk factor.

Cancer in the UK

The most common causes of cancer in the UK are as follows*

- 1. Breast
- 2. Lung
- 3. Colorectal
- 4. Prostate
- 5. Bladder
- 6. Non-Hodgkin's lymphoma
- 7. Melanoma
- 8. Stomach
- 9. Oesophagus
- 10. Pancreas

The most common causes of death from cancer in the UK are as follows:

- 1. Lung
- 2. Colorectal
- 3. Breast
- 4. Prostate
- 5. Oesophagus
- 6. Stomach
- 7. Bladder
- 8. Non-Hodgkin's lymphoma
- 9. Ovarian
- 10. Leukaemia

*excludes non-melanoma skin cancer

Question 75 of 116

Which one of the following is least associated with small cell lung cancer?

- A. Bad prognosis
- B. Cushing's syndrome
- C. PTH-related peptide secretion
- D. Hyponatraemia
- E. Lambert-Eaton syndrome

Question 75 of 116

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- D. Hyponatraemia
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Paraneoplastic features of lung cancer
- squamous cell: PTHrp, clubbing, HPOA
- small cell: ADH, ACTH, Lambert-Eaton syndrome

PTH-related peptide secretion is seen in squamous cell lung cancer

Lung cancer: small cell

Features
- usually central
- arise from APUD* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome
- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

Management
- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- radiotherapy: only used for debulking
- chemotherapy: good response to combination chemotherapy, may extend life by approximately 4 months

*an acronym for
- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

Question 76 of 116

Which one of the following is least associated with thrombocytopenia?

- A. Heparin therapy
- B. Rheumatoid arthritis
- C. Infectious mononucleosis
- D. Liver disease
- E. Pregnancy

Question 76 of 116

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Rheumatoid arthritis, unlike systemic lupus erythematous, is generally associated with a thrombocytosis. In some cases of Felty's syndrome thrombocytopaenia may be seen secondary to hypersplenism. This however represents a small percentage of patients with rheumatoid arthritis

Thrombocytopenia

Causes of severe thrombocytopenia

- ITP
- DIC
- TTP
- haematological malignancy

Causes of moderate thrombocytopenia

- heparin induced thrombocytopenia (HIT)
- drug-induced (e.g. quinine, diuretics, sulphonamides, aspirin, thiazides)
- alcohol
- liver disease
- hypersplenism
- viral infection (EBV, HIV, hepatitis)
- pregnancy
- SLE/antiphospholipid syndrome
- vitamin B12 deficiency

Question 77 of 116

Which one of the following is least associated with eosinophilia?

- A. Churg-Strauss syndrome
- B. Nematode infection
- C. Histoplasmosis
- D. Allergic bronchopulmonary aspergillosis
- E. Asthma

Question 77 of 116

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- C. Histoplasmosis
- D. Allergic bronchopulmonary aspergillosis
- E. Asthma

Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes
- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Loffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes
- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes
- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

Question 78 of 116

Which one of the following therapeutic options is least recognised in the treatment of aplastic anaemia?

- A. Interferon-alpha
- B. Stem cell transplantation
- C. Anti-lymphocyte globulin
- D. Anti-thymocyte globulin
- E. Platelet transfusion

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- E. Platelet transfusion

Aplastic anaemia: management

Supportive
- blood products
- prevention and treatment of infection

Anti-thymocyte globulin (ATG) and anti-lymphocyte globulin (ALG)
- prepared in animals (e.g. rabbits or horses) by injecting human lymphocytes
- is highly allergenic and may cause serum sickness (fever, rash, arthralgia), therefore steroid cover usually given
- immunosuppression using agents such as ciclosporin may also be given

Stem cell transplantation
- allogeneic transplants have a success rate of up to 80%

Question 79 of 116

Which one of the following is least recognised as a treatment modality in idiopathic thrombocytopenic purpura?

- A. Plasma exchange
- B. Splenectomy
- C. IV immunoglobulin
- D. Cyclophosphamide
- E. Oral prednisolone

Question 79 of 116

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- D. Cyclophosphamide
- E. Oral prednisolone

ITP: investigation and management

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

Investigations

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

Management

- oral prednisolone (80% of patients respond)
- splenectomy if platelets < 30 after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide

Question 80 of 116

Which of the following factors is associated with a good prognosis in acute myeloid leukaemia?

- A. Translocation between chromosome 9 and 14
- B. Translocation between chromosome 15 and 17
- C. 25% blast following first course of chemotherapy
- D. Deletion of chromosome 5
- E. Deletion of chromosome 7

Question 80 of 116

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- E. Deletion of chromosome 7

Acute myeloid leukaemia - good prognosis: t(15;17)

A translocation between chromosome 15 and 17 is seen in acute promyelocytic leukaemia, which is known to carry a good prognosis

Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features
- > 60 years
- > 20% blasts after first course of chemo
- cytogenics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3
- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)
- MO - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

Question 81 of 116

A 72-year-old man is diagnosed with prostate cancer and goserelin (Zoladex) is prescribed. Which one of the following is it most important to co-prescribe for the first two weeks of treatment?

- A. Tamoxifen
- B. Lansoprazole
- C. Allopurinol
- D. Cyproterone acetate
- E. Tamsulosin

Question 81 of 116

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- C. Allopurinol
- D. Cyproterone acetate
- E. Tamsulosin

Anti-androgen treatment such as cyproterone acetate should be co-prescribed when starting gonadorelin analogues due to the risk of tumour flare. This phenomenon is secondary to initial stimulation of luteinising hormone release by the pituitary gland resulting in increased testosterone levels.

Prostate cancer: management

Localised prostate cancer (T1/T2)
Treatment depends on life expectancy and patient choice. Options include:

- conservative: active monitoring & watchful waiting
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Localised advanced prostate cancer (T3/T4)
Options include:

- hormonal therapy: see below
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

Metastatic prostate cancer disease - hormonal therapy
Synthetic GnRH agonist

- e.g. Goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen

- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Orchidectomy

Question 82 of 116

A 43-year-old woman is about to start treatment with trastuzumab for metastatic breast cancer. What is the most important investigation to perform prior to initiating treatment?

- A. Pulmonary function tests
- B. Echo
- C. Liver function tests
- D. Chest x-ray
- E. Glucose tolerance test

Question 82 of 116

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- B. Echo
- C. Liver function tests
- D. Chest x-ray
- E. Glucose tolerance test

Trastuzumab (Herceptin) - cardiac toxicity is common

Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Question 83 of 116

Each one of the following is associated with hyposplenism, except:

- A. Sickle-cell anaemia
- B. Liver cirrhosis
- C. Systemic lupus erythematous
- D. Coeliac disease
- E. Splenectomy

Question 83 of 116

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Hyposplenism

Causes
- splenectomy
- sickle-cell
- coeliac disease, dermatitis herpetiformis
- Graves' disease
- systemic lupus erythematosus
- amyloid

Features
- Howell-Jolly bodies
- siderocytes

Question 84 of 116

Which one of the following is least associated with hepatocellular carcinoma?

- A. Hepatitis C
- B. Primary biliary cirrhosis
- C. Aflatoxin
- D. Wilson's disease
- E. Haemochromatosis

Question 84 of 116

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Hepatocellular carcinoma

Risk factors
- hepatitis B and C
- cirrhosis*: alcohol, haemochromatosis, primary biliary cirrhosis
- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda

*Wilson's disease is an exception

Question 85 of 116

Which one of the following haematological disorders is most associated with gingival hyperplasia?

- A. Chronic lymphocytic leukaemia
- B. Myelofibrosis
- C. Polycythaemia rubra vera
- D. Haemophilia A
- E. Acute myeloid leukaemia

Question 85 of 116

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- D. Haemophilia A
- E. Acute myeloid leukaemia

Gingival hyperplasia: phenytoin, ciclosporin, calcium channel blockers and AML

Gingival hyperplasia

Drug causes of gingival hyperplasia
- phenytoin
- ciclosporin
- calcium channel blockers (especially nifedipine)

Other causes of gingival hyperplasia include
- acute myeloid leukaemia (myelomonocytic and monocytic types)

Question 86 of 116

Which electrolyte disturbance is cisplatin most associated with?

- A. Hypocalcaemia
- B. Hyponatraemia
- C. Hypomagnesaemia
- D. Hypokalaemia
- E. Hypercalcaemia

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Cisplatin is associated with hypomagnesaemia

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Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 87 of 116

A 54-year-old woman who has had a hysterectomy presents for advice about hormone replacement therapy. Which one of the following would result from the use of a combined oestrogen-progestogen preparation compared to an oestrogen-only preparation?

- A. Decreased risk of venous thromboembolism
- B. Increased risk of a stroke
- C. Increased risk of breast cancer
- D. Increased risk of endometrial cancer
- E. Better control of symptoms

Question 87 of 116

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HRT: adding a progestogen increases the risk of breast cancer

This is the rationale behind giving women who've had a hysterectomy oestrogen-only treatment

Hormone replacement therapy: adverse effects

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen (combined with a progestogen in women with a uterus) to help alleviate menopausal symptoms.

Side-effects
- nausea
- breast tenderness
- fluid retention and weight gain

Potential complications
- increased risk of breast cancer: increased by the addition of a progestogen
- increased risk of endometrial cancer: reduced by the addition of a progestogen but not eliminated completely. The BNF states that the additional risk is eliminated if a progestogen is given continuously
- increased risk of venous thromboembolism: increased by the addition of a progestogen

Breast cancer
- in the Women's Health Initiative (WHI) study there was a relative risk of 1.26 at 5 years of developing breast cancer
- the increased risk relates to duration of use
- breast cancer incidence is higher in women using combined preparations compared to oestrogen-only preparations
- the risk of breast cancer begins to decline when HRT is stopped and by 5 years it reaches the same level as in women who have never taken HRT

Question 88 of 116

Of the following options, which one is the best diagnostic test for paroxysmal nocturnal haemoglobinuria?

- A. Osmotic fragility test
- B. FMC-7 staining
- C. PAS staining of erythrocytes
- D. Flow cytometry for CD59 and CD55
- E. Immunophenotyping for CD19 and CD20

Question 88 of 116

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Flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

Pathophysiology
- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

Features
- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopaenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

Diagnosis
- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

Management
- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation

Question 89 of 116

A 66-year-old woman is referred by her GP with anaemia. She has been feeling generally unwell for the past 3 weeks. Bloods on admission show:

Hb 8.7 g/dl

MCV 87 fl

Plt 198 * 10^9/l

WBC 5.3 * 10^9/l

Further tests were then ordered:

Reticulocytes	5.2%l
Direct antiglobulin test	Positive, C3d only
Film	Marked red cell agglutination at room temperature

Which one of the following is the most likely underlying cause?

- A. Non-Hodgkin's lymphoma
- B. Mycoplasma pneumonia
- C. Chronic myeloid leukaemia
- D. Acute myeloid leukaemia subtype M3
- E. Cytomegalovirus infection

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The blood results suggest warm autoimmune haemolytic anaemia (AIHA) which may be caused by non-Hodgkin's lymphoma. Mycoplasma pneumonia is associated with cold AIHA. The other three listed conditions are not commonly associated with AIHA.

Autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia (AIHA) may be divided in to 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

Warm AIHA

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyldopa

Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

Question 90 of 116

Which one of the following is least associated with thymomas?

- A. Syndrome inappropriate ADH
- B. Myasthenia gravis
- C. Red cell aplasia
- D. Dermatomyositis
- E. Motor neurone disease

Question 90 of 116

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Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with
- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death
- compression of airway
- cardiac tamponade

Question 91 of 116

Which one of the following is not a risk factor for the development of bladder cancer?

- A. Occupational exposure to aniline dyes
- B. Cyclophosphamide
- C. Strongyloides infection
- D. Smoking
- E. Occupational history involving rubber manufacture

Question 91 of 116

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- B. Cyclophosphamide
- C. Strongyloides infection
- D. Smoking
- E. Occupational history involving rubber manufacture

Schistosomiasis rather than Strongyloides infection is associated with an increased risk of bladder cancer

Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

Question 92 of 116

Which one of the following is the most common inherited thrombophilia?

- A. Protein S deficiency
- B. Antithrombin III deficiency
- C. Protein C deficiency
- D. Activated protein C resistance
- E. Von Willebrand's disease

Question 92 of 116

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- A. Protein S deficiency
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- D. Activated protein C resistance
- E. Von Willebrand's disease

Activated protein C resistance (Factor V Leiden) is the most common inherited thrombophilia

Activated protein C resistance is due a point mutation in the Factor V gene, encoding for the Leiden allele. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Von Willebrand's disease is the most common inherited bleeding disorder

Thrombophilia: causes

Inherited
- activated protein C resistance (factor V Leiden)
- antithrombin III deficiency
- protein C deficiency
- protein S deficiency

Acquired
- antiphospholipid syndrome
- the Pill

Question 93 of 116

A 67-year-old man is investigated for dyspepsia. A gastroscopy reveals a suspicious lesion which is biopsied. Which one of the following findings on biopsy would be most consistent with a diagnosis of gastric adenocarcinoma?

- A. Columnar metaplasia
- B. Histiocytic infiltration
- C. Paneth cell metaplasia
- D. Giant cell granulomas
- E. Signet ring cells

Question 93 of 116

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- C. Paneth cell metaplasia
- D. Giant cell granulomas
- E. Signet ring cells

Gastric adenocarcinoma - signet ring cells

Gastric cancer

Epidemiology
- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Columbia than the West
- more common in males, 2:1

Associations
- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

Investigation
- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Question 94 of 116

A 48-year-old female who has just completed a course of chemotherapy complains of difficulty using her hands associated with 'pins and needles'. She has also experienced urinary hesitancy. Which cytotoxic drug is most likely to be responsible?

- A. Doxorubicin
- B. Cyclophosphamide
- C. Methotrexate
- D. Vincristine
- E. Bleomycin

Question 94 of 116

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- D. Vincristine
- E. Bleomycin

Vincristine is associated with peripheral neuropathy. Urinary hesitancy may develop secondary to bladder atony.

Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Question 95 of 116

A 28-year-old man is investigated for cervical lymphadenopathy. A biopsy shows nodular sclerosing Hodgkin's lymphoma. Which one of the following factors is associated with a poor prognosis?

- A. History of Epstein Barr virus infection
- B. Mediastinal involvement
- C. Female sex
- D. Night sweats
- E. Lymphocytes 20% of total white blood cells

Question 95 of 116

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- C. Female sex
- D. Night sweats
- E. Lymphocytes 20% of total white blood cells

Night sweats are a 'B' symptom and imply a poor prognosis

Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Histological classification
- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis
- weight loss > 10% in last 6 months
- fever > 38ºC
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:
- age = 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/µl or < 8%
- male
- albumin < 40 g/l
- white blood count = 15,000/µl

Question 96 of 116

A 24-year-old man is diagnosed with a deep vein thrombosis of his right leg. He is initially treated with low-molecular weight heparin but is switched after three days to warfarin. He then develops necrotic skin lesions on his lower limbs and forearms. Which one of the following conditions is characteristically associated with this complication?

- A. Protein S deficiency
- B. Antiphospholipid syndrome
- C. Antithrombin III deficiency
- D. Activated protein C resistance
- E. Protein C deficiency

Question 96 of 116

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- C. Antithrombin III deficiency
- D. Activated protein C resistance
- E. Protein C deficiency

Protein C deficiency

Protein C deficiency is an autosomal codominant condition which causes an increased risk of thrombosis

Features

- venous thromboembolism
- skin necrosis following the commencement of warfarin: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis

Question 97 of 116

A 71-year-old woman with no significant past medical history is investigated for lymphocytosis. She has recently lost 7kg in weight and complains of lethargy. The following blood results are obtained:

Hb	9.8 g/dl
Plt	104 * 10^9/l
WBC	70.3 * 10^9/l
Blood film:	Lymphocytosis. Smudge cells seen

Four months previously her white cell count was 30.5 * 10^9/l. What is the most appropriate management?

- A. Imatinib
- B. Cyclophosphamide
- C. No treatment, monitor full blood count
- D. Chlorambucil
- E. Rituximab

Question 97 of 116

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- D. Chlorambucil
- E. Rituximab

CLL - treatment - chlorambucil

This patient has chronic lymphocytic leukaemia. The lymphocyte doubling time is less than 6 months, the patient has some evidence of marrow failure and also has systemic symptoms. She should therefore be treated and of the options given chlorambucil is the most appropriate treatment. As with many haematological cancers such patients are often entered into randomised trials

Chronic lymphocytic leukaemia: management

Indications for treatment*

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

Management

- none early on
- chlorambucil to reduce lymphocyte count
- other options include fludarabine

*taken from the 2005 British Committee for Standards in Haematology guidelines

Question 98 of 116

A 17-year-old man is investigated after he bled excessively following a tooth extraction. The following results are obtained:

Plt 173 * 10^9/l

PT 12.9 secs

APTT 84 secs

Which clotting factor is he most likely to be deficient in?

- A. Factor VI
- B. Factor VII
- C. Factor VIII
- D. Factor IX
- E. Factor X

Question 98 of 116

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Plt 173 * 10^9/l

PT 12.9 secs

APTT 84 secs

Which clotting factor is he most likely to be deficient in?

- A. Factor VI
- B. Factor VII
- C. Factor VIII
- D. Factor IX
- E. Factor X

This man is most likely to have haemophilia A, which accounts for 90% of cases of haemophilia.

Haemophilia

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

Features
- haemoarthroses, haematomas
- prolonged bleeding after surgery or trauma

Blood tests
- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

Question 99 of 116

A 25-year-old woman with primary antiphospholipid syndrome is reviewed. She has just had a booking ultrasound which confirms a viable pregnancy. This is her first pregnancy and she is otherwise fit and well. Which one of the following is the recommend treatment?

- A. Aspirin + prednisolone
- B. Low-molecular weight heparin
- C. Prednisolone + low-molecular weight heparin
- D. Aspirin + low-molecular weight heparin
- E. Aspirin

Question 99 of 116

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- B. Low-molecular weight heparin
- C. Prednisolone + low-molecular weight heparin
- D. Aspirin + low-molecular weight heparin
- E. Aspirin

Antiphospholipid syndrome in pregnancy: aspirin + LMWH

Antiphospholipid syndrome: pregnancy

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

Question 100 of 116

What is the lifetime risk of developing colorectal cancer in the United Kingdom?

- A. 1%
- B. 2%
- C. 5%
- D. 10%
- E. 15%

Question 100 of 116

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- D. 10%
- E. 15%

Colorectal cancer is the third most common cancer in the UK, with approximately 30,000 new cases in England and Wales per year

Colorectal cancer: screening

Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screeing programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligble patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Question 101 of 116

A 34-year-old man is reviewed four years after having an orchidectomy for a testicular teratoma. What are the most useful follow-up investigation(s) to detecf disease recurrence?

- A. CRP + beta-HCG
- B. Testosterone + beta-HCG
- C. ESR + alpha-fetoprotein
- D. Alpha-fetoprotein + beta-HCG
- E. LDH + ESR

Question 101 of 116

A 34-year-old man is reviewed four years after having an orchidectomy for a testicular teratoma. What are the most useful follow-up investigation(s) to detecf disease recurrence?

- A. CRP + beta-HCG
- B. Testosterone + beta-HCG
- C. ESR + alpha-fetoprotein
- D. Alpha-fetoprotein + beta-HCG
- E. LDH + ESR

Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

Question 102 of 116

A 34-year-old man who is known to have type 1 von Willebrand's disease asks for advice. He is due to have a tooth extracted at the dentist next week. Which one of the following is the most appropriate management to reduce the risk of bleeding?

- A. Mefanamic acid
- B. Vitamin K
- C. Desmopressin
- D. Factor VIII concentrate
- E. Factor VII concentrate

Question 102 of 116

A 34-year-old man who is known to have type 1 von Willebrand's disease asks for advice. He is due to have a tooth extracted at the dentist next week. Which one of the following is the most appropriate management to reduce the risk of bleeding?

- A. Mefanamic acid
- B. Vitamin K
- C. Desmopressin
- D. Factor VIII concentrate
- E. Factor VII concentrate

Blood products such as factor VIII concentrate should be avoided when possible to minimise the risk of transfusion acquired viral illnesses.

Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemoarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types

- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Question 103 of 116

A 67-year-old woman is diagnosed with multiple myeloma. Which one of the following complications is she most likely to develop as a result of her primary diagnosis?

- A. Renal failure
- B. Venous thromboembolism
- C. Hypercalcaemia
- D. Carpal tunnel syndrome
- E. Pathological fracture

Question 103 of 116

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- B. Venous thromboembolism
- C. Hypercalcaemia
- D. Carpal tunnel syndrome
- E. Pathological fracture

This is a difficult question as all of the above may be seen with myeloma. However, up to 60% of patients will develop a pathological fracture.

Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

Clinical features
- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:
- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

Hypercalcaemia in myeloma
- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Question 104 of 116

Patients with Sjogren's syndrome are at an increased risk of which one of the following malignancies?

- A. Myeloma
- B. Oesophageal cancer
- C. Intraocular melanoma
- D. Squamous cell skin cancer
- E. Non-Hodgkin's lymphoma

Question 104 of 116

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- D. Squamous cell skin cancer
- E. Non-Hodgkin's lymphoma

Patients with Sjogren's syndrome have an increased risk of lymphoid malignancies

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features
- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation
- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management
- artificial saliva and tears
- pilocarpine may stimulate saliva production

Question 105 of 116

A 48-year-old man is diagnosed with acute myeloid leukaemia and cytogenics are performed. Which one of the following is associated most with a poor prognosis?

- A. Deletions of chromosome 5
- B. Translocation between chromosome 15 and 17
- C. Deletions of chromosome 15
- D. Translocation between chromosome 9 and 14
- E. Deletions of chromosome 8

Question 105 of 116

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- B. Translocation between chromosome 15 and 17
- C. Deletions of chromosome 15
- D. Translocation between chromosome 9 and 14
- E. Deletions of chromosome 8

Acute myeloid leukaemia - poor prognosis: deletion of chromosome 5 or 7

Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features
- > 60 years
- > 20% blasts after first course of chemo
- cytogenics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3
- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)
- MO - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

Question 106 of 116

A 77-year-old man with a history of chronic lymphocytic leukaemia is admitted to the Acute Medical Unit with pneumonia. This is his fourth admission for pneumonia in the past six months. Which one of the following factors is most likely to be responsible?

- A. Hypersplenism
- B. Decreased lymphocyte survival
- C. Hypogammaglobulinaemia
- D. Transformation to high-grade lymphoma
- E. Immature lymphocytes

Question 106 of 116

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- C. Hypogammaglobulinaemia
- D. Transformation to high-grade lymphoma
- E. Immature lymphocytes

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications
- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations
- blood film: smudge cells
- immunophenotyping

Question 107 of 116

A patient with metastatic cancer asks to be switched from MST 90 mg bd to fentanyl patches. What is the equivalent number of patches which should be applied?

- A. Half a fentanyl '25' patch
- B. One fentanyl '25' patch
- C. One fentanyl '50' patch
- D. One fentanyl '75' patch
- E. One fentanyl '100' patch

Question 107 of 116

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- D. One fentanyl '75' patch
- E. One fentanyl '100' patch

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 108 of 116

Which one of the following is associated with a high leucocyte alkaline phosphatase score?

- A. Myelofibrosis
- B. Pernicious anaemia
- C. Infectious mononucleosis
- D. Paroxysmal nocturnal haemoglobinuria
- E. Chronic myeloid leukaemia

Question 108 of 116

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Leucocyte alkaline phosphatase

Raised in
- myelofibrosis
- leukaemoid reactions
- polycythaemia rubra vera
- infections
- steroids, Cushing's syndrome
- pregnancy, oral contraceptive pill

Low in
- chronic myeloid leukaemia
- pernicious anaemia
- paroxysmal nocturnal haemoglobinuria
- infectious mononucleosis

uestion 109 of 116

Which one of the following features is least associated with Waldenstrom's macroglobulinaemia?

- A. Cryoglobulinaemia
- B. Bone pain
- C. Retinal vein thrombosis
- D. Hepatosplenomegaly
- E. Monoclonal IgM paraproteinaemia

Question 109 of 116

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- C. Retinal vein thrombosis
- D. Hepatosplenomegaly
- E. Monoclonal IgM paraproteinaemia

Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

Features

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Question 110 of 116

A 17-year-old male is diagnosed with alpha-thalassaemia. What chromosome is the alpha-globulin genes located on?

- A. Chromosome 4
- B. Chromosome 8
- C. Chromosome 12
- D. Chromosome 16
- E. Chromosome 20

Question 110 of 116

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- B. Chromosome 8
- C. Chromosome 12
- D. Chromosome 16
- E. Chromosome 20

Alpha-thalassaemia

Alpha-thalassaemia is due to a deficiency of alpha chains in haemoglobin

Overview
- 2 separate alpha-globulin genes are located on each chromosome 16

Clinical severity depends on the number of alpha chains present

If 1 or 2 alpha chains are absent then the blood picture would be hypochromic and microcytic, but the Hb level would be typically normal

Loss of 3 alpha chains results in a hypochromic microcytic anaemia with splenomegaly. This is known as Hb H disease

If all 4 alpha chains absent (i.e. homozygote) then death in utero (hydrops fetalis, Bart's hydrops)

Question 111 of 116

A 71-year-old woman with metastatic breast cancer comes to surgery with her husband. She is known to have spinal metastases but her back pain is not controlled with a combination of paracetamol, diclofenac and MST 30mg bd. Her husband reports she is using 10mg of oral morphine solution around 6-7 times a day for breakthrough pain. The palliative care team at the hospice tried using a bisphosphonate but this unfortunately resulted in persistent myalgia and arthralgia. What is the most appropriate next step?

- A. Switch to oxycodone
- B. Increase MST
- C. Increase MST + add dexamethasone
- D. Increase MST + suggest course of complimentary therapies
- E. Increase MST + refer for radiotherapy

Question 111 of 116

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Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Palliative care prescribing: pain

SIGN issued guidance on the control of pain in adults with cancer in 2008.

Selected points
- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Question 112 of 116

Interferon alpha is a recognised treatment for which one of the following haematological disorders?

- A. Acute lymphoblastic leukaemia
- B. Myelofibrosis
- C. Burkitt's lymphoma
- D. Hairy cell leukaemia
- E. Acute myeloid leukaemia

Question 112 of 116

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Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha is produced by leucocytes and has an antiviral action. It has been shown to be useful in the management of hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer and hairy cell leukaemia

Hairy cell leukaemia

Hairy cell leukaemia is a rare malignant proliferation disorder of B cells. It is more common in males (4:1)

Features

- pancytopenia
- splenomegaly
- skin vasculitis in 1/3 patients
- 'dry tap' despite bone marrow hypercellularity
- tartrate resistant acid phosphotase (TRAP) stain positive

Management

- chemotherapy is first-line: cladribine, pentostatin
- immunotherapy is second-line: rituximab, interferon-alpha

Question 113 of 116

A 72-year-old woman is admitted with confusion and pallor. Her daughter reports that she has been getting more confused are tired for the past three months. Blood tests are reported as follows:

Hb 8.9 g/dl

MCV 125 fl

Plt 148 * 10^9/l

WBC 4.4 * 10^9/l

In light of the macrocytic anaemia some further tests are ordered:

Intrinsic factor antibodies	Negative
Vitamin B12	94 ng/l (200-900 ng/l)
Folic acid	1.1 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- A. Oral folic acid + blood transfusion
- B. Oral folic acid + start Intramuscular vitamin B12 when folic acid levels are normal
- C. Intramuscular vitamin B12 + start oral folic acid when vitamin B12 levels are normal
- D. Blood transfusion
- E. Oral prednisolone

Question 113 of 116

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- C. Intramuscular vitamin B12 + start oral folic acid when vitamin B12 levels are normal
- D. Blood transfusion
- E. Oral prednisolone

It is important in a patient who is also deficient in both vitamin B12 and folic acid to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

Macrocytic anaemia

Macrocytic anaemia can be divided into causes associated with a megaloblastic bone marrow and those with a normoblastic bone marrow

Megaloblastic causes	Normoblastic causes
• vitamin B12 deficiency • folate deficiency • cytotoxics e.g. hydroxyurea	• alcohol • liver disease • hypothyroidism • pregnancy • reticulocytosis e.g. haemolysis • aplastic anaemia • myelodysplasia • drugs: cytotoxics

Question 114 of 116

A 4-year-old girl with sickle cell anaemia presents with abdominal pain. On examination she is noted to have splenomegaly and is clinically anaemic. What is the most likely diagnosis?

- A. Liver cirrhosis
- B. Parvovirus infection
- C. Sequestration crisis
- D. *Salmonella* infection
- E. Thrombotic crisis

Question 114 of 116

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Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:
- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

Thrombotic crises
- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain

Sequestration crises
- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO2 - the most common cause of death after childhood

Aplastic crises
- caused by infection with parvovirus
- sudden fall in haemoglobin

Haemolytic crises
- rare
- fall in haemoglobin due an increased rate of haemolysis

Question 115 of 116

A women who is about to commence trastuzumab treatment for breast cancer has an echocardiogram. Which class of chemotherapeutic agent would predispose her to developing cardiac dysfunction?

- A. Vinca alkaloids
- B. Platinium-based compounds
- C. Anthracyclines
- D. Taxanes
- E. Topoisomerase inhibitors

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Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Question 116 of 116

Each one of the following is associated with polycythaemia rubra vera, except:

- A. Splenomegaly
- B. Hyperviscosity
- C. Raised ESR
- D. Hypertension
- E. Pruritus

Question 116 of 116

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B. Hyperviscosity

C. Raised ESR

D. Hypertension

E. Pruritus

Polycythaemia rubra vera is associated with a low ESR

Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

Features

- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphotase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count >450 * 10^9/l)
B2	Neutrophil leucocytosis (neutrophil count > 10 * 10^9/l in non-smokers; > 12.5*10^9/l in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Question 1 of 117

A 30-year-old female in her third trimester of pregnancy mentions during an antenatal appointment that she has noticed an itchy rash around her umbilicus. This is her second pregnancy and she had no similar problems in her first pregnancy. Examination reveals blistering lesions in the peri-umbilical region and on her arms. What is the likely diagnosis?

- A. Seborrhoeic dermatitis
- B. Pompholyx
- C. Polymorphic eruption of pregnancy
- D. Lichen planus
- E. Pemphigoid gestationis

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- D. Lichen planus
- E. Pemphigoid gestationis

Polymorphic eruption of pregnancy is not associated with blistering

Pemphigoid gestationis is the correct answer. Polymorphic eruption of pregnancy is not associated with blistering

Skin disorders associated with pregnancy

Polymorphic eruption of pregnancy
- pruritic condition associated with last trimester
- lesions often first appear in abdominal striae
- management depends on severity: emollients, mild potency topical steroids and oral steroids may be used

Pemphigoid gestationis
- pruritic blistering lesions
- often develop in peri-umbilical region, later spreading to the trunk, back, buttocks and arms
- usually presents 2nd or 3rd trimester and is rarely seen in the first pregnancy
- oral corticosteroids are usually required

Question 2 of 117

A 62-year-old female is referred to dermatology due to a lesion over her shin. It initially started as a small red papule which later became a deep, red, necrotic ulcers with a violaceous border. What is the likely diagnosis?

- A. Necrobiosis lipoidica diabeticorum
- B. Syphilis
- C. Erythema nodosum
- D. Pretibial myxoedema
- E. Pyoderma gangrenosum

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- E. Pyoderma gangrenosum

This is a classic description of pyoderma gangrenosum

Shin lesions

The differential diagnosis of shin lesions includes the following conditions:
- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum
- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema
- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum
- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 3 of 117

A 19-year-old student presents with a three day history of a 1 cm golden, crusted lesion on the border of her lower lip. What is the most suitable management?

- A. Oral co-amoxiclav
- B. Oral penicillin
- C. Oral flucloxacillin
- D. Oral flucloxacillin + penicillin
- E. Topical fusidic acid

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Impetigo - topical fusidic acid --> oral flucloxacillin / topical retapamulin

This history is typical of impetigo. As the lesion is small and localised topical fusidic acid is recommended

Impetigo: management

Limited, localised disease
- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease
- oral flucloxacillin
- oral erythromycin if penicillin allergic

Question 4 of 117

A 22-year-old woman presents due to hypopigmented skin lesions on her chest and back. She has recently returned from the south of France and has tanned skin. On examination the lesions are slightly scaly. What is the most likely diagnosis?

- A. Tinea corporis
- B. Pityriasis versicolor
- C. Porphyria cutanea tarda
- D. Lyme disease
- E. Psoriasis

Question 4 of 117

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- C. Porphyria cutanea tarda
- D. Lyme disease
- E. Psoriasis

Pityriasis versicolor

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by Malassezia furfur (formerly termed Pityrosporum ovale)

Features
- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

Predisposing factors
- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

Management
- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

Question 5 of 117

A 28-year-old man presents with multiple protuberant lesions around the anus which have been present for about 6 weeks. He reports it is painful when he passes a stool although there is no change in bowel habit. What is the most likely diagnosis?

- A. Haemorrhoids
- B. Anal cancer
- C. Genital warts
- D. Anal skin tags
- E. Crohn's disease

Question 5 of 117

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- D. Anal skin tags
- E. Crohn's disease

Ambiguous questions such as this are common in the MRCP. Whilst a case could be made for any of the answers the most likely cause from the above list, in a 28-year-old male, is genital warts

Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

Features
- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

Management
- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment are recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Question 6 of 117

A 74-year-old lady with a history of hypothyroidism presents in January with a rash down the right side of her body. On examination an erythematous rash with patches of hyperpigmentation and telangiectasia is found. What is the likely diagnosis?

- A. Erythema marginatum
- B. Herpes zoster
- C. Pretibial myxoedema
- D. Erythema ab igne
- E. Xanthomata

Question 6 of 117

A 74-year-old lady with a history of hypothyroidism presents in January with a rash down the right side of her body. On examination an erythematous rash with patches of hyperpigmentation and telangiectasia is found. What is the likely diagnosis?

- A. Erythema marginatum
- B. Herpes zoster
- C. Pretibial myxoedema
- D. Erythema ab igne
- E. Xanthomata

This is a classic presentation of erythema ab igne. Despite the name, pretibial myxoedema is associated with hyperthyroidism rather than hypothyroidism.

Hypothyroidism can make patients feel cold and hence more likely to sit next a heater / fire.

Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

Question 7 of 117

A 39-year-old female has a pigmented mole removed from her leg which histology shows to be a malignant melanoma. What is the single most important prognostic marker?

- A. Number of episodes of sunburn before the age of 18 years
- B. Age of patient
- C. Diameter of melanoma
- D. Depth of melanoma
- E. Mutation in the MC1R gene

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Melanoma: the invasion depth of the tumour is the single most important prognostic factor

Malignant melanoma: prognostic factors

The invasion depth of a tumour (Breslow depth) is the single most important factor in determining prognosis of patients with malignant melanoma

Breslow Thickness	Approximate 5 year survival
< 1 mm	95-100%
1 - 2 mm	80-96%
2.1 - 4 mm	60-75%
> 4 mm	50%

Question 8 of 117

A 67-year-old man with a history of Parkinson's disease presents due to the development of an itchy, red rash on his neck, behind his ears and around the nasolabial folds. He had a similar flare up last winter but did not seek medical attention. What is the most likely diagnosis?

- A. Levodopa associated dermatitis
- B. Seborrhoeic dermatitis
- C. Flexural psoriasis
- D. Acne rosacea
- E. Fixed drug reaction to ropinirole

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- E. Fixed drug reaction to ropinirole

Seborrhoeic dermatitis is more common in patients with Parkinson's disease

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short perio

Question 9 of 117

A 62-year-old female is referred due to a long-standing ulcer above the right medial malleolus. Ankle-brachial pressure index readings are as follows:

Right 0.95

Left 0.95

To date it has been managed by the District Nurse with standard dressings. What is the most appropriate management to maximize the likelihood of the ulcer healing?

- A. Compression bandaging
- B. Intermittent pneumatic compression
- C. Hydrocolloid dressings
- D. Refer to vascular surgeon
- E. Topical flucloxacillin

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Management of venous ulceration - compression bandaging

The ankle-brachial pressure index readings indicate a reasonable arterial supply and suggest the ulcers are venous in nature.

Venous ulceration

Venous ulceration is typically seen above the medial malleolus

Investigations

- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

Management

- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

Question 10 of 117

A 43-year-old man comes for review. A few months ago he developed redness around his nose and cheeks. This is worse after drinking alcohol. He is concerned as one of his work colleagues asked him if he had a drink problem despite him drinking 14 units per week. On examination he has erythema as described above with some pustules on the nose and telangiectasia on the cheeks. What is the most likely diagnosis?

- A. Mitral stenosis
- B. Seborrhoeic dermatitis
- C. Alcohol-related skin changes
- D. Acne rosacea
- E. Systemic lupus erythematosus

Question 10 of 117

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- C. Alcohol-related skin changes
- D. Acne rosacea
- E. Systemic lupus erythematosus

This is a typical history of acne rosacea

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 11 of 117

A 25-year-old man presents with a widespread rash over his body. The torso and limbs are covered with multiple erythematous lesions less than 1 cm in diameter which in parts are covered by a fine scale. You note that two weeks earlier he was seen with to a sore throat when it was noted that he had exudative tonsillitis. Other than a history of asthma he is normally fit and well. What is the most likely diagnosis?

- A. Pityriasis Rosea
- B. Pityriasis versicolor
- C. Syphilis
- D. Discoid eczema
- E. Guttate psoriasis

Question 11 of 117

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- E. Guttate psoriasis

Psoriasis: guttate

Guttate psoriasis is more common in children and adolescents. It may be precipitated by a streptococcal infection 2-4 weeks prior to the lesions appearing

Features
- tear drop papules on the trunk and limbs

Management
- most cases resolve spontaneously within 2-3 months
- there is no firm evidence to support the use of antibiotics to eradicate streptococcal infection
- topical agents as per psoriasis
- UVB phototherapy
- tonsillectomy may be necessary with recurrent episodes

Question 12 of 117

A 64-year-old patient is referred to dermatology outpatients due to a rash. A diagnosis necrolytic migratory erythema of is made. What is the most likely underlying diagnosis?

- A. Gastrinoma
- B. Lung cancer
- C. Glucagonoma
- D. Pancreatic cancer
- E. Lymphoma

Question 12 of 117

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- B. Lung cancer
- C. Glucagonoma
- D. Pancreatic cancer
- E. Lymphoma

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 13 of 117

A 54-year-old man presents with a brown velvety rash on the back of his neck around his axilla. A clinical diagnosis of acanthosis nigricans is made. Which one of the following conditions is most associated with this kind of rash?

- A. Hypothyroidism
- B. Psoriasis
- C. Tuberculosis
- D. Ulcerative colitis
- E. Acute pancreatitis

Question 13 of 117

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- C. Tuberculosis
- D. Ulcerative colitis
- E. Acute pancreatitis

Acanthosis nigricans

Describes symmetrical, brown, velvety plaques that are often found on the neck, axilla and groin

Causes

- internal malignancy (esp. gastrointestinal)
- insulin-resistant diabetes mellitus
- obesity
- acromegaly
- Cushing's disease
- hypothyroidism
- polycystic ovarian syndrome
- familial
- Prader-Willi syndrome
- drugs: oral contraceptive pill, nicotinic acid

Question 14 of 117

A 34-year-old man presents for the removal of a mole. Where on the body are keloid scars most likely to form?

- A. Sternum
- B. Lower back
- C. Abdomen
- D. Flexor surfaces of limbs
- E. Scalp

Question 14 of 117

A 34-year-old man presents for the removal of a mole. Where on the body are keloid scars most likely to form?

- A. Sternum
- B. Lower back
- C. Abdomen
- D. Flexor surfaces of limbs
- E. Scalp

Keloid scars are most common on the sternum

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 15 of 117

A 67-year-old man who is a retired builder presents following the development of a number of red, scaly lesions on his left temple. These were initially small and flat but are now erythematous and rough to touch. What is the most likely diagnosis?

- A. Pityriasis versicolor
- B. Seborrhoeic keratosis
- C. Polymorphous light eruption
- D. Actinic keratoses
- E. Malignant melanoma

Question 15 of 117

A 67-year-old man who is a retired builder presents following the development of a number of red, scaly lesions on his left temple. These were initially small and flat but are now erythematous and rough to touch. What is the most likely diagnosis?

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- C. Polymorphous light eruption
- D. Actinic keratoses
- E. Malignant melanoma

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 16 of 117

A 34-year-old man presents to dermatology clinic with an itchy rash on his palms. He has also noticed the rash around the site of a recent scar on his forearm. Examination reveals papules with a white-lace pattern on the surface. Some isolated white streaks are also noted on the mucous membranes of the mouth. What is the diagnosis?

- A. Lichen planus
- B. Scabies
- C. Lichen sclerosus
- D. Morphea
- E. Pityriasis rosea

Question 16 of 117

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- C. Lichen sclerosus
- D. Morphea
- E. Pityriasis rosea

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

This is a typical history of lichen planus.

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 17 of 117

A 55-year-old female is referred to dermatology due to a lesions over both shins. On examination symmetrical erythematous lesions are found with an orange peel texture. What is the likely diagnosis?

- A. Pretibial myxoedema
- B. Pyoderma gangrenosum
- C. Necrobiosis lipoidica diabeticorum
- D. Erythema nodosum
- E. Syphilis

Question 17 of 117

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- D. Erythema nodosum
- E. Syphilis

Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 18 of 117

Which of the following skin conditions is not associated with diabetes mellitus?

- A. Necrobiosis lipoidica
- B. Sweet's syndrome
- C. Granuloma annulare
- D. Vitiligo
- E. Lipoatrophy

Question 18 of 117

Which of the following skin conditions is not associated with diabetes mellitus?

- A. Necrobiosis lipoidica
- B. Sweet's syndrome
- C. Granuloma annulare
- D. Vitiligo
- E. Lipoatrophy

Sweet's syndrome is also known as acute febrile neutrophilic dermatosis has a strong association with acute myeloid leukaemia. It is not associated with diabetes mellitus

Skin disorders associated with diabetes

Note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is often not included in a differential of potential causes

Necrobiosis lipoidica
- shiny, painless areas of yellow/red/brown skin typically on the shin
- often associated with surrounding telangiectasia

Infection
- candidiasis
- staphylococcal

Neuropathic ulcers

Vitiligo

Lipoatrophy

Granuloma annulare*
- papular lesions that are often slightly hyperpigmented and depressed centrally

*it is not clear from recent studies if there is actually a significant association between diabetes mellitus and granuloma annulare, but it is often listed in major textbooks

Question 19 of 117

A 38-year-old woman with a history of rheumatoid arthritis and epilepsy presents with generalised increased hair growth over her trunk and arms. Which one of the following drugs is associated with hypertrichosis?

- A. Sodium valproate
- B. Prednisolone
- C. Phenytoin
- D. Ciclosporin
- E. Methotrexate

Question 19 of 117

A 38-year-old woman with a history of rheumatoid arthritis and epilepsy presents with generalised increased hair growth over her trunk and arms. Which one of the following drugs is associated with hypertrichosis?

- A. Sodium valproate
- B. Prednisolone
- C. Phenytoin
- D. Ciclosporin
- E. Methotrexate

Phenytoin is associated with hirsuitism rather than hypertrichosis

Hirsuitism and hypertrichosis

Hirsuitism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Causes of hirsuitism

- polycystic ovarian syndrome
- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

Causes of hypertrichosis

- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa

Question 20 of 117

A 23-year-old man presents with a three day history of general malaise and low-grade temperature. Yesterday he developed extensive painful ulceration of his mouth and gums. On examination his temperature is 37.4ºC, pulse 84 / min and there is submandibular lymphadenopathy. What is the most likely diagnosis?

- A. Epstein Barr virus
- B. Lichen planus
- C. HIV seroconversion illness
- D. Herpes simplex virus infection
- E. Oral *Candida*

Question 20 of 117

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- B. Lichen planus
- C. HIV seroconversion illness
- D. Herpes simplex virus infection
- E. Oral *Candida*

This man has gingivostomatitis, a characteristic feature of primary herpes simplex virus infection

Herpes simplex virus

There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

Features

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

Question 21 of 117

A 54-year-old man is referred to the dermatology outpatient department due to a facial rash which has persisted for the past 12 months. On examination there is a symmetrical rash consisting of extensive pustules and papules which affects his nose, cheeks and forehead. What is the most appropriate treatment?

- A. Ciprofloxacin
- B. Isotretinoin
- C. Oxytetracycline
- D. Hydroxychloroquine
- E. Prednisolone

Question 21 of 117

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- B. Isotretinoin
- C. Oxytetracycline
- D. Hydroxychloroquine
- E. Prednisolone

As there is extensive involvement oral oxytetracycline should probably be used rather than topical metronidazole

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 22 of 117

A 31-year-old woman develops with painful, purple lesions on her shins. Which one of the following medications is most likely to be responsible?

- A. Montelukast
- B. Lansoprazole
- C. Combined oral contraceptive pill
- D. Sodium valproate
- E. Carbimazole

Question 22 of 117

A 31-year-old woman develops with painful, purple lesions on her shins. Which one of the following medications is most likely to be responsible?

- A. Montelukast
- B. Lansoprazole
- C. Combined oral contraceptive pill
- D. Sodium valproate
- E. Carbimazole

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 23 of 117

Which one of the following conditions is most strongly associated with erythema multiforme?

- A. Crohn's disease
- B. Tuberculosis
- C. Sarcoidosis
- D. Herpes simplex virus
- E. Streptococcal infections

Question 23 of 117

Which one of the following conditions is most strongly associated with erythema multiforme?

- A. Crohn's disease
- B. Tuberculosis
- C. Sarcoidosis
- D. Herpes simplex virus
- E. Streptococcal infections

This is difficult as both herpes simplex and streptococcal infections are known causes of erythema multiforme (EM). However, studies suggest that HSV is the trigger in over 50% of cases. Streptococcal infections and sarcoidosis are more strongly associated with erythema nodosum

Erythema multiforme

Erythema multiforme
- target lesions (typically worse on peripheries e.g. palms and soles)
- severe = Stevens-Johnson syndrome (blistering and mucosal involvement)

Causes
- viruses: herpes simplex virus, Orf
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

Question 24 of 117

An 18-year-old female is reviewed in the dermatology clinic complaining of scalp hair loss. Which one of the following conditions is least likely to be responsible?

- A. Porphyria cutanea tarda
- B. Discoid lupus
- C. Tinea capitis
- D. Alopecia areata
- E. Telogen effluvium

Question 24 of 117

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- B. Discoid lupus
- C. Tinea capitis
- D. Alopecia areata
- E. Telogen effluvium

Porphyria cutanea tarda is a recognised cause of hypertrichosis

Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

Scarring alopecia
- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis*

Non-scarring alopecia
- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

*scarring would develop in untreated tinea capitis if a kerion develops

Question 25 of 117

Which of the following conditions is most associated with onycholysis?

- A. Bullous pemphigoid
- B. Raynaud's disease
- C. Osteogenesis imperfecta
- D. Oesophageal cancer
- E. Scabies

Question 25 of 117

Which of the following conditions is most associated with onycholysis?

- A. Bullous pemphigoid
- B. Raynaud's disease
- C. Osteogenesis imperfecta
- D. Oesophageal cancer
- E. Scabies

Raynaud's disease causes onycholysis, as can any cause of impaired circulation

Onycholysis

Onycholysis describes the separation of the nail plate from the nail bed

Causes

- idiopathic
- trauma e.g. excessive manicuring
- infection: especially fungal
- skin disease: psoriasis, dermatitis
- impaired peripheral circulation e.g. Raynaud's
- systemic disease: hyper- and hypothyroidism

Question 26 of 117

A 85-year-old lady presents to dermatology clinic complaining of itchy white plaques affecting her vulva. There is no history of vaginal discharge or bleeding. A similar plaque is also seen on her inner thigh. What is the likely diagnosis?

- A. *Candida*
- B. Lichen planus
- C. Lichen sclerosus
- D. Herpes simplex
- E. Seborrhoeic dermatitis

Question 26 of 117

A 85-year-old lady presents to dermatology clinic complaining of itchy white plaques affecting her vulva. There is no history of vaginal discharge or bleeding. A similar plaque is also seen on her inner thigh. What is the likely diagnosis?

- A. *Candida*
- B. Lichen planus
- C. Lichen sclerosus
- D. Herpes simplex
- E. Seborrhoeic dermatitis

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

The correct answer is lichen sclerosus. *Candida* may cause pruritus and white plaques but lesions would not also be seen on her inner thigh

Lichen sclerosus

Lichen sclerosus was previously termed lichen sclerosus et atrophicus. It is an inflammatory condition which usually affects the genitalia and is more common in elderly females. Lichen sclerosus leads to atrophy of the epidermis with white plaques forming

Features
- itch is prominent

A biopsy is often performed to exclude other diagnoses

Management
- topical steroids and emollients
- increased risk of vulval cancer

Question 27 of 117

A 43-year-old man is admitted to the Emergency Department with a rash and feeling generally unwell. He is known to have epilepsy and his medication was recently changed to phenytoin three weeks ago. Around one week ago he started to develop mouth ulcers associated with malaise and a cough. Two days ago he started to develop a widespread red rash which has now coalesced to form large fluid-filled blisters, covering around 30% of his body area. The lesions separate when slight pressure is applied. On examination his temperature is 38.3ºC and pulse 126 / min. Blood results show:

Na^+	144 mmol/l
K^+	4.2 mmol/l
Bicarbonate	19 mmol/l
Urea	13.4 mmol/l
Creatinine	121 µmol/l

What is the most likely diagnosis?

- A. Phenytoin-induced neutropaenia
- B. Drug-induced lupus
- C. Kawasaki disease
- D. Toxic epidermal necrolysis
- E. Staphylococcal Scalded Skin syndrome

Question 27 of 117

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- B. Drug-induced lupus
- C. Kawasaki disease
- D. Toxic epidermal necrolysis
- E. Staphylococcal Scalded Skin syndrome

Toxic epidermal necrolysis

Toxic epidermal necrolysis (TEN) is a potentially life-threatening skin disorder that is most commonly seen secondary to a drug reaction. In this condition the skin develops a scalded appearance over an extensive area. Some authors consider TEN to be the severe end of a spectrum of skin disorders which includes erythema multiforme and Stevens-Johnson syndrome

Features
- systemically unwell e.g. pyrexia, tachycardic
- positive Nikolsky's sign: the epidermis separates with mild lateral pressure

Drugs known to induce TEN
- phenytoin
- sulphonamides
- allopurinol
- penicillins
- carbamazepine
- NSAIDs

Management
- stop precipitating factor
- supportive care, often in intensive care unit
- intravenous immunoglobulin has been shown to be effective and is now commonly used first-line
- other treatment options include: immunosuppressive agents (ciclosporin and cyclophosphamide), plasmapheresis

Question 28 of 117

Which one of the following complications is most associated with psoralen + ultraviolet A light (PUVA) therapy?

- A. Squamous cell cancer
- B. Osteoporosis
- C. Basal cell cancer
- D. Dermoid cysts
- E. Malignant melanoma

Question 28 of 117

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- E. Malignant melanoma

The most significant complication of PUVA therapy for psoriasis is squamous cell skin cancer.

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 29 of 117

Which one of the following conditions is least likely to be associated with pyoderma gangrenosum?

- A. Ulcerative colitis
- B. Syphilis
- C. Lymphoma
- D. IgA monoclonal gammopathy
- E. Rheumatoid arthritis

Question 29 of 117

Which one of the following conditions is least likely to be associated with pyoderma gangrenosum?

- A. Ulcerative colitis
- B. Syphilis
- C. Lymphoma
- D. IgA monoclonal gammopathy
- E. Rheumatoid arthritis

Syphilis is not commonly associated with pyoderma gangrenosum

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 30 of 117

A 26-year-old newly qualified nurse presents as she has developed a bilateral erythematous rash on both hands. She has recently emigrated from the Philippines and has no past medical history of note. A diagnosis of contact dermatitis is suspected. What is the most suitable to test to identify the underlying cause?

- A. Radioallergosorbent test (RAST)
- B. Latex IgM levels
- C. Skin prick test
- D. Urinary porphyrins
- E. Skin patch test

Question 30 of 117

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- C. Skin prick test
- D. Urinary porphyrins
- E. Skin patch test

The skin patch test is useful in this situation as it may also identify for irritants, not just allergens

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 31 of 117

A 36-year-old woman is reviewed. She presented 4 weeks ago with itchy dry skin on her arms and was diagnosed as having atopic eczema. She was prescribed hydrocortisone 1% cream with an emollient. Unfortunately there has been no improvement in her symptoms. What is the next step in management, alongside continued regular use of an emollient?

- A. Betamethasone valerate 0.1%
- B. Clobetasone butyrate 0.05%
- C. Clobetasol propionate 0.05%
- D. Topical tetracycline
- E. Regular wet wraps

Question 31 of 117

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- C. Clobetasol propionate 0.05%
- D. Topical tetracycline
- E. Regular wet wraps

Topical steroids
- moderate: Clobetasone butyrate 0.05%
- potent: Betamethasone valerate 0.1%
- very potent: Clobetasol propionate 0.05%

Clobetasone butyrate 0.05% is a moderately potent topical steroid and would be the most suitable next step in management. It is important to note the potency difference between two very similar sounding steroids - Clobetasone butyrate 0.05% (moderate) and Clobetasol propionate 0.05% (very potent)

Eczema: topical steroids

Use weakest steroid cream which controls patients symptoms

The table below shows topical steroids by potency

Mild	Moderate	Potent	Very potent
Hydrocortisone 0.5-2.5%	Betamethasone valerate 0.025% (Betnovate RD) Clobetasone butyrate 0.05% (Eumovate)	Fluticasone propionate 0.05% (Cutivate) Betamethasone valerate 0.1% (Betnovate)	Clobetasol propionate 0.05% (Dermovate)

Finger tip rule
- 1 finger tip unit (FTU) = 0.5 g, sufficient to treat a skin area about twice that of the flat of an adult hand

Topical steroid doses for eczema in adults

Area of skin	Fingertip units per dose
Hand and fingers (front and back)	1.0
A foot (all over)	2.0
Front of chest and abdomen	7.0
Back and buttocks	7.0
Face and neck	2.5
An entire arm and hand	4.0
An entire leg and foot	8.0

Question 32 of 117

A 54-year-old woman with a history of type 1 diabetes mellitus presents with unsightly toenails affecting the lateral three nails of the left foot. On examination the nails and brown and break easily. Nail scrapings demonstrate Trichophyton rubrum infection. What is the treatment of choice?

- A. Oral terbinafine for 12 weeks
- B. Oral itraconazole for 4 weeks
- C. Topical itraconazole for 2 weeks
- D. Topical amorolfine for 6 weeks
- E. Oral itraconazole for 1 weeks

Question 32 of 117

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Dermatophyte nail infections - use oral terbinafine

Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by

- dermatophytes - mainly Trichophyton rubrum, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

Features

- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

Investigation

- nail clippings
- scrapings of the affected nail

Management

- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

Question 33 of 117

A 34-year-old man presents with a three week history of an intensely itchy rash on the back of his elbows. On examination he has a symmetrical vesicular rash on the extensor aspects of his arms. Which one of the following antibodies is most likely to be positive?

- A. Anti-mitochondrial antibody
- B. Anti-gliadin antibody
- C. Anti-nuclear antibody
- D. Anti-neutrophil cytoplasmic antibody
- E. Anti-Jo-1 antibody

Question 33 of 117

A 34-year-old man presents with a three week history of an intensely itchy rash on the back of his elbows. On examination he has a symmetrical vesicular rash on the extensor aspects of his arms. Which one of the following antibodies is most likely to be positive?

- A. Anti-mitochondrial antibody
- B. Anti-gliadin antibody
- C. Anti-nuclear antibody
- D. Anti-neutrophil cytoplasmic antibody
- E. Anti-Jo-1 antibody

Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

Features
- itchy, vesicular skin lesions on the extensor surfaces (e.g. Elbows, knees buttocks)

Diagnosis
- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

Management
- gluten-free diet
- dapsone

Question 34 of 117

You review a 50-year-old man who has psoriasis. Which one of the following medications is most likely exacerbate his condition?

- A. Nicorandil
- B. Simvastatin
- C. Verapamil
- D. Atenolol
- E. Isosorbide mononitrate

Question 34 of 117

You review a 50-year-old man who has psoriasis. Which one of the following medications is most likely exacerbate his condition?

- A. Nicorandil
- B. Simvastatin
- C. Verapamil
- D. Atenolol
- E. Isosorbide mononitrate

Psoriasis: exacerbating factors

The following factors may exacerbate psoriasis:

- trauma
- alcohol
- drugs: beta blockers, lithium, antimalarials (chloroquine and hydroxychloroquine), NSAIDs and ACE inhibitors
- withdrawal of systemic steroids

Question 35 of 117

A 23-year-old man presents with an itchy skin condition. Which one of the following is least relevant when deciding whether a patient has atopic eczema?

- A. History of asthma
- B. Responds to topical steroids
- C. History of flexural involvement
- D. Onset below age 2 years
- E. History of generally dry skin

Question 35 of 117

A 23-year-old man presents with an itchy skin condition. Which one of the following is least relevant when deciding whether a patient has atopic eczema?

- A. History of asthma
- B. Responds to topical steroids
- C. History of flexural involvement
- D. Onset below age 2 years
- E. History of generally dry skin

Whilst response to topical steroids provides useful clinical information it is not part of the diagnostic criteria

Eczema: diagnosis

UK Working Party Diagnostic Criteria for Atopic Eczema

An itchy skin condition in the last 12 months

Plus three or more of
- onset below age 2 years*
- history of flexural involvement**
- history of generally dry skin
- personal history of other atopic disease***
- visible flexural dermatitis

*not used in children under 4 years

**or dermatitis on the cheeks and/or extensor areas in children aged 18 months or under
***in children aged under 4 years, history of atopic disease in a first degree relative may be included

Question 36 of 117

Which of the following skin disorders is least associated with tuberculosis?

- A. Scrofuloderma
- B. Erythema nodosum
- C. Lupus vulgaris
- D. Verrucosa cutis
- E. Lupus pernio

Question 36 of 117

Which of the following skin disorders is least associated with tuberculosis?

- A. Scrofuloderma
- B. Erythema nodosum
- C. Lupus vulgaris
- D. Verrucosa cutis
- E. Lupus pernio

Lupus pernio is sometimes seen in sarcoidosis but is not associated with tuberculosis

Skin disorders associated with TB

Possible skin disorders
- lupus vulgaris (accounts for 50% of cases)
- erythema nodosum
- scarring alopecia
- scrofuloderma: breakdown of skin overlying a tuberculous focus
- verrucosa cutis
- gumma

Lupus vulgaris is the most common form of cutaneous TB seen in the Indian subcontinent. It generally occurs on the face and is common around the nose and mouth. The initial lesion is an erythematous flat plaque which gradually becomes elevated and may ulcerate later

Question 37 of 117

Which of the following statements regarding psoriasis is incorrect?

- A. Often occurs on extensor surfaces
- B. Psoriatic arthropathy may occur prior to the development of skin lesions
- C. Mediated by type 2 helper T cells
- D. Abnormal T cell activity stimulates keratinocyte proliferation
- E. Nail signs include pitting and onycholysis

Question 37 of 117

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- C. Mediated by type 2 helper T cells
- D. Abnormal T cell activity stimulates keratinocyte proliferation
- E. Nail signs include pitting and onycholysis

Psoriasis is mediated by type 1 helper T cells which are involved in the cell mediated response, rather than type 2 helper T cells

Psoriasis

Psoriasis can be divided into type 1 and 2:

Type 1
- presents < 40 years old
- positive family history
- associated with HLA-CW6

Type 2
- presents > 50 years old
- no family history

Cause
- abnormal T cell activity stimulates keratinocyte proliferation (rather than an actual primary keratinocyte disorder)
- mediated by type 1 helper T cells

Features
- red, scaly plaques
- scalp, extensor surfaces elbows/knees, sacrum
- nail signs: pitting, onycholysis
- arthritis

Complications
- psoriatic arthropathy (around 10%)
- psychological distress
- increased incidence of cardiovascular disease

Question 38 of 117

Which one of the following statements regarding acne vulgaris is incorrect?

- A. Follicular epidermal hyperproliferation results in obstruction of the pilosebaceous follicle
- B. Acne vulgaris affects at least 80% of teenagers
- C. Propionibacterium acnes is an anaerobic bacterium
- D. Typical lesions include comedones and pustules
- E. Beyond the age of 25 years acne vulgaris is more common in males

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- C. Propionibacterium acnes is an anaerobic bacterium
- D. Typical lesions include comedones and pustules
- E. Beyond the age of 25 years acne vulgaris is more common in males

Acne is actually more common in females after the age of 25 years

Acne vulgaris

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Epidemiology

- affects around 80-90% of teenagers, 60% of whom seek medical advice
- acne may also persist beyond adolescence, with 10-15% of females and 5% of males over 25 years old being affected

Pathophysiology is multifactorial

- follicular epidermal hyperproliferation resulting in the formation of a keratin plug. This in turn causes obstruction of the pilosebaceous follicle. Activity of sebaceous glands may be controlled by androgen, although levels are often normal in patients with acne
- colonisation by the anaerobic bacterium Propionibacterium acnes
- inflammation

Question 39 of 117

A 81-year-old man is investigated after he develops a number of itchy blisters on his trunk. A skin biopsy suggests a diagnosis bullous pemphigoid. This is most likely to be caused by antibodies directed against:

- A. Adherens
- B. Desmoglein-3
- C. Hemidesmosomal BP antigens
- D. Occludin-2
- E. Desmoglein-1

Question 39 of 117

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- B. Desmoglein-3
- C. Hemidesmosomal BP antigens
- D. Occludin-2
- E. Desmoglein-1

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 40 of 117

A 62-year-old male is referred to dermatology with a lesion over his shin. On examination shiny, painless areas of yellow skin over the shin are found with abundant telangiectasia. What is the most likely diagnosis?

- A. Pretibial myxoedema
- B. Necrobiosis lipoidica diabeticorum
- C. Erythema nodosum
- D. Pyoderma gangrenosum
- E. Syphilis

Question 40 of 117

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Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabeticorum

Below are the characteristic features:

Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Question 41 of 117

A 17-year-old man presents with a 2 week history of abdominal pain, diarrhoea and repeated episodes of flushing. Examination reveals urticarial skin lesions on the trunk. What test is most likely to reveal the diagnosis?

- A. Chest x-ray
- B. Urinary catecholamines
- C. Serum amylase
- D. Urinary 5-HIAA
- E. Urinary histamine

Question 41 of 117

A 17-year-old man presents with a 2 week history of abdominal pain, diarrhoea and repeated episodes of flushing. Examination reveals urticarial skin lesions on the trunk. What test is most likely to reveal the diagnosis?

- A. Chest x-ray
- B. Urinary catecholamines
- C. Serum amylase
- D. Urinary 5-HIAA
- E. Urinary histamine

Urinary histamine is used to diagnose systemic mastocytosis

Given the history of diarrhoea and flushing a diagnosis of carcinoid syndrome should be considered, which would be investigated with urinary 5-HIAA levels. This would not however explain the urticarial skin lesions. In a young person a diagnosis of systemic mastocytosis should be considered. Another factor against carcinoid syndrome is the age of the patient - the average age of a patient with a carcinoid tumour is 61 years

Systemic mastocytosis

Systemic mastocytosis results from a neoplastic proliferation of mast cells

Features
- urticaria pigmentosa - produces a wheal on rubbing (Darier's sign)
- flushing
- abdominal pain
- monocytosis on the blood film

Diagnosis
- raised serum tryptase levels
- urinary histamine

Question 42 of 117

A 54-year-old man presents with a two month history of a rapidly growing lesion on his right forearm. The lesion initially appeared as a red papule but in the last two weeks has become a crater filled centrally with yellow/brown material. On examination the man has skin type II, the lesion is 4 mm in diameter and is morphologically as described above. What is the most likely diagnosis?

- A. Seborrhoeic keratosis
- B. Keratoacanthoma
- C. Pyoderma gangrenosum
- D. Basal cell carcinoma
- E. Malignant melanoma

Question 42 of 117

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- C. Pyoderma gangrenosum
- D. Basal cell carcinoma
- E. Malignant melanoma

Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

Question 43 of 117

A 62-year-old with a history of acne rosacea presents for advice regarding treatment. Which one of the following interventions has the least role in management?

- A. Camouflage creams
- B. Topical metronidazole
- C. Low-dose topical corticosteroids
- D. Laser therapy
- E. Use of high-factor sun block

Question 43 of 117

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- C. Low-dose topical corticosteroids
- D. Laser therapy
- E. Use of high-factor sun block

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 44 of 117

A 49-year-old man is reviewed in the dermatology clinic complaining of losing hair. Examination reveals generalised scalp hair loss that does not follow the typical male-pattern distribution. Which one of the following medications is least likely to be responsible?

- A. Colchicine
- B. Cyclophosphamide
- C. Heparin
- D. Carbimazole
- E. Phenytoin

Question 44 of 117

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- C. Heparin
- D. Carbimazole
- E. Phenytoin

Phenytoin is a recognised cause of hirsuitism, rather than alopecia

Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

Scarring alopecia
- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis*

Non-scarring alopecia
- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

*scarring would develop in untreated tinea capitis if a kerion develops

Question 45 of 117

A 26-year-old male presents with a rash. Examination reveals erythematous oval lesions on his back and upper arms which have a slight scale just inside the edge. They vary in size from 1 to 5 cm in diameter. What is the most likely diagnosis?

- A. Lichen planus
- B. Guttate psoriasis
- C. Lichen sclerosus
- D. Pityriasis rosea
- E. Pityriasis versicolor

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- C. Lichen sclerosus
- D. Pityriasis rosea
- E. Pityriasis versicolor

The skin lesions seen in pityriasis rosea are generally larger than those found in guttate psoriasis and scaling is typically confined to just inside the edges

Pityriasis rosea

Overview
- cause unknown, herpes hominis virus 7 (HHV-7) a possibility
- tends to affect young adults

Features
- herald patch (usually on trunk)
- followed by erythematous, oval, scaly patches which follow a characteristic distribution with the longitudinal diameters of the oval lesions running parallel to the line of Langer. This may produce a 'fir-tree' appearance

Management
- self-limiting, usually disappears after 4-6 weeks

Question 46 of 117

A 25-year-old male presents with extensive patches of altered pigmentation on his front, back, face and thighs. There is mild pruritus. A diagnosis of extensive pityriasis versicolor is made. What is the most appropriate management?

- A. Oral metronidazole
- B. Topical terbinafine
- C. Oral itraconazole
- D. Topical selenium sulphide
- E. Oral terbinafine

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- C. Oral itraconazole
- D. Topical selenium sulphide
- E. Oral terbinafine

Given the extensive nature of the lesions systemic therapy is indicated in this case

Pityriasis versicolor

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by Malassezia furfur (formerly termed Pityrosporum ovale)

Features
- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

Predisposing factors
- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

Management
- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

Question 47 of 117

A 64-year-old woman presents with severe mucosal ulceration associated with the development of blistering lesions over her torso and arms. On examination the blisters are flaccid and easily ruptured when touched. What is the most likely diagnosis?

- A. Pemphigus vulgaris
- B. Pemphigoid
- C. Dermatitis herpetiformis
- D. Psoriasis
- E. Epidermolysis bullosa

Question 47 of 117

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- B. Pemphigoid
- C. Dermatitis herpetiformis
- D. Psoriasis
- E. Epidermolysis bullosa

Blisters/bullae
- no mucosal involvement: bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

Features
- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

Management
- steroids
- immunosuppressants

Question 48 of 117

A 21-year-old woman who is 16 weeks pregnant present with worsening acne which she is finding distressing. She is currently using topical benzyl peroxide with limited effect. On examination there is widespread non-inflammatory lesions and pustules on her face. What is the most appropriate next management step?

- A. Oral trimethoprim
- B. Oral lymecycline
- C. Oral erythromycin
- D. Topical retinoid
- E. Oral doxycycline

Question 48 of 117

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- C. Oral erythromycin
- D. Topical retinoid
- E. Oral doxycycline

Oral erythromycin may be used for acne in pregnancy. The other drugs are contraindicated

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 49 of 117

Which one of the following factors would predispose a patient to forming keloid scars?

- A. Having white skin
- B. Incisions along relaxed skin tension lines
- C. Being aged 20-40 years
- D. Being female
- E. Having a wound on the lower back

Question 49 of 117

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- B. Incisions along relaxed skin tension lines
- C. Being aged 20-40 years
- D. Being female
- E. Having a wound on the lower back

Keloid scars - more common in young, black, male adults

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 50 of 117

A 26-year-old man who is HIV positive is noted to have developed seborrhoeic dermatitis. Which of the following two complications are most associated with this condition?

- A. Alopecia and otitis externa
- B. Blepharitis and otitis externa
- C. Photosensitivity and alopecia
- D. Photosensitivity and blepharitis
- E. Blepharitis and alopecia

Question 50 of 117

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- B. Blepharitis and otitis externa
- C. Photosensitivity and alopecia
- D. Photosensitivity and blepharitis
- E. Blepharitis and alopecia

Alopecia is not commonly seen in seborrhoeic dermatitis, but may develop if a severe secondary infection develops

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 51 of 117

A 65-year-old woman presents with bullae on her forearms following a recent holiday in Spain. She also notes that the skin on her hands is extremely fragile and tears easily. In the past the patient has been referred to dermatology due to troublesome hypertrichosis. What is the most likely diagnosis?

- A. Pellagra
- B. Pemphigus vulgaris
- C. Epidermolysis bullosa
- D. Bullous pemphigoid
- E. Porphyria cutanea tarda

Question 51 of 117

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- D. Bullous pemphigoid
- E. Porphyria cutanea tarda

Porphyria cutanea tarda
• blistering photosensitive rash • hypertrichosis • hyperpigmentation

Porphyria cutanea tarda

Porphyria cutanea tarda is the most common hepatic porphyria. It is due to an inherited defect in uroporphyrinogen decarboxylase or caused by hepatocyte damage e.g. alcohol, oestrogens

Features
- classically presents with photosensitive rash with blistering and skin fragility on the face and dorsal aspect of hands (most common feature)
- hypertrichosis
- hyperpigmentation

Investigations
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp

Management
- chloroquine
- venesection

Question 52 of 117

A 60-year-old woman presents with a swelling just proximal to the nailbed on the left ring finger. She has a history of osteoarthritis but is usually well. On examination a 4mm, firm dome-shaped swelling is seen. What is the most likely diagnosis?

- A. Fibrokeratoma
- B. Epidermoid cyst
- C. Orf
- D. Myxoid cyst
- E. Rheumatoid nodule

Question 52 of 117

A 60-year-old woman presents with a swelling just proximal to the nailbed on the left ring finger. She has a history of osteoarthritis but is usually well. On examination a 4mm, firm dome-shaped swelling is seen. What is the most likely diagnosis?

- A. Fibrokeratoma
- B. Epidermoid cyst
- C. Orf
- D. Myxoid cyst
- E. Rheumatoid nodule

Myxoid cyst

Myxoid cysts (also known as mucous cysts) are benign ganglion cysts usually found on the distal, dorsal aspect of the finger. There is usually osteoarthritis in the surrounding joint. They are more common in middle-aged women.

Question 53 of 117

A 23-year-old man presents as he is concerned over recent hair loss. Examination reveals a discrete area of hair loss on the left temporal region with no obvious abnormality of the underlying scalp. What is the most likely diagnosis?

- A. Telogen effluvium
- B. Alopecia areata
- C. Tinea capitis
- D. Male-pattern baldness
- E. Discoid lupus erythematous

Question 53 of 117

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- A. Telogen effluvium
- B. Alopecia areata
- C. Tinea capitis
- D. Male-pattern baldness
- E. Discoid lupus erythematous

Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

Question 54 of 117

Which of the following skin conditions associated with malignancy are not correctly paired?

- A. Necrolytic migratory erythema and glucagonoma
- B. Migratory thrombophlebitis and pancreatic cancer
- C. Erythema gyratum repens and lymphoma
- D. Acanthosis nigricans and gastrointestinal cancer
- E. Erythroderma and lymphoma

Question 54 of 117

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- C. Erythema gyratum repens and lymphoma
- D. Acanthosis nigricans and gastrointestinal cancer
- E. Erythroderma and lymphoma

Erythema gyratum repens is generally associated with solid organ malignancies such as lung and breast cancer

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	**Associated malignancies**
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 55 of 117

Which one of the following conditions is least associated with pruritus?

- A. Pemphigus vulgaris
- B. Iron-deficiency anaemia
- C. Polycythaemia
- D. Chronic renal failure
- E. Scabies

Question 55 of 117

Which one of the following conditions is least associated with pruritus?

- A. Pemphigus vulgaris
- B. Iron-deficiency anaemia
- C. Polycythaemia
- D. Chronic renal failure
- E. Scabies

Pemphigus vulgaris is an autoimmune bullous disease of the skin. It is not commonly associated with pruritus

Pruritus

The table below lists the main characteristics of the most important causes of pruritus

Liver disease	History of alcohol excess Stigmata of chronic liver disease: spider naevi, bruising, palmar erythema, gynaecomastia etc Evidence of decompensation: ascites, jaundice, encephalopathy
Iron deficiency anaemia	Pallor Other signs: koilonychia, atrophic glossitis, post-cricoid webs, angular stomatitis
Polycythaemia	Pruritus particularly after warm bath 'Ruddy complexion' Gout Peptic ulcer disease
Chronic kidney disease	Lethargy & pallor Oedema & weight gain Hypertension
Lymphoma	Night sweats Lymphadenopathy Splenomegaly, hepatomegaly Fatigue

Other causes:

- hyper- and hypothyroidism
- diabetes
- pregnancy
- 'senile' pruritus
- urticaria
- skin disorders: eczema, scabies, psoriasis, pityriasis rosea

Question 56 of 117

A 24-year-old woman presents due to a rash on her neck and forehead. She returned from a holiday in Cyprus 1 week ago and had her hair dyed 2 days ago. On examination there is a weepy, vesicular rash around her hairline although the scalp itself is not badly affected. What is the most likely diagnosis?

- A. Cutaneous leishmaniasis
- B. Irritant contact dermatitis
- C. Allergic contact dermatitis
- D. Syphilis
- E. Photocontact dermatitis

Question 56 of 117

A 24-year-old woman presents due to a rash on her neck and forehead. She returned from a holiday in Cyprus 1 week ago and had her hair dyed 2 days ago. On examination there is a weepy, vesicular rash around her hairline although the scalp itself is not badly affected. What is the most likely diagnosis?

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- C. Allergic contact dermatitis
- D. Syphilis
- E. Photocontact dermatitis

Contact dermatitis

There are two main types of contact dermatitis

- irritant contact dermatitis: common - non-allergic reaction due to weak acids or alkalis (e.g. detergents). Often seen on the hands. Erythema is typical, crusting and vesicles are rare
- allergic contact dermatitis: type IV hypersensitivity reaction. Uncommon - often seen on the head following hair dyes. Presents as an acute weeping eczema which predominately affects the margins of the hairline rather than the hairy scalp itself. Topical treatment with a potent steroid is indicated

Cement is a frequent cause of contact dermatitis. The alkaline nature of cement may cause an irritant contact dermatitis whilst the dichromates in cement also can cause an allergic contact dermatitis

Question 57 of 117

A 24-year-old female with a history of anorexia nervosa presents with red crusted lesions around the corner of her mouth and below her lower lip. What is she most likely to be deficient in?

- A. Zinc
- B. Tocopherol
- C. Pantothenic acid
- D. Thiamine
- E. Magnesium

Question 57 of 117

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- B. Tocopherol
- C. Pantothenic acid
- D. Thiamine
- E. Magnesium

Vitamin B12 deficiency may also cause angular cheilosis

Zinc deficiency

Features
- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Question 58 of 117

Which of the following conditions is least likely to exhibit the Koebner phenomenon?

- A. Vitiligo
- B. Molluscum contagiosum
- C. Lichen planus
- D. Psoriasis
- E. Lupus vulgaris

Question 58 of 117

Which of the following conditions is least likely to exhibit the Koebner phenomenon?

- A. Vitiligo
- B. Molluscum contagiosum
- C. Lichen planus
- D. Psoriasis
- E. Lupus vulgaris

Lupus vulgaris is not associated with the Koebner phenomenon

Koebner phenomenon

The Koebner phenomenon describes skin lesions which appear at the site of injury. It is seen in:

- psoriasis
- vitiligo
- warts
- lichen planus
- lichen sclerosus
- molluscum contagiosum

Question 59 of 117

A 34-year-old female is reviewed in the dermatology clinic with a skin rash under her new wrist watch. An allergy to nickel is suspected. What is the best investigation?

- A. Skin prick test
- B. Skin patch test
- C. Skin biopsy
- D. Serum IgE
- E. Serum nickel antibodies

Question 59 of 117

A 34-year-old female is reviewed in the dermatology clinic with a skin rash under her new wrist watch. An allergy to nickel is suspected. What is the best investigation?

- A. Skin prick test
- B. Skin patch test
- C. Skin biopsy
- D. Serum IgE
- E. Serum nickel antibodies

Nickel dermatitis

Nickel is a common cause allergic contact dermatitis and is an example of a type IV hypersensitivity reaction. It is often caused by jewellery such as watches

It is diagnosed by a skin patch test

Question 60 of 117

A 45-year-old man with a history of seborrhoeic dermatitis presents in late winter due a flare in his symptoms, affecting both his face and scalp. Which one of the following agents is least likely to be beneficial?

- A. Topical ketoconazole
- B. Selenium sulphide shampoo
- C. Topical hydrocortisone
- D. Tar shampoo
- E. Aqueous cream

Question 60 of 117

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- B. Selenium sulphide shampoo
- C. Topical hydrocortisone
- D. Tar shampoo
- E. Aqueous cream

There is less of a role for emollients in the management of seborrhoeic dermatitis than in other chronic skin disorders

Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 61 of 117

An 84-year-old woman with a history of ischaemic heart disease is reviewed in the dermatology clinic. She has developed tense blistering lesions on her legs. Each lesion is around 1 to 3 cm in diameter and she reports that they are slightly pruritic. Examination of her mouth and vulva is unremarkable. What is the most likely diagnosis?

- A. Pemphigus
- B. Drug reaction to aspirin
- C. Epidermolysis bullosa
- D. Scabies
- E. Bullous pemphigoid

Question 61 of 117

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- B. Drug reaction to aspirin
- C. Epidermolysis bullosa
- D. Scabies
- E. Bullous pemphigoid

Blisters/bullae
- no mucosal involvement (in exams at least*): bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 62 of 117

A woman presents with painful erythematous lesions on her shins. Which one of the following is least associated with this presentation?

- A. Pregnancy
- B. Behcet's syndrome
- C. Streptococcal infection
- D. Penicillin
- E. Amyloidosis

Question 62 of 117

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- B. Behcet's syndrome
- C. Streptococcal infection
- D. Penicillin
- E. Amyloidosis

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 63 of 117

A 23-year-old man presents with a 4 day history of an itchy and sore right ear. He has recently returned from holiday in Spain. On examination the right ear canal is inflamed but no debris is seen. The tympanic membrane is clearly visible and is unremarkable. What is the most appropriate management?

- A. Topical corticosteroid + aminoglycoside
- B. Topical corticosteroid
- C. Refer to ENT
- D. Topical corticosteroid + clotrimazole
- E. Oral flucloxacillin

Question 63 of 117

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- A. Topical corticosteroid + aminoglycoside
- B. Topical corticosteroid
- C. Refer to ENT
- D. Topical corticosteroid + clotrimazole
- E. Oral flucloxacillin

This patient has otitis externa. The first line management is either a topical antibiotic or a combined topical antibiotic and steroid

Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes of otitis externa include:
- infection: bacterial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*) or fungal
- seborrhoeic dermatitis
- contact dermatitis (allergic and irritant)

Features
- ear pain, itch, discharge
- otoscopy: red, swollen, or eczematous canal

The recommend initial management of otitis externa is:
- topical antibiotic or a combined topical antibiotic with steroid
- if the tympanic membrane is perforated aminoglycosides should not be used
- if there is canal debris then consider removal
- if the canal is extensively swollen then an ear wick is sometimes inserted

Second line options include
- consider contact dermatitis secondary to neomycin
- oral antibiotics if the infection is spreading
- taking a swab inside the ear canal
- empirical use of an antifungal agent

Malignant otitis externa is more common in elderly diabetics. In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal. Intravenous antibiotics may be required.

Question 64 of 117

A 45-year-old woman is presents with itchy, violaceous papules on the flexor aspects of her wrists. She is normally fit and well and has not had a similar rash previously. Given the likely diagnosis, what other feature is she most likely to have?

- A. Onycholysis
- B. Raised ESR
- C. Mucous membrane involvement
- D. Pain in small joints
- E. Microscopic haematuria

Question 64 of 117

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- D. Pain in small joints
- E. Microscopic haematuria

Lichen
- **p**lanus: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- sclerosus: itchy white spots typically seen on the vulva of elderly women

Mucous membrane involvement is common in lichen planus

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 65 of 117

A 78-year-old nursing home resident is reviewed due to the development of an intensely itchy rash. On examination white linear lesions are seen on the wrists and elbows, and red papules are present on the penis. What is the most appropriate management?

- A. Topical permethrin
- B. Referral to GUM clinic
- C. Topical betnovate
- D. Topical ketoconazole
- E. Topical selenium sulphide

Question 65 of 117

A 78-year-old nursing home resident is reviewed due to the development of an intensely itchy rash. On examination white linear lesions are seen on the wrists and elbows, and red papules are present on the penis. What is the most appropriate management?

- A. Topical permethrin
- B. Referral to GUM clinic
- C. Topical betnovate
- D. Topical ketoconazole
- E. Topical selenium sulphide

Lichen planus may give a similar picture but the intense itching is more characteristic of scabies. It is also less common for lichen planus to present in the elderly - it typical affects patients aged 30-60 years.

Scabies

Scabies is caused by the mite Sarcoptes scabiei and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8–12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Question 66 of 117

A 72-year-old woman is diagnosed with a number of erythematous, rough lesions on the back of her hands. A diagnosis of actinic keratoses is made. What is the most appropriate management?

- A. Reassurance
- B. Urgent referral to a dermatologist
- C. Topical fluorouracil cream
- D. Review in 3 months
- E. Topical betnovate

Question 66 of 117

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- C. Topical fluorouracil cream
- D. Review in 3 months
- E. Topical betnovate

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 67 of 117

A 15-year-old male returns to the dermatology clinic for review. He has a past history of acne and is currently treated with oral lymecycline. There has been no response to treatment and examination reveals evidence of scarring on his face. What is the most suitable treatment?

- A. Oral doxycycline
- B. Oral cyproterone acetate
- C. Oral retinoin
- D. IV retinoin
- E. Topical retinoids

Question 67 of 117

A 15-year-old male returns to the dermatology clinic for review. He has a past history of acne and is currently treated with oral lymecycline. There has been no response to treatment and examination reveals evidence of scarring on his face. What is the most suitable treatment?

- A. Oral doxycycline
- B. Oral cyproterone acetate
- C. Oral retinoin
- D. IV retinoin
- E. Topical retinoids

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 68 of 117

Each one of the following is associated with yellow nail syndrome except:

- A. Chronic sinus infections
- B. Bronchiectasis
- C. Azoospermia
- D. Congenital lymphoedema
- E. Pleural effusions

Question 68 of 117

Each one of the following is associated with yellow nail syndrome except:

- A. Chronic sinus infections
- B. Bronchiectasis
- C. Azoospermia
- D. Congenital lymphoedema
- E. Pleural effusions

Yellow nail syndrome

Slowing of nail growth leads to the characteristic thickened and discoloured nails seen in yellow nail syndrome

Associations

- congenital lymphoedema
- pleural effusions
- bronchiectasis
- chronic sinus infections

Question 69 of 117

A 29-year-old man presents due to the development of 'hard skin' on his scalp. On examination he has a 4cm circular, white, hyperkeratotic lesion on the crown of his head. He has no past history of any skin or scalp disorder. Skin scrapings are reported as follows:

No fungal elements seen

What is the most likely diagnosis?

- A. Psoriasis
- B. Dissecting cellulitis
- C. Kerion
- D. Systemic lupus erythematous
- E. Seborrhoeic dermatitis

Question 69 of 117

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- C. Kerion
- D. Systemic lupus erythematous
- E. Seborrhoeic dermatitis

As the skin scraping is negative for fungi the most likely diagnosis is psoriasis. Scalp psoriasis may occur in isolation in patients with no history of psoriasis elsewhere. Please see the link for more information.

The white appearance of the lesion is secondary to the 'silver scale' covering the psoriatic plaque.

Psoriasis

Psoriasis can be divided into type 1 and 2:

Type 1
- presents < 40 years old
- positive family history
- associated with HLA-CW6

Type 2
- presents > 50 years old
- no family history

Cause
- abnormal T cell activity stimulates keratinocyte proliferation (rather than an actual primary keratinocyte disorder)
- mediated by type 1 helper T cells

Features
- red, scaly plaques
- scalp, extensor surfaces elbows/knees, sacrum
- nail signs: pitting, onycholysis
- arthritis

Complications
- psoriatic arthropathy (around 10%)
- psychological distress
- increased incidence of cardiovascular disease

Question 70 of 117

A 54-year-old woman is prescribed topical fusidic acid for a small patch of impetigo around her nose. She has recently been discharged from hospital following varicose vein surgery. Seven days after starting treatment there has been no change in her symptoms. Examination reveals a persistent small, crusted area around the right nostril. Whilst awaiting the results of swabs, what is the most appropriate management?

- A. Oral vancomycin
- B. Oral erythromycin
- C. Topical metronidazole
- D. Topical mupirocin
- E. Oral flucloxacillin

Question 70 of 117

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- C. Topical metronidazole
- D. Topical mupirocin
- E. Oral flucloxacillin

MRSA should be considered given the recent hospital stay and lack of response to fusidic acid. Topical mupirocin is therefore the most appropriate treatment.

Impetigo: management

Limited, localised disease
- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease
- oral flucloxacillin
- oral erythromycin if penicillin allergic

Question 71 of 117

A 63-year-old man who is known to have type 2 diabetes mellitus presents with a number of lesions over his shins. On examination there are a number of 3-4 mm smooth, firm, papules which are hyperpigmented and centrally depressed. What is the most likely diagnosis?

- A. Lupus vulgaris
- B. Necrobiosis lipoidica diabeticorum
- C. Guttate psoriasis
- D. Granuloma annulare
- E. Pyoderma gangrenosum

Question 71 of 117

A 63-year-old man who is known to have type 2 diabetes mellitus presents with a number of lesions over his shins. On examination there are a number of 3-4 mm smooth, firm, papules which are hyperpigmented and centrally depressed. What is the most likely diagnosis?

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- C. Guttate psoriasis
- D. Granuloma annulare
- E. Pyoderma gangrenosum

Granuloma annulare

Basics

- papular lesions that are often slightly hyperpigmented and depressed centrally
- typically occur on the dorsal surfaces of the hands and feet, and on the extensor aspects of the arms and legs

A number of associations have been proposed to conditions such as diabetes mellitus but there is only weak evidence for this

Question 72 of 117

A 43-year-old presents with itchy lesions on the instep of both feet. These have been present for the past two months. On examination small blisters are seen with surrounding dry and cracked skin. What is the most likely diagnosis?

- A. Porphyria cutanea tarda
- B. Pustular psoriasis
- C. Pompholyx
- D. Bullous pemphigoid
- E. Pemphigus

Question 72 of 117

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- A. Porphyria cutanea tarda
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- C. Pompholyx
- D. Bullous pemphigoid
- E. Pemphigus

Pompholyx

Pompholyx is a type of eczema which affects both the hands (cheiropompholyx) and the feet (pedopompholyx). It is also known as dyshidrotic eczema

Features
- small blisters on the palms and soles
- pruritic, sometimes burning sensation
- once blisters burst skin may become dry and crack

Management
- cool compresses
- emollients
- topical steroids

Question 73 of 117

Café-au-lait spots are seen in each of the following, except:

- A. McCune-Albright syndrome
- B. Friedreich's ataxia
- C. Neurofibromatosis
- D. Fanconi anaemia
- E. Tuberous sclerosis

Question 73 of 117

Café-au-lait spots are seen in each of the following, except:

- A. McCune-Albright syndrome
- B. Friedreich's ataxia
- C. Neurofibromatosis
- D. Fanconi anaemia
- E. Tuberous sclerosis

Café-au-lait spots

Hyperpigmented lesions that vary in colour from light brown to dark brown, with borders that may be smooth or irregular

Causes

- neurofibromatosis type I & II
- tuberous sclerosis
- Fanconi anaemia
- McCune-Albright syndrome

Question 74 of 117

A 58-year-old woman presents with a persistent erythematous rash on her cheeks and a 'red nose'. She describes occasional episodes of facial flushing. On examination erythematous skin is noted on the nose and cheeks associated with occasional telangiectasia. What is the most appropriate management?

- A. Topical metronidazole
- B. Topical isotretinoin
- C. Benzyl peroxide
- D. Daktacort
- E. Topical hydrocortisone

Question 74 of 117

A 58-year-old woman presents with a persistent erythematous rash on her cheeks and a 'red nose'. She describes occasional episodes of facial flushing. On examination erythematous skin is noted on the nose and cheeks associated with occasional telangiectasia. What is the most appropriate management?

- A. Topical metronidazole
- B. Topical isotretinoin
- C. Benzyl peroxide
- D. Daktacort
- E. Topical hydrocortisone

Given that this woman has mild symptoms, topical metronidazole should be used first line

Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

Features
- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

Management
- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

Question 75 of 117

A 34-year-old man with a history of polyarthralgia, back pain and diarrhoea is found to have a 3 cm red lesion on his shin which is starting to ulcerate. What is the most likely diagnosis?

- A. Systemic *Shigella* infection
- B. Syphilis
- C. Metastatic colon cancer
- D. Erythema nodosum
- E. Pyoderma gangrenosum

Question 75 of 117

A 34-year-old man with a history of polyarthralgia, back pain and diarrhoea is found to have a 3 cm red lesion on his shin which is starting to ulcerate. What is the most likely diagnosis?

- A. Systemic *Shigella* infection
- B. Syphilis
- C. Metastatic colon cancer
- D. Erythema nodosum
- E. Pyoderma gangrenosum

This patient is likely to have ulcerative colitis, which has a known association with large-joint arthritis, sacroilitis and pyoderma gangrenosum

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 76 of 117

A 48-year-old man with a history of psoriasis develops plaques on his face. Of the following options, which one is the most appropriate treatment?

- A. Hydrocortisone 1%
- B. Calcipotriol
- C. Coal tar
- D. Dithranol
- E. Tacrolimus

Question 76 of 117

A 48-year-old man with a history of psoriasis develops plaques on his face. Of the following options, which one is the most appropriate treatment?

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- B. Calcipotriol
- C. Coal tar
- D. Dithranol
- E. Tacrolimus

Difficult question, particularly as there is an emphasis on patient-doctor choice when deciding upon treatment in psoriasis. Vitamin D analogues can be used in this situation but calcipotriol is not recommended as it may cause irritation - calcitriol and tacalcitol are alternatives. Mild potency topical steroids are useful for the management of facial psoriasis. Coal tar is smelly and messy - most patients would not tolerate facial application

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 77 of 117

Which one of the following conditions is least associated with photosensitivity?

- A. Discoid lupus erythematous
- B. Systemic lupus erythematous
- C. Herpes labialis
- D. Acute intermittent porphyria
- E. Xeroderma pigmentosum

Question 77 of 117

Which one of the following conditions is least associated with photosensitivity?

- A. Discoid lupus erythematous
- B. Systemic lupus erythematous
- C. Herpes labialis
- D. Acute intermittent porphyria
- E. Xeroderma pigmentosum

Photosensitivity is not a feature of acute intermittent porphyria unlike porphyria cutanea tarda

Photosensitive skin disorders

Diseases aggravated by exposure to sunlight

- systemic lupus erythematosus, discoid lupus
- porphyria (not acute intermittent)
- herpes labialis (cold sores)
- pellagra
- xeroderma pigmentosum
- solar urticaria
- polymorphic light eruption

Question 78 of 117

A 20-year-old man presents with acute gingivitis assoociated with oral ulceration. A diagnosis of primary herpes simplex infection is suspected. Which one of the following types of rash is he most likely to go an develop?

- A. Erythema ab igne
- B. Erythema nodosum
- C. Erythema chronicum migrans
- D. Erythema marginatum
- E. Erythema multiforme

Question 78 of 117

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- B. Erythema nodosum
- C. Erythema chronicum migrans
- D. Erythema marginatum
- E. Erythema multiforme

Erythema multiforme

Erythema multiforme
- target lesions (typically worse on peripheries e.g. palms and soles)
- severe = Stevens-Johnson syndrome (blistering and mucosal involvement)

Causes
- viruses: herpes simplex virus, Orf
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

Question 79 of 117

A 17-year-old female originally from Nigeria presents due to a swelling around her earlobe. She had her ears pierced around three months ago and has noticed the gradual development of an erythematous swelling since. On examination a keloid scar is seen. What is the most appropriate management?

- A. Intralesional diclofenac
- B. Advise no treatment is available
- C. Intralesional triamcinolone
- D. Advise will spontaneously regress within 4-6 months
- E. Intralesional sclerotherapy

Question 79 of 117

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- C. Intralesional triamcinolone
- D. Advise will spontaneously regress within 4-6 months
- E. Intralesional sclerotherapy

Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines*

Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

Question 80 of 117

A 22-year-old male is referred to dermatology clinic with a longstanding problem of bilateral excessive axillary sweating. He is otherwise well but the condition is affecting his confidence and limiting his social life. What is the most appropriate management?

- A. Non-sedating antihistamine
- B. Topical hydrocortisone 1%
- C. Perform thyroid function tests
- D. Topical aluminium chloride
- E. Trial of desmopressin

Question 80 of 117

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- C. Perform thyroid function tests
- D. Topical aluminium chloride
- E. Trial of desmopressin

Hyperhidrosis

Hyperhidrosis describes the excessive production of sweat

Management options include

- topical aluminium chloride preparations are first-line. Main side effect is skin irritation
- iontophoresis: particularly useful for patients with palmar, plantar and axillary hyperhidrosis
- botulinum toxin: currently licensed for axillary symptoms
- surgery: e.g. Endoscopic transthoracic sympathectomy. Patients should be made aware of the risk of compensatory sweating

Question 81 of 117

A 15-year-old girl presents with an urticarial rash, angioedema and wheezing. Her mother states that she has just come from her younger sister's party where she had been helping to blow up balloons. What is the most likely diagnosis?

- A. C1-esterase deficiency (hereditary angioedema)
- B. Allergic contact dermatitis
- C. Peanut allergy
- D. Latex allergy
- E. Irritant contact dermatitis

Question 81 of 117

A 15-year-old girl presents with an urticarial rash, angioedema and wheezing. Her mother states that she has just come from her younger sister's party where she had been helping to blow up balloons. What is the most likely diagnosis?

- A. C1-esterase deficiency (hereditary angioedema)
- B. Allergic contact dermatitis
- C. Peanut allergy
- D. Latex allergy
- E. Irritant contact dermatitis

This is a typical history of latex allergy. Adrenaline should be given immediately and usual anaphylaxis management followed

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

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

Type IV - Delayed hypersensitivity
- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 82 of 117

A 29-year-old man consults you regarding a rash he has noticed around his groin. It has been present for the past 3 months and is asymptomatic. On examination there is a symmetrical well-demarcated, brown-red macular rash around the groin. What is the most likely diagnosis?

- A. Erythrasma
- B. Pityriasis versicolor
- C. Secondary syphilis
- D. Acanthosis nigricans
- E. *Candida*l intertrigo

Question 82 of 117

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- B. Pityriasis versicolor
- C. Secondary syphilis
- D. Acanthosis nigricans
- E. *Candida*l intertrigo

Erythrasma

Erythrasma is a generally asymptomatic, flat, slightly scaly, pink or brown rash usually found in the groin or axillae. It is caused by an overgrowth of the diphtheroid Corynebacterium minutissimum

Examination with Wood's light reveals a coral-red fluorescence.

Topical miconazole or antibacterial are usually effective. Oral erythromycin may be used for more extensive infection

Question 83 of 117

A patient who is suspected of having dermatitis herpetiformis undergoes a skin biopsy. Which one of the following antibodies is most likely to be found in the dermis?

- A. IgM
- B. IgA
- C. IgD
- D. IgE
- E. IgG

Question 83 of 117

A patient who is suspected of having dermatitis herpetiformis undergoes a skin biopsy. Which one of the following antibodies is most likely to be found in the dermis?

- A. IgM
- B. IgA
- C. IgD
- D. IgE
- E. IgG

Dermatitis herpetiformis - caused by IgA deposition in the dermis

Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

Features
- itchy, vesicular skin lesions on the extensor surfaces (e.g. Elbows, knees buttocks)

Diagnosis
- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

Management
- gluten-free diet
- dapsone

Question 84 of 117

Which one of the following is least recognised as a cause of erythroderma in the UK?

- A. Lymphoma
- B. Drug eruption
- C. Lichen planus
- D. Psoriasis
- E. Eczema

Question 84 of 117

Which one of the following is least recognised as a cause of erythroderma in the UK?

- A. Lymphoma
- B. Drug eruption
- C. Lichen planus
- D. Psoriasis
- E. Eczema

Erythroderma

Erythroderma is a term used when more than 95% of the skin is involved in a rash of any kind

Causes of erythroderma
- eczema
- psoriasis
- drugs e.g. gold
- lymphoma, leukaemia
- idiopathic

Erythrodermic psoriasis
- may result from progression of chronic disease to an exfoliative phase with plaques covering most of the body. Associated with mild systemic upset
- more serious form is an acute deterioration. This may be triggered by a variety of factors such as withdrawal of systemic steroids. Patients need to be admitted to hospital for management

Question 85 of 117

A patient develops an eczematous, weeping rash on his wrist following the purchase of a new watch. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

Question 85 of 117

A patient develops an eczematous, weeping rash on his wrist following the purchase of a new watch. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- A. Type I reaction
- B. Type II reaction
- C. Type III reaction
- D. Type IV reaction
- E. Type V reaction

This patient has allergic contact dermatitis, which is commonly precipitated by nickel

Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic
- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound
- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex
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In recent times a further category has been added:

Type V - Stimulated hypersensitivity
- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Question 86 of 117

A 62-year-old woman mentions in diabetes clinic that she has a 'volcano' like spot on her left cheek, which has appeared over the past 3 months. She initially thought it may be a simple spot but it has not gone away. On examination she has a 5 mm red, raised lesion with a central keratin filled crater. A clinical diagnosis of probable keratoacanthoma is made. What is the most suitable management?

- A. Reassure will spontaneously involute within 3 months
- B. Urgent referral to dermatology
- C. Topical 5-FU
- D. Non-urgent referral to dermatology
- E. Oral prednisolone

Question 86 of 117

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- B. Urgent referral to dermatology
- C. Topical 5-FU
- D. Non-urgent referral to dermatology
- E. Oral prednisolone

Whilst keratoacanthoma is a benign lesion it is difficult clinically to exclude squamous cell carcinoma so urgent excision is advised

Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater
- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

Question 87 of 117

A 67-year-old man with recurrent actinic keratoses on his scalp is reviewed. Which one of the following is not a treatment option for the management of this condition?

- A. Topical diclofenac
- B. Topical betnovate
- C. Topical fluorouracil
- D. Topical imiquimod
- E. Cryotherapy

Question 87 of 117

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- A. Topical diclofenac
- B. Topical betnovate
- C. Topical fluorouracil
- D. Topical imiquimod
- E. Cryotherapy

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 88 of 117

A 69-year-old woman with a history of learning difficulties is reviewed in clinic. She is known to have erythema ab igne on her legs but according to her carer still spends long hours in front of her electric fire. Which one of the following skin lesions is she at risk of developing?

- A. Squamous cell carcinoma
- B. Cutaneous T-cell lymphoma of the skin
- C. Dermatofibrosarcoma protuberans
- D. Basal cell carcinoma
- E. Malignant melanoma

Question 88 of 117

A 69-year-old woman with a history of learning difficulties is reviewed in clinic. She is known to have erythema ab igne on her legs but according to her carer still spends long hours in front of her electric fire. Which one of the following skin lesions is she at risk of developing?

- A. Squamous cell carcinoma
- B. Cutaneous T-cell lymphoma of the skin
- C. Dermatofibrosarcoma protuberans
- D. Basal cell carcinoma
- E. Malignant melanoma

Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

Question 89 of 117

A 31-year-old female with polycystic ovarian syndrome consults you as she is troubled with excessive facial hair. Switching her combined oral contraceptive pill to co-cyprindiol has had no effect. On examination she has hirsuitism affecting her moustache, beard, and temple areas. What is the most appropriate treatment?

- A. Topical salicylic acid
- B. Topical adapalene
- C. Oral clomifene
- D. Topical eflornithine
- E. Topical tazarotene

Question 89 of 117

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- B. Topical adapalene
- C. Oral clomifene
- D. Topical eflornithine
- E. Topical tazarotene

Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based

General
- weight reduction if appropriate
- if a women requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

Hirsuitism and acne
- a COC pill may be used help manage hirsuitism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

Infertility
- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen* therapies such as clomifene
- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

Question 90 of 117

A 72-year-old man is investigated for oral ulceration. A biopsy suggests pemphigus vulgaris. This is most likely to be caused by antibodies directed against:

- A. Hemidesmosomal BP180
- B. Occludin-2
- C. Hemidesmosomal BP230
- D. Desmoglein
- E. Adherens

Question 90 of 117

A 72-year-old man is investigated for oral ulceration. A biopsy suggests pemphigus vulgaris. This is most likely to be caused by antibodies directed against:

- A. Hemidesmosomal BP180
- B. Occludin-2
- C. Hemidesmosomal BP230
- D. Desmoglein
- E. Adherens

Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

Features

- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

Management

- steroids
- immunosuppressants

Question 91 of 117

Which one of the following drugs is most likely to result in a photosensitive rash?

- A. Gentamicin
- B. Erythromycin
- C. Penicillin
- D. Tetracycline
- E. Amoxicillin

Question 91 of 117

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- C. Penicillin
- D. Tetracycline
- E. Amoxicillin

Drugs causing photosensitivity

Causes of drug-induced photosensitivity

- thiazides
- tetracyclines, sulphonamides, ciprofloxacin
- amiodarone
- NSAIDs e.g. piroxicam
- psoralens
- sulphonylureas

Question 92 of 117

A 17-year-old female presents with multiple comedones, pustules and papules on her face. Which one of the following is least likely to improve her condition?

- A. Topical retinoids
- B. Dietary advice
- C. Sunlight
- D. Oral trimethoprim
- E. Ethinylestradiol with cyproterone acetate

Question 92 of 117

A 17-year-old female presents with multiple comedones, pustules and papules on her face. Which one of the following is least likely to improve her condition?

- A. Topical retinoids
- B. Dietary advice
- C. Sunlight
- D. Oral trimethoprim
- E. Ethinylestradiol with cyproterone acetate

There is no role for dietary modification in patients with acne vulgaris. Ethinylestradiol with cyproterone acetate (Dianette) is useful in some female patients with acne unresponsive to standard treatment. Oral trimethoprim is useful in patients on long-term antibiotics who develop Gram negative folliculitis

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 93 of 117

Which one of the following is least likely to cause a bullous rash?

- A. Frusemide
- B. Friction
- C. Lichen planus
- D. Insect bite
- E. Epidermolysis bullosa

Question 93 of 117

Which one of the following is least likely to cause a bullous rash?

- A. Frusemide
- B. Friction
- C. Lichen planus
- D. Insect bite
- E. Epidermolysis bullosa

The bullous variant of lichen planus is extremely rare

Bullous disorders

Causes of skin bullae
- congenital: epidermolysis bullosa
- autoimmune: bullous pemphigoid, pemphigus
- insect bite
- trauma/friction
- drugs: barbiturates, furosemide

Question 94 of 117

A 64-year-old female is referred to dermatology due to a non-healing skin ulcer on her lower leg. This has been present for around 6 weeks and the appearance didn't improve following a course of oral flucloxacillin. What is the most important investigation to perform first?

- A. MRI
- B. Rheumatoid factor titres
- C. Ankle-brachial pressure index
- D. Swab of ulcer for culture and sensitivity
- E. X-ray

Question 94 of 117

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- C. Ankle-brachial pressure index
- D. Swab of ulcer for culture and sensitivity
- E. X-ray

An ankle-brachial pressure index measurement would help exclude arterial insufficiency as a contributing factor. If this was abnormal then a referral to the vascular surgeons should be considered.

If the ulcer fails to heal with active management (e.g. Compression bandaging) then referral for consideration of biopsy to exclude a malignancy should be made.

Ongoing infection is not a common cause of non-healing leg ulcers.

Venous ulceration

Venous ulceration is typically seen above the medial malleolus

Investigations
- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

Management
- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

Question 95 of 117

A 14-year-old male is reviewed due to a patch of scaling and hair loss on the right side of his head. A skin scraping is sent which confirms a diagnosis of tinea capitis. Which organism is most likely to be responsible?

- A. Trichophyton tonsurans
- B. Microsporum distortum
- C. Trichophyton verrucosum
- D. Microsporum audouinii
- E. Microsporum canis

Question 95 of 117

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- E. Microsporum canis

Tinea

Tinea is a term given to dermatophyte fungal infections. Three main types of infection are described depending on what part of the body is infected

- tinea capitis - scalp
- tinea corporis - trunk, legs or arms
- tinea pedis - feet

Tinea capitis (scalp ringworm)

- a cause of scarring alopecia mainly seen in children
- if untreated a raised, pustular, spongy/boggy mass called a kerion may form
- most common cause is Trichophyton tonsurans in the UK and the USA
- may also be caused by Microsporum canis acquired from cats or dogs
- diagnosis: lesions due to Microsporum canis green fluorescence under Wood's lamp*. However the most useful investigation is scalp scapings
- management (based on CKS guidelines): oral antifungals: terbinafine for Trichophyton tonsurans infections and griseofulvin for Microsporum infections. Topical ketoconazole shampoo should be given for the first two weeks to reduce transmission

Tinea corporis

- causes include Trichophyton rubrum and Trichophyton verrucosum (e.g. From contact with cattle)
- well-defined annular, erythematous lesions with pustules and papules
- may be treated with oral fluconazole

Tinea pedis (athlete's foot)

- characterised by itchy, peeling skin between the toes
- common in adolescence

*lesions due to Trichophyton species do not readily fluoresce under Wood's lamp

Question 96 of 117

Each of the following drugs may be used in psoriasis, except:

- A. Interferon alpha
- B. Infliximab
- C. Retinoids
- D. Methotrexate
- E. Ciclosporin

Question 96 of 117

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Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 97 of 117

A 34-year-old female with a history of discoid lupus erythematous is reviewed in clinic. The erythematous, scaly rash on her face has not responded to topical steroid creams. What is the most appropriate next step in management?

- A. UV light therapy
- B. Oral hydroxychloroquine
- C. Topical dapsone
- D. Oral prednisolone
- E. Topical hydroxychloroquine

Question 97 of 117

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- C. Topical dapsone
- D. Oral prednisolone
- E. Topical hydroxychloroquine

Discoid lupus erythematous - topical steroids --> oral hydroxychloroquine

Discoid lupus erythematous

Discoid lupus erythematous is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematous is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

Features
- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Management
- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure

Question 98 of 117

A 33-year-old woman is reviewed in the dermatology clinic with patchy, well demarcated hair loss on the scalp. This is affecting around 20% of her total scalp, and causing significant psychological distress. A diagnosis of alopecia areata is suspected. Which one of the following is an appropriate management plan?

- A. Topical 5-FU cream
- B. Autoimmune screen
- C. Topical ketoconazole
- D. Topical corticosteroid
- E. Autoimmune screen + topical ketoconazole

Question 98 of 117

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- A. Topical 5-FU cream
- B. Autoimmune screen
- C. Topical ketoconazole
- D. Topical corticosteroid
- E. Autoimmune screen + topical ketoconazole

Watchful waiting for spontaneous remission is another option. Neither the British Association of Dermatologists or Clinical Knowledge Summaries recommend screening for autoimmune disease

Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

Question 99 of 117

A 33-year-old is investigated for lethargy. The full blood count is reported as follows:

Hb 10.1 g/dl

Plt 156 * 10^9/l

WBC 3.7 * 10^9/l

His daughter was unwell one week previously with a pyrexial illness associated with a red rash on her cheeks. What is the most likely cause?

- A. Measles
- B. Coxsackie a16
- C. Group A haemolytic streptococci
- D. Parvovirus B19
- E. HHV-6 (Human Herpesvirus-6)

Question 99 of 117

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- D. Parvovirus B19
- E. HHV-6 (Human Herpesvirus-6)

Parvovirus B19

Parvovirus B19 is a DNA virus which causes a variety of clinical presentations. It was identified in the 1980's as the cause of erythema infectiosum

Erythema infectiosum (also known as fifth disease or 'slapped-cheek syndrome')

- most common presenting illness
- systemic symptoms: lethargy, fever, headache
- 'slapped-cheek' rash spreading to proximal arms and extensor surfaces

Other presentations

- asymptomatic
- pancytopaenia in immunosuppressed patients
- aplastic crises e.g. in sickle-cell disease (parvovirus B19 suppresses erythropoiesis for about a week so aplastic anaemia is rare unless there is a chronic haemolytic anaemia)

Question 100 of 117

A 35-year-old female presents tender, erythematous nodules over her forearms. Blood tests reveal:

Calcium 2.78 mmol/l

What is the most likely diagnosis?

- A. Granuloma annulare
- B. Erythema nodosum
- C. Lupus pernio
- D. Erythema multiforme
- E. Necrobiosis lipoidica

Question 100 of 117

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- C. Lupus pernio
- D. Erythema multiforme
- E. Necrobiosis lipoidica

The likely underlying diagnosis is sarcoidosis

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 101 of 117

A 72-year-old woman who is known to have type 2 diabetes mellitus and heart failure is reviewed. One week ago she was treated with oral flucloxacillin and penicillin V for a right lower limb cellulitis. Unfortunately there has been no response to treatment. What is the most appropriate next line antibiotic?

- A. Co-amoxiclav
- B. Erythromycin
- C. Clindamycin
- D. Vancomycin
- E. Gentamicin

Question 101 of 117

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Cellulitis: management

The BNF recommends penicillin + flucloxacillin as first-line treatment for cellulitis. Erythromycin is recommend in patients allergic to penicillin. Treatment failure is now commonly treated with oral clindamycin.

Question 102 of 117

A 78-year-old woman asks you for cream to treat a lesion on her left cheek. It has been present for the past nine months and is asymptomatic. On examination you find a 2 * 3 cm area of flat brown pigmentation with a jagged, irregular edge. The pigmentation on the anterior aspect of the lesion is a darker brown. What is the most likely diagnosis?

- A. Solar lentigo
- B. Dermatofibroma
- C. Lentigo maligna
- D. Bowen's disease
- E. Seborrhoeic keratosis

Question 102 of 117

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- A. Solar lentigo
- B. Dermatofibroma
- C. Lentigo maligna
- D. Bowen's disease
- E. Seborrhoeic keratosis

These lesions often present a diagnostic dilemma. The asymmetrical nature of the lesion would however point away from a diagnosis of solar lentigo.

Lentigo maligna

Lentigo maligna is a type of melanoma in-situ. It typically progresses slowly but may at some stage become invasive causing lentigo maligna melanoma.

Question 103 of 117

A 36-year-old female with a history of ulcerative colitis is diagnosed as having pyoderma gangrenosum. She presented 4 days ago with a 1 cm lesion on her right shin which rapidly ulcerated and is now painful. What is the most appropriate management?

- A. Topical hydrocortisone
- B. Oral prednisolone
- C. Surgical debridement
- D. Topical tacrolimus
- E. Infliximab

Question 103 of 117

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- B. Oral prednisolone
- C. Surgical debridement
- D. Topical tacrolimus
- E. Infliximab

Topical therapy does have a role in pyoderma gangrenosum and it may seem intuitive to try this first before moving on to systemic treatment. However, pyoderma gangrenosum has the potential to evolve rapidly and for this reason oral prednisolone is usually given as initial treatment. For a review see BMJ 2006;333:181-184

Pyoderma gangrenosum

Features
- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

Causes*
- idiopathic in 50%
- IBD: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

Management
- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Question 104 of 117

Each one of the following is associated with hypertrichosis, except:

- A. Anorexia nervosa
- B. Porphyria cutanea tarda
- C. Psoriasis
- D. Minoxidil
- E. Ciclosporin

Question 104 of 117

Each one of the following is associated with hypertrichosis, except:

- A. Anorexia nervosa
- B. Porphyria cutanea tarda
- C. Psoriasis
- D. Minoxidil
- E. Ciclosporin

Hirsuitism and hypertrichosis

Hirsuitism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Causes of hirsuitism
- polycystic ovarian syndrome
- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

Causes of hypertrichosis
- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa

Question 105 of 117

A 19-year-old man is started on isotretinoin for severe nodulo-cystic acne. Which one of the following side-effects is most likely to occur?

- A. Low mood
- B. Thrombocytopaenia
- C. Raised plasma triglycerides
- D. Reversible alopecia
- E. Dry skin

Question 105 of 117

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- A. Low mood
- B. Thrombocytopaenia
- C. Raised plasma triglycerides
- D. Reversible alopecia
- E. Dry skin

Dry skin is the most common side-effect of isotretinoin

Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

Adverse effects

- teratogenicity: females MUST be using two forms of contraception (e.g. combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Question 106 of 117

A 45-year-old man who presented with itchy lesions on his hands is diagnosed with scabies. It is decided to treat him with permethrin 5%. You have explained the need to treat all members of the household and hot wash all bedding and clothes. What advice should be given about applying the cream?

- A. From neck down + leave for 12 hours
- B. All skin including scalp + leave for 12 hours + retreat in 2 days
- C. All skin including scalp + leave for 12 hours + retreat in 7 days
- D. From neck down + leave for 4 hours
- E. From neck down + leave for 12 hours + retreat in 7 days

Question 106 of 117

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- D. From neck down + leave for 4 hours
- E. From neck down + leave for 12 hours + retreat in 7 days

Scabies - permethrin treatment: all skin including scalp + leave for 12 hours + retreat in 7 days

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation (and common practice).

Scabies

Scabies is caused by the mite Sarcoptes scabiei and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8–12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

Question 107 of 117

Which one of the following antibiotics is most associated with the development of Stevens-Johnson syndrome?

- A. Co-trimoxazole
- B. Ethambutol
- C. Chloramphenicol
- D. Ciprofloxacin
- E. Gentamicin

Question 107 of 117

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- E. Gentamicin

Stevens-Johnson syndrome

Stevens-Johnson syndrome severe form of erythema multiforme associated with mucosal involvement and systemic symptoms

Features
- rash is typically maculopapular with target lesions being characteristic. May develop into vesicles or bullae
- mucosal involvement
- systemic symptoms: fever, arthralgia

Causes
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- viruses: herpes simplex virus, Orf
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill
- connective tissue disease e.g. SLE
- sarcoidosis
- malignancy

Question 108 of 117

A 33-year-old man presents complaining of an itchy scalp and dandruff. On examination he is noted to have eczema on his scalp, behind his ears and around his nose. He has tried 'Head and Shoulders' and 'Neutrogen T-gel' but with poor results. Which one of the following is the most appropriate treatment for his scalp?

- A. Topical hydrocortisone
- B. Oral metronidazole
- C. Topical selenium sulphide
- D. Oral terbinafine
- E. Topical ketoconazole

Question 108 of 117

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Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called Malassezia (formerly known as Pityrosporum ovale). It is common, affecting around 2% of the general population

Features
- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

Associated conditions include
- HIV
- Parkinson's disease

Scalp disease management
- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

Face and body management
- topical antifungals: e.g. ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

Question 109 of 117

A 34-year-old patient who is known to have psoriasis presents with erythematous skin in the groin and genital area. He also has erythematous skin in the axilla. In the past he has expressed a dislike of messy or cumbersome creams. What is the most appropriate treatment?

- A. Topical steroid
- B. Topical dithranol
- C. Topical clotrimazole
- D. Coal tar
- E. Topical calcipotriol

Question 109 of 117

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- C. Topical clotrimazole
- D. Coal tar
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Flexural psoriasis - topical steroid

This patient has flexual psoriasis which responds well to topical steroids. Topical calcipotriol is usually irritant in flexures. Mild tar preparations are an option but may be messy and cumbersome.

Psoriasis: management

Chronic plaque psoriasis
- simple emollients
- coal tar: probably inhibit DNA synthesis
- topical corticosteroids: mild steroids are sometimes used in facial psoriasis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Flexural psoriasis
- emollients
- topical steroids

Scalp psoriasis
- calcipotriol lotion
- steroid lotion + shampoo
- combination shampoo: betamethasone with vitamin D analogues
- coconut oil compound shampoos (combination of coal tar, salicylic acid and sulphur)
- tar shampoo

Phototherapy
- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy
- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab

Ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials.

Question 110 of 117

A 50-year-old man presents with shiny, flat-topped papules on the palmar aspect of the wrists. He is mainly bothered by the troublesome and persistent itching. A diagnosis of lichen planus is suspected. What is the most appropriate treatment?

- A. Refer for punch biopsy
- B. Emollients + oral antihistamine
- C. Topical dapsone
- D. Topical clotrimazole
- E. Topical clobetasone butyrate

Question 110 of 117

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- C. Topical dapsone
- D. Topical clotrimazole
- E. Topical clobetasone butyrate

Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

Features
- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon seen
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:
- gold
- quinine
- thiazides

Management
- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Question 111 of 117

A 17-year-old male is reviewed six weeks after starting an oral antibiotic for acne vulgaris. He stopped taking the drug two weeks ago due to perceived alteration in his skin colour, and denies been exposed to strong sunlight for the past six months. On examination he has generalised increased skin pigmentation, including around the buttocks. Which one of the following antibiotics was he likely to be taking?

- A. Doxycycline
- B. Oxytetracycline
- C. Tetracycline
- D. Erythromycin
- E. Minocycline

Question 111 of 117

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- A. Doxycycline
- B. Oxytetracycline
- C. Tetracycline
- D. Erythromycin
- E. Minocycline

Minocycline can cause irreversible skin pigmentation and is now considered a second line drug in acne. Photosensitivity secondary to tetracycline/doxycycline is less likely given the generalised distribution of the pigmentation and the failure to improve following drug withdrawal

Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions.
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Question 112 of 117

A 30-year-old man presents with painful, purple coloured lesions on his shins. Some of these lesions have started to heal and no evidence of scarring is seen. These have been present for the past 2 weeks. There is no past medical history of note and he takes no regular medications. What is the most useful next investigation?

- A. Liver function tests
- B. Anti-nuclear antibody
- C. ECG
- D. HIV test
- E. Chest x-ray

Question 112 of 117

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- A. Liver function tests
- B. Anti-nuclear antibody
- C. ECG
- D. HIV test
- E. Chest x-ray

The likely diagnosis here is erythema nodosum (EN). All these tests may have a place but a chest x-ray is important as it helps exclude sarcoidosis and tuberculosis, two important cause of EN

Erythema nodosum

Overview
- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

Causes
- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Question 113 of 117

A 67-year-old man is diagnosed with actinic keratoses on his right temple and prescribed fluorouracil cream. One week later he presents as the skin where he is applying treatment has become red and sore. On examination there is no sign of weeping or blistering. What is the most appropriate action?

- A. Continue fluorouracil cream + review in 1 week
- B. Complete a 'Yellow Card'
- C. Stop fluorouracil cream + prescribe topical hydrocortisone
- D. Continue fluorouracil cream + prescribe topical hydrocortisone to use concurrently
- E. Stop fluorouracil cream

Question 113 of 117

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- E. Stop fluorouracil cream

This is a normal reaction to treatment. Fluorouracil should be continued for at least another week before starting topical steroids.

Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

Features
- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

Management options include
- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

Question 114 of 117

A 65-year-old woman with blistering lesions on her leg is diagnosed as having bullous pemphigoid. What is the most appropriate initial management?

- A. Reassurance
- B. Topical corticosteroids
- C. Oral itraconazole
- D. Screen for solid-tumour malignancies
- E. Oral corticosteroids

Question 114 of 117

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- D. Screen for solid-tumour malignancies
- E. Oral corticosteroids

Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include
- itchy, tense blisters typically around flexures
- mouth is usually spared*

Skin biopsy
- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management
- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Question 115 of 117

Which one of the following statements regarding fungal nail infections is incorrect?

- A. *Candida* accounts for less than 10% of cases
- B. Diagnosis should be confirmed by microbiology before starting treatment
- C. Treatment is successful in around 90-95% of people
- D. Thickened, rough, opaque nails are typical
- E. Suitable investigations include nail clippings

Question 115 of 117

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- D. Thickened, rough, opaque nails are typical
- E. Suitable investigations include nail clippings

Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by
- dermatophytes - mainly Trichophyton rubrum, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

Features
- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

Investigation
- nail clippings
- scrapings of the affected nail

Management
- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

Question 116 of 117

Which of the following skin conditions associated with malignancy are not correctly paired?

- A. Erythroderma and lymphoma
- B. Necrolytic migratory erythema and gastrinoma
- C. Acanthosis nigricans and gastrointestinal cancer
- D. Sweet's syndrome and myelodysplasia
- E. Erythema gyratum repens and lung cancer

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- E. Erythema gyratum repens and lung cancer

Necrolytic migratory erythema is associated with glucagonomas

Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	**Associated malignancies**
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Bronchial and breast cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Question 117 of 117

A man presents with an area of dermatitis on his left wrist. He thinks he may be allergic to nickel. Which one of the following is the best test to investigate this possibility?

- A. Skin patch test
- B. Radioallergosorbent test (RAST)
- C. Nickel IgG levels
- D. Skin prick test
- E. Nickel IgM levels

Question 117 of 117

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- C. Nickel IgG levels
- D. Skin prick test
- E. Nickel IgM levels

Allergy tests

Skin prick test	Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes Useful for food allergies and also pollen
Radioallergosorbent test (RAST)	Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive) Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines
Skin patch testing	Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The results are read 48 hours later by a dermatologist

Question 1 of 138

Which one of the following is a recognised cause of hypokalaemia associated with hypertension

- A. Liddle's syndrome
- B. Bartter's syndrome
- C. Gitelman syndrome
- D. Ciclosporin
- E. Renal tubular acidosis

Question 1 of 138

Which one of the following is a recognised cause of hypokalaemia associated with hypertension

- A. Liddle's syndrome
- B. Bartter's syndrome
- C. Gitelman syndrome
- D. Ciclosporin
- E. Renal tubular acidosis

Liddle's syndrome: hypokalaemia + hypertension

Liddle's syndrome is an autosomal dominant disorder that mimics hyperaldosteronism, resulting in hypokalaemia associated with hypertension.

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension.

Gitelman's syndrome is due to a defect in the thiazide-sensitive Na^+ Cl- transporter in the distal convoluted tubule. It is associated with hypokalaemia and normotension.

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 2 of 138

A 15-year-old girl is investigated for primary amenorrhoea, despite having developed secondary sexual characteristics at 11 years of age. On examination she has well developed breasts with scanty pubic hair and small bilateral groin swellings. What is the most likely diagnosis?

A. Congenital adrenal hyperplasia

B. Polycystic ovarian syndrome

C. Turner's syndrome

D. Complete androgen insensitivity syndrome

E. Mullerian duct agenesis

Question 2 of 138

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- A. Congenital adrenal hyperplasia
- B. Polycystic ovarian syndrome
- C. Turner's syndrome
- D. Complete androgen insensitivity syndrome
- E. Mullerian duct agenesis

Androgen insensitivity syndrome

Androgen insensitivity syndrome is an X-linked recessive condition due to end-organ resistance to testosterone causing genotypically male children (46XY) to have a female phenotype. Complete androgen insensitivity syndrome is the new term for testicular feminisation syndrome

Features
- 'primary amennorhoea'
- undescended testes causing groin swellings
- breast development may occur as a result of conversion of testosterone to oestradiol

Diagnosis
- buccal smear or chromosomal analysis to reveal 46XY genotype

Management
- counselling - raise child as female
- bilateral orchidectomy (increased risk of testicular cancer due to undescended testes)
- oestrogen therapy

Question 3 of 138

A 48-year-old man who was diagnosed with type 2 diabetes mellitus presents for review. During his annual review he was noted to have the following results:

Total cholesterol	5.3 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	3.1 mmol/l
Triglyceride	1.7 mmol/l
HbA1c	6.4%

His current medication is metformin 500mg tds. According to recent NICE guidelines, what is the most appropriate action?

- A. Simvastatin 40mg on
- B. Lifestyle advice, repeat lipid profile in 3 months
- C. Nicotinic acid
- D. Atorvastatin 40mg on
- E. Increase his metformin slowly to 1g tds

Question 3 of 138

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- D. Atorvastatin 40mg on
- E. Increase his metformin slowly to 1g tds

Patients over the age of 40 years with type 2 diabetes mellitus should be started on a statin if they have any other risk factors for cardiovascular disease, such as smoking and hypertension. This patient has a 'high-risk lipid profile' and should therefore be offered statin therapy. Please see the link for more details.

Question 4 of 138

A 45-year-old man is referred to the acute medical unit. He had presented earlier in the day to the GP complaining of ongoing fatigue and polydipsia. A BM taking in the surgery was 22.3. On examination he is an obese man (BMI 36) with a pulse of 84 bpm and blood pressure of 144/84 mmHg. Blood tests reveal the following:

Na^+	140 mmol/l
K^+	3.9 mmol/l
Bicarbonate	23 mmol/l
Urea	5.2 mmol/l
Creatinine	101 µmol/l
Glucose	21.2 mmol/l

What is the most appropriate initial management?

- A. Gliclazide
- B. Pioglitazone
- C. Weight loss
- D. Metformin
- E. Commence insulin therapy

Question 4 of 138

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- C. Weight loss
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- E. Commence insulin therapy

Weight reduction alone would be insufficient in this patient with frank diabetes

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis* with severe liver disease or renal failure

Contraindications**

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 5 of 138

A 46-year-old man with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.7
2	7.6

How should these results be interpreted?

- A. Normal
- B. Impaired fasting glucose and impaired glucose tolerance
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Question 5 of 138

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- A. Normal
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- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Both the fasting and two-hour glucose are within normal limits.

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.
Diabetes mellitus

If the patient is symptomatic:
- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:
- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 6 of 138

A 45-year-old man is investigated following referral to the endocrinology clinic with polydipsia. Plasma glucose and calcium are normal. A water deprivation test is performed with the following results:

Starting plasma osm.	292 mOsmol/l
Final urine osm.	142 mOsmol/l
Urine osm. post-DDAVP	885 mOsmol/l

What is the most likely diagnosis?

- A. Psychogenic polydipsia
- B. Nephrogenic diabetes insipidus
- C. Primary hyperparathyroidism
- D. Pseudohypoparathyroidism
- E. Cranial diabetes insipidus

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- E. Cranial diabetes insipidus

A dramatic improvement is seen in the ability of the kidneys to concentrate urine following the administration of DDAVP. This points towards a diagnosis of cranial diabetes insipidus

Water deprivation test

Method

- prevent patient drinking water
- ask patient to empty bladder
- hourly urine and plasma osmolalities

	Starting plasma osm.	**Final urine osm.**	**Urine osm. post-DDAVP**
Normal	Normal	> 600	> 600
Psychogenic polydipsia	Low	> 400	> 400
Cranial DI	High	< 300	> 600
Nephrogenic DI	High	< 300	< 300

Question 7 of 138

A 56-year-old man is reviewed in the Cardiology outpatient clinic following a myocardial infarction one year previously. During his admission he was found to be hypertensive and diabetic. He complains that he has put on 5kg in weight in the past 6 months. Which of his medications may be contributing to his weight gain?

- A. Metformin
- B. Losartan
- C. Clopidogrel
- D. Gliclazide
- E. Simvastatin

Question 7 of 138

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- A. Metformin
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- D. Gliclazide
- E. Simvastatin

Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present.

Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- increased appetite and weight gain

Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- photosensitivity
- peripheral neuropathy

Sulfonylureas should be avoided in breast feeding and pregnancy

Question 8 of 138

What causes increased sweating in patients with acromegaly?

A. Increased sodium content in sweat

B. Decreased LH and FSH secondary to hypopituitarism

C. Episodic hypoglycaemia

D. Low-grade chronic pyrexia

E. Sweat gland hypertrophy

Question 8 of 138

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- D. Low-grade chronic pyrexia
- E. Sweat gland hypertrophy

Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

Features

- coarse, oily skin , large tongue, prognathism, interdental spaces
- spade-like hands, increase in shoe size
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

Complications

- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Question 9 of 138

Each one of the following is a cause of cranial diabetes insipidus, except:

- A. Pituitary surgery
- B. Lithium
- C. Histiocytosis X
- D. Craniopharyngioma
- E. Post head-injury

Question 9 of 138

Each one of the following is a cause of cranial diabetes insipidus, except:

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- B. Lithium
- C. Histiocytosis X
- D. Craniopharyngioma
- E. Post head-injury

Lithium causes a nephrogenic diabetes insipidus

Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 10 of 138

Which one of the following statements regarding maturity-onset diabetes of the young (MODY) is true?

- A. There is usually a strong family history
- B. Body mass index is typically > 30
- C. Doesn’t respond to glimepiride
- D. Autosomal recessive inheritance
- E. Frequent episodes of diabetic ketoacidosis are typical

Question 10 of 138

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MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

MODY 3
- 60% of cases
- due to a defect in the HNF-1 alpha gene

MODY 2
- 20% of cases
- due to a defect in the glucokinase gene

Question 11 of 138

A 45-year-old woman is investigated for weight gain. She had had been unwell for around four months and described a combination of symptoms including depression, facial male-pattern hair growth and reduced libido. During the work-up she was found to be hypertensive with a blood pressure of 170/100 mmHg. Which one of the following tests is most likely to be diagnostic?

- A. Renin:aldosterone levels
- B. High-dose dexamethasone suppression test
- C. Pelvic ultrasound
- D. Overnight dexamethasone suppression test
- E. 24 hr urinary free cortisol

Question 11 of 138

A 45-year-old woman is investigated for weight gain. She had had been unwell for around four months and described a combination of symptoms including depression, facial male-pattern hair growth and reduced libido. During the work-up she was found to be hypertensive with a blood pressure of 170/100 mmHg. Which one of the following tests is most likely to be diagnostic?

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The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

This patient has Cushing's syndrome as evidenced by the weight gain, hirsuitism, depression and hypertension. Polycystic ovarian syndrome may give some of these features but would not cause such an elevated blood pressure.

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 12 of 138

A 9-year-old boy is investigated for lethargy. Examination is unremarkable with a blood pressure of 102/62 mmHg. Blood tests reveal:

Na^+	140 mmol/l
K^+	2.6 mmol/l
Bicarbonate	33 mmol/l
Urea	4.2 mmol/l
Creatinine	91 µmol/l

Which one of the following conditions is most likely to be responsible?

- A. Cushing's syndrome
- B. Conn's syndrome
- C. 11-beta hydroxylase deficiency
- D. Bartter's syndrome
- E. Liddle's syndrome

Question 12 of 138

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- E. Liddle's syndrome

Bartter's syndrome is associated with normotension

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 13 of 138

A 35-year-old female who has recently being diagnosed with Grave's disease presents for review 3 months after starting a 'block and replace' regime with carbimazole and thyroxine. She is concerned about developing thyroid eye disease. What is the best way that her risk of developing thyroid eye disease can be reduced?

- A. Reduce alcohol intake
- B. A diet rich in omega-3 fatty acids
- C. Regular exercise
- D. Stop smoking
- E. Lose weight

Question 13 of 138

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- E. Lose weight

Smoking is the most important modifiable risk factor for the development of thyroid eye disease

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 14 of 138

A 46-year-old woman is referred to endocrine with a tender neck swelling. Blood results are as follows:

TSH <0.1 mU/l

T4 188 nmol/l

Hb 14.2 g/dl

Plt 377 * 10^9/l

WBC 6.4 * 10^9/l

ESR 65 mm/hr

Technetium thyroid scan shows decreased uptake globally

What is the most likely diagnosis?

- A. Sick thyroid syndrome
- B. Acute bacterial thyroiditis
- C. Hashimoto's thyroiditis
- D. Subacute thyroiditis
- E. Toxic multinodular goitre

Question 14 of 138

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- C. Hashimoto's thyroiditis
- D. Subacute thyroiditis
- E. Toxic multinodular goitre

Subacute thyroiditis is suggested by the tender goitre, hyperthyroidism and raised ESR. The globally reduced uptake on technetium thyroid scan is also typical

Subacute (De Quervain's) thyroiditis

Subacute thyroiditis (also known as De Quervain's thyroiditis) is thought to occur following viral infection and typically presents with hyperthyroidism

Features

- hyperthyroidism
- painful goitre
- raised ESR
- globally reduced uptake on iodine-131 scan

Management

- usually self-limiting - most patients do not require treatment
- thyroid pain may respond to aspirin or other NSAIDs
- in more severe cases steroids are used, particularly if hypothyroidism develops

Question 15 of 138

A 68-year-old woman is found to have the following blood tests:
TSH 0.05 mu/l
Free T4 19 pmol/l (range 9-25 pmol/l)
Free T3 7 pmol/l (range 3-9 pmol/l)

If left untreated, what are the most likely possible consequences?

- A. Supraventricular arrhythmias and osteoporosis
- B. Supraventricular arrhythmias and hyperlipidaemia
- C. Hypothyroidism and impaired glucose tolerance
- D. Myasthenia gravis and hypothyroidism
- E. Impaired glucose tolerance and hyperlipidaemia

Question 15 of 138

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- D. Myasthenia gravis and hypothyroidism
- E. Impaired glucose tolerance and hyperlipidaemia

Subclinical hyperthyroidism

Subclinical hyperthyroidism is an entity which is gaining increasing recognition. It is defined as:

- normal serum free thyroxine and triiodothyronine levels
- with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l)

Causes

- multinodular goitre, particularly in elderly females
- excessive thyroxine may give a similar biochemical picture

The importance in recognising subclinical hyperthyroidism lies in the potential effect on the cardiovascular system (atrial fibrillation) and bone metabolism (osteoporosis). It may also impact on quality of life and increase the likelihood of dementia

Management

- TSH levels often revert back to normal - therefore levels must be persistently low to warrant intervention
- a reasonable treatment option is a therapeutic trial of low-dose antithyroid agents for approximately 6 months in an effort to induce a remission

Question 16 of 138

A 61-year-old man presents as he developed enlargement of his breast tissue. He has become very self-conscious and is worried about going on holiday in the summer. Which one of the following drugs is most likely to be responsible?

- A. Amitriptyline
- B. Isoniazid
- C. Verapamil
- D. Methyldopa
- E. Spironolactone

Question 16 of 138

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- D. Methyldopa
- E. Spironolactone

All the above drugs may cause gynaecomastia but spironolactone is the most common cause.

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia
- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

Drug causes of gynaecomastia
- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia
- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

Question 17 of 138

A 53 year man presents as his wife has noticed a change in his appearance. He has also noticed his hands seem larger. On examination blood pressure is 170/94 and he is noted to have bitemporal hemianopia. What is the most appropriate first-line treatment?

- A. Octreotide
- B. External irradiation
- C. Pegvisomant
- D. Trans-sphenoidal surgery
- E. Bromocriptine

Question 17 of 138

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- D. Trans-sphenoidal surgery
- E. Bromocriptine

Trans-sphenoidal surgery is the treatment of choice in acromegaly. There is no significant evidence base supporting the use of pre-operative octreotide

Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists
- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue
- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant
- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

Question 18 of 138

A 45-year-old female is admitted to the Emergency Department with abdominal pain associated with vomiting. She has a past medical history of hypothyroidism and takes thyroxine. On examination she is pyrexial at 37.6ºC. Pulse is 110 bpm with a blood pressure of 100/64 mmHg. Blood results show the following:

Na^+	131 mmol/l
K^+	4.9 mmol/l
Urea	8.1 mmol/l
Creatinine	110 µmol/l
Glucose	3.3 mmol/l

What treatment should be given first?

- A. Ceftriaxone + benzylpenicillin
- B. Glucagon
- C. Propranolol
- D. Triiodothyronine
- E. Hydrocortisone

Question 18 of 138

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This is a typical history of Addison's. Patients may have a history of other autoimmune conditions such as thyroid disorders. Steroids should be given as soon as possible

Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

Features

- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

Other causes of hypoadrenalism

Primary causes

- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

Secondary causes

- pituitary disorders (e.g. tumours, irradiation, infiltration)

Exogenous glucocorticoid therapy

Question 19 of 138

A 46-year-old man presents as he is concerned about reduced libido, erectile dysfunction and excessive thirst. His wife also reports that he has 'no energy' and is generally listless. During the review of systems he also complains of pains in both hands. Which one of the following investigations is most likely to reveal the diagnosis?

- A. Ferritin
- B. Testosterone
- C. Cortisol
- D. Blood glucose
- E. Prolactin

Question 19 of 138

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- B. Testosterone
- C. Cortisol
- D. Blood glucose
- E. Prolactin

The above patient has symptoms consistent with haemochromatosis. The excessive thirst is secondary to untreated diabetes mellitus. Diabetes mellitus itself would not normally cause reduced libido or arthralgia.

Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 20 of 138

In patients with suspected insulinoma, which one of the following is considered the best investigation?

- A. Oral glucose tolerance test
- B. Insulin tolerance test
- C. Early morning C-peptide levels
- D. Glucagon stimulation test
- E. Supervised fasting

Question 20 of 138

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- E. Supervised fasting

Insulinoma is diagnosed with supervised prolonged fasting

CT of the pancreas is also useful in demonstrating a lesion

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 21 of 138

A diabetic man is diagnosed as having painful diabetic neuropathy in his feet. He has no other medical history of note. What is the most suitable first-line treatment to relieve his pain?

- A. Duloxetine
- B. Gabapentin
- C. Carbamazepine
- D. Referral to pain management clinic
- E. Pregabalin

Question 21 of 138

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- C. Carbamazepine
- D. Referral to pain management clinic
- E. Pregabalin

Diabetic neuropathy

NICE updated it's guidance on the management of diabetic neuroopathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

Question 22 of 138

An 18-year-old girl is admitted to the Emergency Department with an episode of sweating and dizziness. She is brought in by her father who has type 2 diabetes mellitus as he is worried she may be diabetic. He describes a number of similar episodes for the past two weeks. Her BM on admission is 1.9 mmol/l so the following bloods are taken:

Plasma glucose	1.8 mmol/l
Insulin	15 mg/ml (6-10 mg/ml)
Proinsulin	22% (22-24%)
C-peptide	0.15 nmol/l (0.2-0.4 nmol/l)

What is the most likely diagnosis?

- A. Diabetes mellitus
- B. Insulinoma
- C. Nesidioblastosis
- D. Insulin abuse
- E. Sulfonylurea abuse

Question 22 of 138

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- A. Diabetes mellitus
- B. Insulinoma
- C. Nesidioblastosis
- D. Insulin abuse
- E. Sulfonylurea abuse

The raised insulin with low c-peptide level points to a diagnosis of insulin abuse. C-peptide levels would be raised in a patient following sulfonylurea abuse

Hypoglycaemia

Causes
- insulinoma - increased ratio of proinsulin to insulin
- self-administration of insulin/sulphonylureas
- liver failure
- Addison's disease
- alcohol

Other possible causes in children
- nesidioblastosis - beta cell hyperplasia

Question 23 of 138

A 55-year-old woman is investigated following an osteoporotic hip fracture. The following results are obtained:

TSH < 0.05 mu/l

Free T4 29 pmol/l

Which one of the following autoantibodies is most likely to be present?

- A. Anti-TSH receptor stimulating autoantibodies
- B. Anti-nuclear antibodies
- C. Anti-thyroglobulin autoantibodies
- D. Anti-microsomal antibodies
- E. Anti-thyroid peroxidase autoantibodies

Question 23 of 138

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- E. Anti-thyroid peroxidase autoantibodies

Anti-TSH receptor stimulating autoantibodies (often referred to as Thyroid Stimulating Immunoglobulins) are almost diagnostic of Graves' disease, the most common cause of thyrotoxicosis in the UK

Graves' disease: features

Features seen in Graves' but not in other causes of thyrotoxicosis
- eye signs: exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

Autoantibodies
- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

Question 24 of 138

Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

- A. Diabetes mellitus
- B. Bendrofluazide
- C. Nephrotic syndrome
- D. Alcohol
- E. Obesity

Question 24 of 138

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- A. Diabetes mellitus
- B. Bendrofluazide
- C. Nephrotic syndrome
- D. Alcohol
- E. Obesity

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia
- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia
- nephrotic syndrome
- cholestasis
- hypothyroidism

Question 25 of 138

A 71-year-old woman with a history of type 2 diabetes mellitus presents with lethargy and polyuria. A diagnosis of hyperosmolar hyperglycaemic state is considered. Which one of the following findings would be least consistent with this diagnosis?

- A. pH of 7.38
- B. Ketones 1+ in urine
- C. Serum osmolality of 310 mosmol/kg
- D. Serum bicarbonate of 19 mmol/l
- E. Glucose of 45 mmol/l

Question 25 of 138

A 71-year-old woman with a history of type 2 diabetes mellitus presents with lethargy and polyuria. A diagnosis of hyperosmolar hyperglycaemic state is considered. Which one of the following findings would be least consistent with this diagnosis?

- A. pH of 7.38
- B. Ketones 1+ in urine
- C. Serum osmolality of 310 mosmol/kg
- D. Serum bicarbonate of 19 mmol/l
- E. Glucose of 45 mmol/l

A trace of ketones may be found in hyperosmolar hyperglycaemic state. Serum osmolality is typically > 320 mosmol/kg

Hyperosmolar hyperglycaemic state

The American Diabetes Association criteria for the diagnosis of hyperosmolar hyperglycaemic state (HHS) is as follows:

- glucose > 33.3 mmol/l
- pH > 7.30
- serum bicarbonate > 15 mmol/l
- serum osmolality > 320 mosmol/kg
- traces of ketones may be present in urines

Question 26 of 138

A 64-year-old man with a history of type 2 diabetes mellitus is admitted with chest pain to the Emergency Department. An ECG shows ST elevation in the anterior leads and he is thrombolysed and transferred to the Coronary Care Unit (CCU). His usual medication includes simvastatin, gliclazide and metformin. How should his diabetes be managed whilst in CCU?

- A. Stop metformin + continue gliclazide at a higher dose
- B. Subcutaneous insulin: basal-bolus regime
- C. Continue metformin + gliclazide at same dose
- D. Intravenous insulin
- E. Subcutaneous insulin: biphasic insulin regime

Question 26 of 138

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- C. Continue metformin + gliclazide at same dose
- D. Intravenous insulin
- E. Subcutaneous insulin: biphasic insulin regime

The benefits of tight glycaemic control following a myocardial infarction were initially established by the DIGAMI study.

Myocardial infarction: management

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

In the absence of contraindications, all patients should be given

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

NICE suggest the following in terms of oxygen therapy:

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

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

With regards to thrombolysis:

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

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

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

Question 27 of 138

A 28-year-old woman with polycystic ovarian syndrome consults you as she is having problems becoming pregnant. She has a past history of oligomenorrhea and has previously recently stopped taking a combined oral contraceptive pill. Despite stopping the pill 6 months ago she is still not having regular periods. Her body mass index is 28 kg/m^2. Apart from advising her to lose weight, which one of the following interventions is most effective in increasing her chances of conceiving?

- A. Metformin
- B. Bromocriptine
- C. Laparoscopic ovarian cautery
- D. Clomifene
- E. Orlistat

Question 27 of 138

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- B. Bromocriptine
- C. Laparoscopic ovarian cautery
- D. Clomifene
- E. Orlistat

Infertility in PCOS - clomifene is superior to metformin

Whilst metformin has a role in the management of infertility it should be used second-line to anti-oestrogens such as clomifene. Similar questions to this often appear in which clomifene is not an option, in this case metformin is clearly the right answer.

Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based

General

- weight reduction if appropriate
- if a women requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

Hirsuitism and acne

- a COC pill may be used help manage hirsuitism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

Infertility

- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen* therapies such as clomifene
- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

Question 28 of 138

What is the mechanism of action of rosiglitazone?

- A. PPAR-gamma receptor antagonist
- B. PPAR-alpha receptor antagonist
- C. PPAR-alpha receptor agonist
- D. PPAR-gamma receptor agonist
- E. Increases endogenous insulin secretion

Question 28 of 138

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- C. PPAR-alpha receptor agonist
- D. PPAR-gamma receptor agonist
- E. Increases endogenous insulin secretion

Glitazones are agonists of PPAR-gamma receptors

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 29 of 138

A 45-year-old female is reviewed in the medical clinic with a two month history of lethargy. Blood tests reveal the following:

Na^+	129 mmol/l
K^+	5.1 mmol/l
Urea	5.3 mmol/l
Creatinine	99 µmol/l
Total T4	66 nmol/l

Which one of the following investigations is most likely to reveal the diagnosis?

- A. Serum glucose
- B. TSH
- C. Free T4
- D. Overnight dexamethasone suppression test
- E. Short synacthen test

Question 29 of 138

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- E. Short synacthen test

The short synacthen test is the best test to diagnose Addison's disease

Hyponatraemia and a high potassium in a patient with lethargy is highly suggestive of Addison's disease. The thyroxine level is slightly low and she may indeed have co-existing hypothyroidism but this would not explain the high potassium

Many labs have an upper reference range for potassium of 5.5 mmol/l, but in the context of the other results hypoadrenalism should be suspected

Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a short ACTH test. Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Question 30 of 138

A 45-year-old man is reviewed in the diabetes clinic. The following results are obtained:

Urinalysis NAD

HbA1c 8.6%

Gliclazide is added to the metformin he already takes. What is the minimum time period after which the HbA1c should be repeated ?

- A. 6 months
- B. 1 month
- C. 2 weeks
- D. 3 months
- E. 4 months

Question 30 of 138

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- B. 1 month
- C. 2 weeks
- D. 3 months
- E. 4 months

HbA1C - recheck after 2-3 months

A more accurate answer would probably be 2 months but this is not given as an option. See the explanation below

Glycosylated haemoglobin

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HBA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose = (2 * HbA1c) - 4.5

Question 31 of 138

A 36-year-old woman presents with feeling tired and cold all the time. On examination a firm, non-tender goitre is noted. Blood tests reveal the following:

TSH 24.2 mU/l

Free T4 5.4 pmol/l

What is the most likely diagnosis?

- A. Primary atrophic hypothyroidism
- B. Pituitary failure
- C. De Quervain's thyroiditis
- D. Iodine deficiency
- E. Hashimoto's thyroiditis

Question 31 of 138

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- D. Iodine deficiency
- E. Hashimoto's thyroiditis

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

The combination of a goitre with hypothyroidism points to a diagnosis of Hashimoto's.

Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

Features

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

Question 32 of 138

Which one of the following is not part of the diagnostic criteria for the metabolic syndrome?

- A. High triglycerides
- B. Low HDL
- C. High LDL
- D. Central obesity
- E. Hypertension

Question 32 of 138

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- C. High LDL
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High LDL levels are not part of the World Health Organization or International Diabetes Federation diagnostic criteria

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 33 of 138

A 45-year-old man presents with bitemporal hemianopia and spade-like hands. What is the definite test to confirm the diagnosis?

- A. Early morning growth hormone
- B. Insulin tolerance test
- C. Oral glucose tolerance with growth hormone measurements
- D. Random insulin-like growth factor 1 (IGF-!)
- E. Short ACTH test

Question 33 of 138

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- C. Oral glucose tolerance with growth hormone measurements
- D. Random insulin-like growth factor 1 (IGF-!)
- E. Short ACTH test

The diagnostic test for acromegaly is an oral glucose tolerance with growth hormone measurements

Acromegaly: investigations

Growth hormone (GH) levels vary during the day and are therefore not diagnostic. The definitive test is the oral glucose tolerance (OGTT) with serial GH measurements. Serum IGF-1 may also be used as a screening test and is sometimes used to monitor disease

Oral glucose tolerance test

- in normal patients GH is suppressed to < 2 mu/L with hyperglycaemia
- in acromegaly there is no suppression of GH
- may also demonstrate impaired glucose tolerance which is associated with acromegaly

A pituitary MRI may demonstrate a pituitary tumour

Question 34 of 138

A 54-year-old woman presents to the Emergency Department with confusion and fever. She has a past history of thyrotoxicosis previously treated with radioiodine therapy. On examination she has a pulse of 120/min regular, blood pressure 150/90 mmHg, temperature of 39.1ºC and a respiratory rate of 18/min. Examination of the cardiorespiratory system is unremarkable and urine dipstick is clear. Blood results showed the following:

Free T4 84 pmol/l (normal range 10–22 pmol/l)

Free T3 29 pmol/l (2.5–5.5 pmol/l)

TSH < 0.01 mU/l (0.5–4.0 mU/l)

Which one of the following does not have a role in the subsequent management?

- A. Lugol's iodine
- B. Propranolol
- C. Propylthiouracil
- D. Bicarbonate
- E. Dexamethasone

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- C. Propylthiouracil
- D. Bicarbonate
- E. Dexamethasone

There is no indication for giving bicarbonate in this scenario.

Thyroid storm

Thyroid storm is a rare but life-threatening complication of thyrotoxicosis. It is typically seen in patients with established thyrotoxicosis and is rarely seen as the presenting feature. Iatrogenic thyroxine excess does not usually result in thyroid storm

Clinical features include:

- fever > 38.5ºC
- tachycardia
- confusion and agitation
- nausea and vomiting
- hypertension
- heart failure
- abnormal liver function test

Management

- symptomatic treatment e.g. paracetamol
- treatment of underlying precipitating event
- anti-thyroid drugs: e.g. methimazole or propylthiouracil
- Lugol's iodine
- dexamethasone - e.g. 4mg IV qds - blocks the conversion of T4 to T3
- propranolol

Question 35 of 138

Which one of the following is not associated with primary hyperparathyroidism?

- A. Hypotension
- B. Multiple endocrine neoplasia type 1
- C. Multiple endocrine neoplasia type 2a
- D. Depression
- E. Pancreatitis

Question 35 of 138

Which one of the following is not associated with primary hyperparathyroidism?

- A. Hypotension
- B. Multiple endocrine neoplasia type 1
- C. Multiple endocrine neoplasia type 2a
- D. Depression
- E. Pancreatitis

Primary hyperparathyroidism is associated with hypertension

Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism
- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'
- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations
- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations
- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment
- total parathyroidectomy

Question 36 of 138

A 25-year-old Asian woman who is 26 weeks pregnant has an oral glucose tolerance test (OGTT). This was requested due to a combination of her ethnicity and a background of obesity. A recent ultrasound shows that the fetus is large for dates. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	9.2
2	14.2

What is the most appropriate management?

- A. Start insulin
- B. Give advice about a diabetic diet
- C. Give advice about a diabetic diet + repeat OGTT in 4 weeks
- D. Start metformin
- E. Start insulin + aspirin

Question 36 of 138

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- D. Start metformin
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Insulin should be started straight away given the blood glucose levels and evidence of macrosomia

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes

- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 37 of 138

A 36-year-old female with a BMI of 34 kg/m^2 is reviewed after managing to lose 3 kg in the past month. She asks about the possibility of starting a drug to help her lose weight. What is the primary mode of action of orilistat?

- A. Leptin antagonist
- B. Pancreatic lipase inhibitor
- C. Blocks intestinal absorption of lipids
- D. HMG-CoA reductase inhibitor
- E. Centrally-acting appetite suppressant

Question 37 of 138

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- E. Centrally-acting appetite suppressant

The primary mode of action of orilistat is to inhibit pancreatic lipases, which in turn will decrease the absorption of lipids from the intestine

Obesity: therapeutic options

The management of obesity consists of a step-wise approach:
- conservative: diet, exercise
- medical
- surgical

Orlistat is a pancreatic lipase inhibitor used in the management of obesity. Adverse effects include faecal urgency/incontinence and flatulence. A lower dose version is now available without prescription ('Alli'). NICE have defined criteria for the use of orlistat. It should only be prescribed as part of an overall plan for managing obesity in adults who have:
- BMI of 28 kg/m^2 or more with associated risk factors, or
- BMI of 30 kg/m^2 or more
- continued weight loss e.g. 5% at 3 months
- orlistat is normally used for < 1 year

Sibutramine
- withdrawn January 2010 by the European Medicines Agency due to an increased risk of cardiovascular events
- centrally acting appetite suppressant (inhibits uptake of serotonin and noradrenaline at hypothalamic sites that regular food intake)
- adverse effects include hypertension (monitor blood pressure and pulse during treatment), constipation, headache, dry mouth, insomnia and anorexia
- contraindicated in psychiatric illness, hypertension, IHD, stroke, arrhythmias

Rimonabant, a specific CB1 cannabinoid receptor antagonist, was withdrawn in October 2008 after the European Medicines Agency warned of serious psychiatric problems including suicide

Question 38 of 138

A 27-year-old female develops eye pain and reduced visual acuity following the initiation of treatment for her recently diagnosed Grave's disease. Which one of the following treatments is likely to have been started?

- A. Radioiodine treatment
- B. Thyroidectomy
- C. Propylthiouracil
- D. Carbimazole and thyroxine
- E. Carbimazole

Question 38 of 138

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- E. Carbimazole

Radioiodine treatment may lead to the development / worsening of thyroid eye disease in up to 15% of patients with Grave's disease

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 39 of 138

Which one of the following statements regarding polycystic ovarian syndrome (PCOS) is incorrect?

- A. A slightly elevated prolactin is consistent with a diagnosis of PCOS
- B. Luteinizing hormone levels are usually raised
- C. Hyperinsulinaemia is seen
- D. Acanthosis nigricans may be seen
- E. Affects between 2-3% of women of reproductive age

Question 39 of 138

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- D. Acanthosis nigricans may be seen
- E. Affects between 2-3% of women of reproductive age

Polycystic ovarian syndrome is extremely common, affecting between 5-20% of women of reproductive age

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features
- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations
- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 40 of 138

A 22-year-old female presents with recurrent painful oral ulceration. Examination reveals signs of oral *Candida*l infection. Which one of the following would most suggest type 1 polyglandular syndrome?

- A. Hypocalcaemia
- B. Rheumatoid arthritis
- C. Type II diabetes mellitus
- D. Coeliac disease
- E. Hypercalcaemia

Question 40 of 138

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- B. Rheumatoid arthritis
- C. Type II diabetes mellitus
- D. Coeliac disease
- E. Hypercalcaemia

Primary hypoparathyroidism is usually the first endocrine manifestation of type 1 autoimmune polyendocrinopathy syndrome. The contrast to multiple endocrine neoplasia (MEN), where hyperparathyroidism is a common finding, should be noted

The question gives a slightly atypical history as this is the upper end of the age range in which patients would be expected to present

Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

Question 41 of 138

A 33-year-old female is referred to endocrinology with thyrotoxicosis. Following a discussion of management options she elects to have radioiodine therapy. Which one of the following is the most likely adverse effect?

- A. Hypothyroidism
- B. Thyroid malignancy
- C. Agranulocytosis
- D. Oesophagitis
- E. Precipitation of thyroid eye disease

Question 41 of 138

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- A. Hypothyroidism
- B. Thyroid malignancy
- C. Agranulocytosis
- D. Oesophagitis
- E. Precipitation of thyroid eye disease

It is well documented that radioiodine therapy can precipitate thyroid eye disease but a majority of patients will eventually require thyroxine replacement

Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

Question 42 of 138

A 64-year-old patient is prescribed pegvisomant for the treatment of acromegaly. What is the mechanism of action of pegvisomant?

- A. IGF-1 receptor antagonist
- B. Growth hormone receptor antagonist
- C. IGF-1 receptor agonist
- D. Growth hormone receptor agonist
- E. Long-acting somatostatin analogue

Question 42 of 138

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Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists
- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue
- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant
- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

Question 43 of 138

A 24-year-old female with a history of type 1 diabetes mellitus presents to the Emergency Department with vomiting and abdominal pain. Finger-prick testing estimates the blood sugar to be 25 mmol/l. Arterial blood gases record a pH of 7.22. On examination the patient is dehydrated and weighs 84 kg. An intravenous line is sited and bloods are sent. One litre of 0.9% saline is infused and an intravenous insulin pump is set-up. What rate should insulin be initially given?

- A. 10 unit / hour
- B. 1 unit / hour
- C. 2 unit / hour
- D. 8 unit / hour
- E. 6 unit / hour

Question 43 of 138

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- D. 8 unit / hour
- E. 6 unit / hour

Diabetic ketoacidosis

The most common precipitating factors of diabetic ketoacidosis (DKA) are infection, missed insulin doses and myocardial infarction

American Diabetes Association diagnostic criteria are as follows:

- blood glucose >13.8 mmol/l
- pH < 7.30
- serum bicarbonate
- anion gap > 10
- ketonaemia

Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially
- insulin: an intravenous infusion should be started at 6u/hour. Once blood glucose is < 15 mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

Complications of DKA and its treatment

- gastric stasis
- cerebral oedema
- thromboembolism
- acute respiratory distress syndrome
- acute renal failure

Question 44 of 138

Liddle's syndrome is associated with each one of the following, except:

- A. Alkalosis
- B. Response to treatment with amiloride
- C. Hypertension
- D. Autosomal recessive inheritance
- E. Hypokalaemia

Question 44 of 138

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- A. Alkalosis
- B. Response to treatment with amiloride
- C. Hypertension
- D. Autosomal recessive inheritance
- E. Hypokalaemia

Question 45 of 138

Each one of the following is associated with pseudohypoparathyroidism, except:

- A. Low calcium levels
- B. Low PTH levels
- C. Shortened 4th and 5th metacarpals
- D. Low IQ
- E. Short stature

Question 45 of 138

Each one of the following is associated with pseudohypoparathyroidism, except:

- A. Low calcium levels
- B. Low PTH levels
- C. Shortened 4th and 5th metacarpals
- D. Low IQ
- E. Short stature

Hypoparathyroidism

Primary hypoparathyroidism
- decrease PTH secretion
- e.g. secondary to thyroid surgery
- low calcium, high phosphate
- treat with alfacalcidol

Pseudohypoparathyroidism
- target cells being insensitive to PTH
- due to abnormality in a G protein
- associated with low IQ, short stature, shortened 4th and 5th metacarpals
- low calcium, high phosphate, high PTH
- diagnosis is made by measuring urinary cAMP and phosphate levels following an infusion of PTH. In hypoparathyroidism this will cause an increase in both cAMP and phosphate levels. In pseudohypoparathyroidism type I neither cAMP nor phosphate levels are increased whilst in pseudohypoparathyroidism type II only cAMP rises.

Pseudopseudohypoparathyroidism
- similar phenotype to pseudohypoparathyroidism but normal biochemistry

Question 46 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypercalcaemia
- B. Demeclocycline
- C. Histiocytosis X
- D. Lithium
- E. Hypokalaemia

Question 46 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypercalcaemia
- B. Demeclocycline
- C. Histiocytosis X
- D. Lithium
- E. Hypokalaemia

Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 47 of 138

Which one of the following is not an indication for treating a patient with subclinical hypothyroidism?

- A. Previous treatment of Graves' disease
- B. TSH > 10
- C. Raised ESR
- D. Positive thyroid autoantibodies
- E. Other autoimmune disorder

Question 47 of 138

Which one of the following is not an indication for treating a patient with subclinical hypothyroidism?

- A. Previous treatment of Graves' disease
- B. TSH > 10
- C. Raised ESR
- D. Positive thyroid autoantibodies
- E. Other autoimmune disorder

Subclinical hypothyroidism

Basics
- TSH raised but T3, T4 normal
- no obvious symptoms

Significance
- risk of progressing to overt hypothyroidism is 2-5% per year (higher in men)
- risk increased by presence of thyroid autoantibodies

Treat if
- TSH > 10
- thyroid autoantibodies positive
- other autoimmune disorder
- previous treatment of Graves' disease

Question 48 of 138

The first-line treatment in remnant hyperlipidaemia (dysbetalipoproteinaemia) is:

- A. Ursodeoxycholic acid
- B. Vitamin A
- C. Statins
- D. Fish oil
- E. Fibrates

Question 48 of 138

The first-line treatment in remnant hyperlipidaemia (dysbetalipoproteinaemia) is:

- A. Ursodeoxycholic acid
- B. Vitamin A
- C. Statins
- D. Fish oil
- E. Fibrates

Remnant hyperlipidaemia

Overview
- rare cause of mixed hyperlipidaemia (raised cholesterol and triglyceride levels)
- also known as Fredrickson type III hyperlipidaemia, broad-beta disease and dysbetalipoproteinaemia
- associated with apo-e2 homozygosity
- high incidence of ischaemic heart disease and peripheral vascular disease
- thought to be caused by impaired removal of intermediate density lipoprotein from the circulation by the liver

Features
- yellow palmar creases
- palmer xanthomas
- tuberous xanthomas

Management
- fibrates are first line treatment

Question 49 of 138

A 45-year-old man is reviewed in the diabetic clinic. His current medication is basal bolus insulin regime combined with ramipril 10mg od, amlodipine 10mg od, simvastatin 40mg on and aspirin 75mg od. On examination blood pressure is 134/84 mmHg. The following results are obtained:

HbA1c	7.3%
Albumin:Creatinine ratio	10.5

What is the most appropriate change to his treatment?

- A. Stop aspirin
- B. Increase dose of ramipril
- C. Add an angiotensin-II receptor antagonist
- D. Add doxazosin
- E. Stop ramipril

Question 49 of 138

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- B. Increase dose of ramipril
- C. Add an angiotensin-II receptor antagonist
- D. Add doxazosin
- E. Stop ramipril

The patient is on the maximum daily dose of ramipril. Given the persistently raised albumin:creatinine ratio dual blockade with an angiotensin-II receptor antagonist is indicated

Diabetic nephropathy: management

Screening
- all patients should be screened annually
- albumin:creatinine ratio (ACR) in early morning specimen
- ACR > 2.5 = microalbuminuria

Management
- dietary protein restriction
- tight glycaemic control
- BP control: aim for < 130/80 mmHg
- benefits independent of blood pressure control have been demonstrated for ACE inhibitors and angiotensin II receptor blockers - these may be used alone or in combination
- control dyslipidaemia e.g. Statins

Question 50 of 138

A 51-year-old woman who is known to have poorly controlled type 1 diabetes mellitus is reviewed. Her main presenting complaint is bloating and vomiting after eating. She also notes that her blood glucose readings have become more erratic recently. Which one of the following medications is most likely to be beneficial?

- A. *Helicobacter pylori* eradication therapy
- B. Lansoprazole
- C. Amitriptyline
- D. Metoclopramide
- E. Cyclizine

Question 50 of 138

A 51-year-old woman who is known to have poorly controlled type 1 diabetes mellitus is reviewed. Her main presenting complaint is bloating and vomiting after eating. She also notes that her blood glucose readings have become more erratic recently. Which one of the following medications is most likely to be beneficial?

- A. *Helicobacter pylori* eradication therapy
- B. Lansoprazole
- C. Amitriptyline
- D. Metoclopramide
- E. Cyclizine

Diabetic neuropathy

NICE updated it's guidance on the management of diabetic neuroopathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

Question 51 of 138

Which one of the following skin disorders is least associated with hypothyroidism?

- A. Xanthomata
- B. Pruritus
- C. Pretibial myxoedema
- D. Eczema
- E. Dry, coarse hair

Question 51 of 138

Which one of the following skin disorders is least associated with hypothyroidism?

- A. Xanthomata
- B. Pruritus
- C. Pretibial myxoedema
- D. Eczema
- E. Dry, coarse hair

For the purposes of postgraduate exams pretibial myxoedema is associated with thyrotoxicosis. There are however case reports of it been found in hypothyroid patients, especially the diffuse non-pitting variety

Skin disorders associated with thyroid disease

Skin manifestations of hypothyroidism
- dry (anhydrosis), cold, yellowish skin
- non-pitting oedema (e.g. hands, face)
- dry, coarse scalp hair, loss of lateral aspect of eyebrows
- eczema
- xanthomata

Skin manifestations of hyperthyroidism
- pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli
- thyroid acropachy: clubbing
- scalp hair thinning
- increased sweating

Pruritus can occur in both hyper- and hypothyroidism

Question 52 of 138

A 53-year-old female with a history of primary atrophic hypothyroidism is assessed two months following a change in her dose of levothyroxine. Which one of the following best describes what the TSH should ideally be?

- A. Between 0.5 to 1.0 mU/l
- B. Between 0.5 to 2.5 mU/l
- C. Between 2.5 to 4.5 mU/l
- D. Between 1.5 to 3.5 mU/l
- E. Between 3.5 to 5.5 mU/l

Question 52 of 138

A 53-year-old female with a history of primary atrophic hypothyroidism is assessed two months following a change in her dose of levothyroxine. Which one of the following best describes what the TSH should ideally be?

- A. Between 0.5 to 1.0 mU/l
- B. Between 0.5 to 2.5 mU/l
- C. Between 2.5 to 4.5 mU/l
- D. Between 1.5 to 3.5 mU/l
- E. Between 3.5 to 5.5 mU/l

A TSH value between 0.5 to 2.5 mU/l is now considered preferable. Dosage changes should of course also take account of symptoms

Hypothyroidism: management

Key points

- initial starting dose of levothyroxine should be lower in elderly patients and those with ischaemic heart disease (e.g. 25–50 mcg/day)
- following a change in thyroxine dose thyroid function tests should be checked after 6-8 weeks
- the therapeutic goal is 'normalisation' of the thyroid stimulating hormone (TSH) level. As the majority unaffected people have a TSH value 0.5–2.5 mU/l it is now thought preferable to aim for a TSH in this range
- there is no evidence to support combination therapy with levothyroxine and liothyronine

Side-effects of thyroxine therapy

- hyperthyroidism: due to over treatment
- reduced bone mineral density
- worsening of angina
- atrial fibrillation

Question 53 of 138

A 36-year-old woman who presented with a goitre is diagnosed with autoimmune thyroiditis. Which one of the following types of thyroid cancer is she predisposed to developing?

- A. Anaplastic
- B. Lymphoma
- C. Medullary
- D. Follicular
- E. Papillary

Question 53 of 138

A 36-year-old woman who presented with a goitre is diagnosed with autoimmune thyroiditis. Which one of the following types of thyroid cancer is she predisposed to developing?

- A. Anaplastic
- B. Lymphoma
- C. Medullary
- D. Follicular
- E. Papillary

Hashimoto's thyroiditis is associated with thyroid lymphoma

Thyroid cancer

Features of hyperthyroidism or hypothyroidism are not commonly seen in patients with thyroid malignancies as they rarely secrete thyroid hormones

Type	**Percentage**	
Papillary	70%	Often young females - excellent prognosis
Follicular	20%	
Medullary	5%	Cancer of parafollicular cells, secrete calcitonin, part of MEN-2
Anaplastic	1%	Not responsive to treatment, can cause pressure symptoms
Lymphoma	Rare	Associated with Hashimoto's

Management of papillary and follicular cancer

- total thyroidectomy
- followed by radioiodine (I-131) to kill residual cells
- yearly thyroglobulin levels to detect early recurrent disease

Question 54 of 138

Which one of the following features is not seen in carcinoid syndrome?

- A. Flushing
- B. Diarrhoea
- C. Bronchospasm
- D. Hypertension
- E. Pellagra

Question 54 of 138

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- D. Hypertension
- E. Pellagra

Flushing, diarrhoea, bronchospasm, tricuspid stenosis, pellagra --> carcinoid with liver mets - diagnosis: urinary 5-HIAA

Hypo- not hypertension is seen in carcinoid syndrome secondary to serotonin release

Carcinoid tumours

Carcinoid syndrome
- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

Features
- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation
- urinary 5-HIAA
- plasma chromogranin A y

Management
- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help

Question 55 of 138

A 47-year-old woman is referred to the general medical clinic. She has gained 10 kg in weight in the past 3 months but her main problem is episodic sweating. These episodes of sweating are associated with double vision and typically occur early in the morning. Clinical examination is unremarkable. What is the most likely diagnosis?

- A. Bronchial carcinoid
- B. Hashimoto's thyroiditis
- C. Menopause
- D. Cushing's syndrome
- E. Insulinoma

Question 55 of 138

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- A. Bronchial carcinoid
- B. Hashimoto's thyroiditis
- C. Menopause
- D. Cushing's syndrome
- E. Insulinoma

This is a typical presentation of insulinoma

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 56 of 138

A 56-year-old female is admitted to ITU with a severe pneumonia. Thyroid function tests are most likely to show:

- A. TSH normal; thyroxine high; T3 high
- B. TSH normal / low; thyroxine low; T3 low
- C. TSH high; thyroxine low; T3 low
- D. TSH low; thyroxine high; T3 high
- E. TSH high; thyroxine normal; T3 high

Question 56 of 138

A 56-year-old female is admitted to ITU with a severe pneumonia. Thyroid function tests are most likely to show:

- A. TSH normal; thyroxine high; T3 high
- B. TSH normal / low; thyroxine low; T3 low
- C. TSH high; thyroxine low; T3 low
- D. TSH low; thyroxine high; T3 high
- E. TSH high; thyroxine normal; T3 high

Sick euthyroid syndrome

In sick euthyroid syndrome (now referred to as non-thyroidal illness) it is often said that everything (TSH, thyroxine and T3) is low. In the majority of cases however the TSH level is within the normal range (inappropriately normal given the low thyroxine and T3).

Changes are reversible upon recovery from the systemic illness.

Question 57 of 138

A 30-year-old female is diagnosed with having Grave's disease. What is her chance of developing thyroid eye disease?

- A. 2-5%
- B. 5-10&
- C. 10-15%
- D. 15-25%
- E. 25-50%

Question 57 of 138

A 30-year-old female is diagnosed with having Grave's disease. What is her chance of developing thyroid eye disease?

- A. 2-5%
- B. 5-10&
- C. 10-15%
- D. 15-25%
- E. 25-50%

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 58 of 138

A 43-year-old man is found to have a phaeochromocytoma. Which anti-hypertensive medication should be started first?

- A. Propranolol
- B. Ramipril
- C. Atenolol
- D. Phenoxybenzamine
- E. Doxazosin

Question 58 of 138

A 43-year-old man is found to have a phaeochromocytoma. Which anti-hypertensive medication should be started first?

- A. Propranolol
- B. Ramipril
- C. Atenolol
- D. Phenoxybenzamine
- E. Doxazosin

PHaeochromocytoma - give **PH**enoxybenzamine before beta-blockers

Phenoxybenzamine is a non-selective alpha-adrenoceptor antagonist and should be started before a beta-blocker is introduced

There is ongoing debate about the optimal medical management of phaeochromocytoma, with the suggestion that antihypertensive treatment regimes other than nonspecific alpha-blockade are just as effective and safe. There are however no trials to provide an answer to this question yet

Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

Basics

- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

Tests

- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:

- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

Question 59 of 138

A 69-year-old man who had a stroke 6 months ago is reviewed. After his diagnosis he was started on simvastatin 40mg on for secondary prevention of further cardiovascular disease. A fasting lipid profile taken one week ago is reported as follows:

Total cholesterol	5.4 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	4.1 mmol/l
Triglyceride	1.5 mmol/l

According to recent NICE guidelines, what is the most appropriate action?

- A. Switch to simvastatin 80mg on
- B. No change in medication, repeat lipid profile in 6 months
- C. Add nicotinic acid
- D. Switch to atorvastatin 80mg on
- E. Add ezetimibe

Question 59 of 138

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- B. No change in medication, repeat lipid profile in 6 months
- C. Add nicotinic acid
- D. Switch to atorvastatin 80mg on
- E. Add ezetimibe

Nicotinic acid can raise HDL levels by up to 30% but in practice its use is limited by flushing. Any change to treatment should of course be in conjunction with continued lifestyle advice.

The increased risk of myopathy with the 80mg dose of simvastatin was recently highlighted by the Medicines and Healthcare products Regulatory Agency. Please see the link for more details.

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 60 of 138

A 62-year-old HGV driver is reviewed. He was diagnosed last year with type 2 diabetes mellitus. Following weight loss and metformin his HbA1c has decreased from 8.8% to 8.4%. What is the most suitable next step in management?

- A. Add exenatide
- B. Make no changes to management
- C. Add gliclazide
- D. Stop metformin for a period to ensure hypoglycaemic awareness is not lost
- E. Add pioglitazone

Question 60 of 138

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- C. Add gliclazide
- D. Stop metformin for a period to ensure hypoglycaemic awareness is not lost
- E. Add pioglitazone

Pioglitazone is the best option here as it would not put him at risk of hypoglycaemia, which obviously could be dangerous given his job.

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c

- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 61 of 138

Which one of the following statements regarding impaired glucose regulation is correct?

- A. All patient should have a repeat oral glucose tolerance test every 2 years
- B. Patients with impaired glucose tolerance are more likely to develop diabetes than patients with impaired fasting glycaemia
- C. Impaired glucose tolerance (IGT) is defined as a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l
- D. Around 1 in 20 adults in the UK have impaired glucose regulation
- E. Patients should be offered metformin if lifestyle changes fail to improve their glucose profile

Question 61 of 138

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- D. Around 1 in 20 adults in the UK have impaired glucose regulation
- E. Patients should be offered metformin if lifestyle changes fail to improve their glucose profile

Impaired glucose regulation

Impaired glucose regulation (IGR) may also be referred to as non-diabetic hyperglycaemia (NDH) or prediabetes. It describes blood glucose levels which are above the normal range but not high enough for a diagnosis of diabetes mellitus. Diabetes UK estimate that around 1 in 7 adults in the UK have IGR. Many individuals with IGR will progress on to developing type 2 diabetes mellitus (T2DM) and they are therefore at greater risk of microvascular and macrovascular complications.

There are two main types of IGR:

- impaired fasting glucose (IFG) - due to hepatic insulin resistance
- impaired glucose tolerance (IGT) - due to muscle insulin resistance
- patients with IGT are more likely to develop T2DM and cardiovascular disease than patients with IFG

Definitions

- a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)
- impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l
- the role of HbA1c is diagnosing IGR and diabetes is currently under review
- people with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT

Management

- Diabetes UK suggests using the term 'prediabetes' when discussing the condition with patients as research has shown that this term has the most impact and is most easily understood
- lifestyle modification: weight loss, increased exercise, change in diet
- drug therapy is not currently licensed or recommended for patients with IGR in the UK
- at least yearly follow-up with blood tests is recommended

Question 62 of 138

Which of the following results establishes a diagnosis of diabetes mellitus?

- A. Asymptomatic patient with fasting glucose 7.9 mmol/L on one occasion
- B. Symptomatic patient with fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria +++
- D. Asymptomatic patient with random glucose 22.0 mmol/L on one occasion
- E. Symptomatic patient with random glucose 12.0 mmol/L on one occasion

Question 62 of 138

Which of the following results establishes a diagnosis of diabetes mellitus?

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- B. Symptomatic patient with fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria +++
- D. Asymptomatic patient with random glucose 22.0 mmol/L on one occasion
- E. Symptomatic patient with random glucose 12.0 mmol/L on one occasion

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 63 of 138

A 56-year-old lady with a BMI of 27 is reviewed in the diabetic clinic due to poor glycaemic control. She is currently being treated with gliclazide 160mg bd. Her latest bloods show:

Na^+	139 mmol/l
K^+	4.1 mmol/l
Urea	8.4 mmol/l
Creatinine	170 µmol/l
ALT	25 iu/l
yGT	33 iu/l
HbA1c	9.4%

Which one of the following medications should be added next?

- A. Guar gum
- B. Pioglitazone
- C. Metformin
- D. Acarbose
- E. Repaglinide

Question 63 of 138

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- A. Guar gum
- B. Pioglitazone
- C. Metformin
- D. Acarbose
- E. Repaglinide

Given that she is overweight metformin would be a natural choice to add. The creatinine however is elevated so pioglitazone is the next best option

One possible drawback of using pioglitazone is that it may lead to weight gain, especially given her BMI is already 27

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 64 of 138

A 34-year-old female with a history of Addison's disease presents for review in endocrinology clinic. She is generally well but complains of a decrease in her libido. On examination there is a slight loss of pubic hair. What is the most likely cause?

- A. Adverse effect of hydrocortisone therapy
- B. 11-hydroxylase deficiency
- C. Diethylstilbestrol deficiency
- D. Oestrogen deficiency
- E. Dehydroepiandrosterone (DHEA) deficiency

Question 64 of 138

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- C. Diethylstilbestrol deficiency
- D. Oestrogen deficiency
- E. Dehydroepiandrosterone (DHEA) deficiency

Dehydroepiandrosterone is the most abundant circulating adrenal steroid. Adrenal glands are the main source of dehydroepiandrosterone in females - loss of functioning adrenal tissue as in Addison's disease may result in symptoms secondary to androgen deficiency, such as loss of libido. Research is ongoing as to whether routine replacement of DHEA is beneficial

Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

Features
- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

Other causes of hypoadrenalism

Primary causes
- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

Secondary causes
- pituitary disorders (e.g. tumours, irradiation, infiltration)

Exogenous glucocorticoid therapy

Question 65 of 138

Which one of the following is most likely to be seen in a patient with multiple endocrine neoplasia (MEN) type I?

- A. Phaeochromocytoma
- B. Insulinoma
- C. Marfanoid body habitus
- D. Medullary thyroid carcinoma
- E. RET gene

Question 65 of 138

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Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	**MEN type IIa**	**MEN type IIb**
Mnemonic 'three P's': • parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia • pituitary (70%) • pancreas (50%, e.g. insulinoma, gastrinoma) • also: adrenal and thyroid	• phaeochromocytoma (95%, e.g. Phaeochromocytoma) • medullary thyroid cancer (70%) • parathyroid (60%)	• medullary thyroid cancer • phaeochromocytoma • marfanoid body habitus • neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene

MEN is inherited as an autosomal dominant disorder

Question 66 of 138

Cushing's syndrome is most typically associated with which one of the following abnormalities:

- A. Hypokalaemic metabolic acidosis
- B. Hyperkalaemic metabolic alkalosis
- C. Hypocalcaemic metabolic acidosis
- D. Hypokalaemic metabolic alkalosis
- E. Hyperkalaemic metabolic acidosis

Question 66 of 138

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- D. Hypokalaemic metabolic alkalosis
- E. Hyperkalaemic metabolic acidosis

Cushing's syndrome - hypokalaemic metabolic alkalosis

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:
- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test
- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation
- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 67 of 138

An insulin stress test is most useful in the investigation of:

- A. Glucagonoma
- B. Insulinoma
- C. Addison's disease
- D. Hypopituitarism
- E. Diabetes mellitus

Question 67 of 138

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- A. Glucagonoma
- B. Insulinoma
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- D. Hypopituitarism
- E. Diabetes mellitus

Insulin stress tests are also occasionally used to differentiate Cushing's from pseudo-Cushing's

Insulin stress test

Basics

- used in investigation of hypopituitarism
- IV insulin given, GH and cortisol levels measured
- with normal pituitary function GH and cortisol should rise

Contraindications

- epilepsy
- ischaemic heart disease
- adrenal insufficiency

Question 68 of 138

A 23-year-old woman presents for review. She has not a normal period for around 8 months now. A recent pregnancy test was negative. Blood tests are ordered:

FSH	2.2 IU/L (0-20 IU/L)
Oestradiol	84 pmol/l (100-500 pmol/l)
Thyroid stimulating hormone	3.1 mIU/L
Prolactin	2 ng/ml (0-10 ng/ml)
Free androgen index	3 (< 7)

What is the most likely cause of her symptoms?

- A. Prolactinoma
- B. Premature ovarian failure
- C. Polycystic ovarian syndrome
- D. Addison's disease
- E. Excessive exercise

Question 68 of 138

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- B. Premature ovarian failure
- C. Polycystic ovarian syndrome
- D. Addison's disease
- E. Excessive exercise

The bloods show a hypothalamic amenorrhoea which may be caused by stress or excessive exercise. The FSH would be raised in premature ovarian failure.

Amenorrhoea

Amenorrhoea may be divided into primary (failure to start menses by the age of 16 years) or secondary (cessation of established, regular menstruation for 6 months or longer).

Causes of primary amenorrhoea
- Turner's syndrome
- testicular feminisation
- congenital adrenal hyperplasia
- congenital malformations of the genital tract

Causes of secondary amenorrhoea (after excluding pregnancy)
- hypothalamic amenorrhoea (e.g. Stress, excessive exercise)
- polycystic ovarian syndrome (PCOS)
- hyperprolactinaemia
- premature ovarian failure
- thyrotoxicosis*

Initial investigations
- exclude pregnancy with urinary or serum bHCG
- gonadotrophins: low levels indicate a hypothalamic cause where as raised levels suggest an ovarian problem (e.g. Premature ovarian failure)
- prolactin
- androgen levels: raised levels may be seen in PCOS
- oestradiol
- thyroid function tests

*hypothyroidism may also cause amenorrhoea

Question 69 of 138

Which one of the following is the most common non-iatrogenic cause of Cushing's syndrome?

- A. Ectopic ACTH production
- B. Adrenal adenoma
- C. Micronodular adrenal dysplasia
- D. Adrenal carcinoma
- E. Pituitary tumour

Question 69 of 138

Which one of the following is the most common non-iatrogenic cause of Cushing's syndrome?

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- C. Micronodular adrenal dysplasia
- D. Adrenal carcinoma
- E. Pituitary tumour

Cushing's disease is the most common, non-iatrogenic, cause of Cushing's syndrome

Cushing's syndrome: causes

ACTH dependent causes
- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes
- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's
- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Question 70 of 138

Which one of the following may be associated with galactorrhoea?

- A. Primary hypothyroidism
- B. Addison's disease
- C. Cushing's syndrome
- D. Grave's disease
- E. Bromocriptine

Question 70 of 138

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- C. Cushing's syndrome
- D. Grave's disease
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Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin
- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin
- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin
- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

Question 71 of 138

A 54-year-old man with type 2 diabetes mellitus is found on annual review to have new vessel formation at the optic disc. Visual acuity in both eyes is not affected (6/9). Blood pressure is155/84 mmHg.

HbA1c 8.4%

What is the most important intervention in this patient?

- A. Follow-up ophthalmoscopy in 3 months
- B. Add aspirin
- C. Blood pressure control
- D. Tight glycaemic control
- E. Laser therapy

Question 71 of 138

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This patient has proliferative diabetic retinopathy and urgent referral to an ophthalmologist for panretinal photocoagulation is indicated

Diabetic retinopathy

Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovasculization is thought to be caused by the production of growth factors in response to retinal ischaemia

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proposed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	**New classification**
Background retinopathy • microaneurysms (dots) • blot haemorrhages (=3) • hard exudates Pre-proliferative retinopathy • cotton wool spots (soft exudates; ischaemic nerve fibres) • > 3 blot haemorrhages • venous beading/looping • deep/dark cluster haemorrhages • more common in Type I DM, treat with laser photocoagulation	Mild NPDR • 1 or more microaneurysm Moderate NPDR • microaneurysms • blot haemorrhages • hard exudates • cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR Severe NPDR • blot haemorrhages and microaneurysms in 4 quadrants • venous beading in at least 2 quadrants • IRMA in at least 1 quadrant

Proliferative retinopathy

- retinal neovascularisation - may lead to vitrous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

Maculopathy

- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

Question 72 of 138

Which of the following is least recognised as a potential complication of acromegaly?

- A. Colorectal cancer
- B. Hypertension
- C. Cardiomyopathy
- D. Diabetes mellitus
- E. Pulmonary hypertension

Question 72 of 138

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- B. Hypertension
- C. Cardiomyopathy
- D. Diabetes mellitus
- E. Pulmonary hypertension

Acromegaly is associated with systemic rather than pulmonary hypertension.

Secondary causes of pulmonary hypertension include COPD, congenital heart disease (Eisenmenger's syndrome), recurrent pulmonary embolism, HIV and sarcoidosis.

Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

Features
- coarse, oily skin , large tongue, prognathism, interdental spaces
- spade-like hands, increase in shoe size
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

Complications
- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Question 73 of 138

A 29-year-old female who is 14 weeks into her first pregnancy is investigated for excessive sweating and tremor. Blood tests reveal the following:

TSH < 0.05 mu/l

T4 188 nmol/l

What is the most appropriate management?

- A. Immediate surgery
- B. Carbimazole
- C. Surgery at start of third trimester
- D. Propylthiouracil
- E. Radioiodine

Question 73 of 138

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- C. Surgery at start of third trimester
- D. Propylthiouracil
- E. Radioiodine

Propylthiouracil is traditionally taught as the antithyroid drug of choice in pregnancy. This approach was supported by the 2007 Endocrine Society consensus guidelines. It also has the advantage of being excreted to a lesser extent than carbimazole in breast milk.

Despite this some endocrinologists use carbimazole and the BNF states both drugs may be used in pregnancy. Carbimazole has rarely been associated with aplasia cutis of the neonate

Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

Thyrotoxicosis
Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

Management
- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

Hypothyroidism
Key points
- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

Question 74 of 138

Which one of the following features of haemochromatosis may be reversible with treatment?

- A. Cardiomyopathy
- B. Hypogonadotrophic hypogonadism
- C. Diabetes mellitus
- D. Arthropathy
- E. Liver cirrhosis

Question 74 of 138

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- B. Hypogonadotrophic hypogonadism
- C. Diabetes mellitus
- D. Arthropathy
- E. Liver cirrhosis

Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Epidemiology
- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

Presenting features
- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 75 of 138

Which one of the following statements regarding the metabolic syndrome is correct?

- A. The WHO criteria are used to define impaired glucose tolerance
- B. The central pathophysiological change is thought to be reduced insulin production
- C. A diagnosis cannot be made without weighing the patient
- D. A raised LDL concentration is one of the key criteria in most definitions
- E. Decisions on cardiovascular risk factor modification should be made regardless of whether patients meet the criteria for metabolic syndrome

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E. Decisions on cardiovascular risk factor modification should be made regardless of whether patients meet the criteria for metabolic syndrome

Decisions on primary prevention of cardiovascular disease should be made using standard tools and are not dependant on whether a diagnosis of metabolic syndrome is made.

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 76 of 138

A 43-year-old man requests a 'medical' as he is concerned about his risk of heart disease. His father died at the age of 45-years following a myocardial infarction. His lipid profile is as follows:

HDL	1.4 mmol/l
LDL	5.7 mmol/l
Triglycerides	2.3 mmol/l
Total cholesterol	8.2 mmol/l

Clinical examination reveals tendon xanthomata around his ankles. What is the most likely diagnosis?

- A. Familial hypercholesterolaemia (heterozygous)
- B. Nephrotic syndrome
- C. Mixed hyperlipidaemia
- D. Familial hypercholesterolaemia (homozygous)
- E. Hypothyroidism

Question 76 of 138

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- B. Nephrotic syndrome
- C. Mixed hyperlipidaemia
- D. Familial hypercholesterolaemia (homozygous)
- E. Hypothyroidism

The presence of tendon xanthomata and cholesterol levels meet the diagnostic criteria for familial hypercholesterolaemia. Homozygous familial hypercholesterolaemia is exceedingly rare - most patients die in their teenage years from a myocardial infarction.

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

Question 77 of 138

A 49-year-old man with type 2 diabetes mellitus is reviewed. Despite weight loss and therapy with metformin and gliclazide his last HbA1c is 7.2%. Which one of the following factors would suggest that the patient may benefit from a meglitinide?

- A. Obesity
- B. Not adhering to diabetic diet
- C. Problems with hypoglycaemia from gliclazide
- D. Erratic lifestyle
- E. Elderly and frail patients

Question 77 of 138

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- D. Erratic lifestyle
- E. Elderly and frail patients

Meglitinides - stimulate insulin release - good for erratic lifestyle

Meglitinides stimulate insulin release and are particularly useful for post-prandial hyperglycaemia or an erratic eating schedule, as patients take them shortly before meals

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin

- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 78 of 138

What is the mode of inheritance of haemochromatosis?

- A. Autosomal recessive
- B. X-linked dominant
- C. Mitochondrial inheritance
- D. Autosomal dominant
- E. X-linked recessive

Question 78 of 138

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Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	**Irreversible complications**
• Cardiomyopathy • Skin pigmentation	• Liver cirrhosis** • Diabetes mellitus • Hypogonadotrophic hypogonadism • Arthropathy

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Question 79 of 138

Which one of the following is least characteristic of Addison's disease?

- A. Hypoglycaemia
- B. Metabolic alkalosis
- C. Hyponatraemia
- D. Hyperkalaemia
- E. Positive short ACTH test

Question 79 of 138

Which one of the following is least characteristic of Addison's disease?

- A. Hypoglycaemia
- B. Metabolic alkalosis
- C. Hyponatraemia
- D. Hyperkalaemia
- E. Positive short ACTH test

Addison's disease is associated with a metabolic acidosis

Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a short ACTH test. Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Question 80 of 138

A 26-year-old obese female is investigated for menstrual disturbance. A diagnosis of polycystic ovarian syndrome is made. Which of the following findings is most consistently seen in polycystic ovarian syndrome?

- A. Obesity
- B. Hirsuitism
- C. Ovarian cysts on ultrasound
- D. Raised LH:FSH ratio
- E. Clitoromegaly

Question 80 of 138

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- E. Clitoromegaly

Polycystic ovarian syndrome - ovarian cysts are the most consistent feature

Whilst all of the features listed above may be seen in polycystic ovarian syndrome, ovarian cysts are the most consistent feature.

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features
- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations
- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 81 of 138

Dynamic pituitary function tests may be used to assess each one of the following, except:

- A. Cortisol
- B. Prolactin
- C. Growth hormone
- D. Follicular stimulating hormone
- E. Antidiuretic hormone

Question 81 of 138

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- A. Cortisol
- B. Prolactin
- C. Growth hormone
- D. Follicular stimulating hormone
- E. Antidiuretic hormone

Dynamic pituitary function tests

A dynamic pituitary function test is used to assess patients with suspected primary pituitary dysfunction

Insulin, TRH and LHRH are given to the patient following which the serum glucose, cortisol, growth hormone, TSH, LH and FSH levels are recorded at regular intervals. Prolactin levels are also sometimes measured*

A normal dynamic pituitary function test has the following characteristics:

- GH level rises > 20mu/l
- cortisol level rises > 550 mmol/l
- TSH level rises by > 2 mu/l from baseline level
- LH and FSH should double

*dopamine antagonist tests using metoclopramide may also be used in the investigation of hyperprolactinaemia. A normal response is at least a twofold rise in prolactin. A blunted prolactin response suggests a prolactinoma

Question 82 of 138

Which of the following statements is true regarding the pathophysiology of diabetes mellitus?

- A. Concordance between identical twins is higher in type 2 diabetes mellitus than type 1
- B. Patients with type 1 diabetes mellitus are rarely HLA-DR4 positive
- C. Type 2 diabetes mellitus is associated with HLA-DR3
- D. Haemochromatosis is an example of primary diabetes
- E. Type 1 diabetes mellitus is thought to be inherited in an autosomal dominant fashion

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C. Type 2 diabetes mellitus is associated with HLA-DR3

D. Haemochromatosis is an example of primary diabetes

E. Type 1 diabetes mellitus is thought to be inherited in an autosomal dominant fashion

Type 1 diabetes mellitus is caused by autoimmune destruction of the Beta-cells of the pancreas. Identical twins show a genetic concordance of 40%. It is associated with HLA-DR3 and DR4. It is inherited in a polygenic fashion

Type 2 diabetes mellitus is thought to be caused by a relative deficiency of insulin and the phenomenon of insulin resistance. Age, obesity and ethnicity are important aetiological factors. There is almost 100% concordance in identical twins and no HLA associations.

Haemochromatosis is an example of secondary diabetes

Diabetes: pathophysiology

Type 1 DM

- autoimmune disease
- antibodies against beta cells of pancreas
- HLA DR4 > HLA DR3
- various antibodies such as islet-associated antigen (IAA) antibody and glutamic acid decarboxylase (GAD) antibody are detected in patients who later go on to develop type 1 DM - their prognostic significance is not yet clear

Question 83 of 138

A 49-year-old woman is investigated for thyrotoxicosis. On examination she is noted to have a goitre containing multiple irregular nodules. Nuclear scintigraphy with technetium 99m reveals patchy uptake. What is the treatment of choice?

- A. Corticosteroids
- B. Radioiodine
- C. Block-and-replace regime
- D. Surgery
- E. Anti-thyroid drug titration regime

Question 83 of 138

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- B. Radioiodine
- C. Block-and-replace regime
- D. Surgery
- E. Anti-thyroid drug titration regime

Toxic multinodular goitre

Toxic multinodular goitre describes a thyroid gland that contains a number of autonomously functioning thyroid nodules that secrete excess thyroid hormones

Nuclear scintigraphy reveals patchy uptake

The treatment of choice is radioiodine therapy

Question 84 of 138

A 52-year-old woman who was diagnosed as having primary atrophic hypothyroidism 12 months ago is reviewed following recent thyroid function tests (TFTs):

TSH 12.5 mU/l

Free T4 14 pmol/l

She is currently taking 75mcg of levothyroxine once a day. How should these results be interpreted?

- A. Poor compliance with medication
- B. Taking extra thyroxine
- C. Evidence of recent systemic steroid therapy
- D. Keep on same dose
- E. T4 to T3 conversion disorder

Question 84 of 138

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- D. Keep on same dose
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Thyroid function tests

The interpretation of thyroid function tests is usually straightforward:

	TSH	**Free T4**	
Thyrotoxicosis (e.g. Graves' disease)	Low	High	In T3 thyrotoxicosis the free T4 will be normal
Primary hypothyroidism (primary atrophic hypothyroidism)	High	Low	
Secondary hypothyroidism	Low	Low	Replacement steroid therapy is required prior to thyroxine
Sick euthyroid syndrome*	Low**	Low	Common in hospital inpatients
Poor compliance with thyroxine	High	Normal / high	
Steroid therapy	Low	Normal	

*now referred to as non-thyroidal illness

**TSH may be normal in some cases

Question 85 of 138

A 54-year-old female presents to the Emergency Department concerned about double vision. She is noted to have exophthalmos and conjunctival oedema on examination and a diagnosis of thyroid eye disease is suspected. What can be said regarding her thyroid status?

- A. Hyper- or euthyroid
- B. Hypothyroid
- C. Hyperthyroid
- D. Hypo- or euthyroid
- E. Eu-, hypo- or hyperthyroid

Question 85 of 138

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- C. Hyperthyroid
- D. Hypo- or euthyroid
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Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Question 86 of 138

A 45-year woman who you have treated for obesity comes for review. Despite ongoing lifestyle interventions and trials of orlistat and sibutramine she has failed to lose a significant amount of weight. She is currently taking ramipril for hypertension but a recent fasting glucose was normal. For this patient, what is the cut-off body mass index (BMI) that would trigger a referral for consideration of bariatric surgery?

- A. BMI > 35 kg/m^2
- B. BMI > 40 kg/m^2
- C. BMI > 30 kg/m^2
- D. BMI > 38 kg/m^2
- E. BMI > 45 kg/m^2

Question 87 of 138

Which one of the following is the most common cause of hypothyroidism in the UK?

- A. Pituitary failure
- B. Dietary iodine deficiency
- C. Lithium therapy
- D. Primary atrophic hypothyroidism
- E. Hashimoto's thyroiditis

Question 87 of 138

Which one of the following is the most common cause of hypothyroidism in the UK?

- A. Pituitary failure
- B. Dietary iodine deficiency
- C. Lithium therapy
- D. Primary atrophic hypothyroidism
- E. Hashimoto's thyroiditis

In European countries primary atrophic hypothyroidism is the most cause causes of hypothyroidism, whereas in North America Hashimoto's thyroiditis appears to account for the majority of cases. The reason for this discrepancy is unclear

Hypothyroidism: causes

Hypothyroidism affects around 1-2% of women in the UK and is around 5-10 times more common in females than males.

Primary hypothyroidism

Primary atrophic hypothyroidism
- most common cause
- autoimmune disease, associated with IDDM, Addison's or pernicious anaemia
- 5 times more common in women

Hashimoto's thyroiditis
- autoimmune disease as above with goitre (positive microsomal antibodies)
- may cause transient thyrotoxicosis in the acute phase
- 10 times more common in women

After thyroidectomy or radioiodine treatment
Drug therapy (e.g. lithium, amiodarone or anti-thyroid drugs such as carbimazole)
Dietary iodine deficiency

Secondary hypothyroidism (rare)

From pituitary failure

Other associated conditions
- Down's syndrome
- Turner's syndrome
- coeliac disease

Question 88 of 138

Which one of the following features is least commonly seen in Gitelman's syndrome?

- A. Hypokalaemia
- B. Hypertension
- C. Metabolic alkalosis
- D. Hypocalciuria
- E. Hypomagnesaemia

Question 89 of 138

What is the most common cause of primary hyperaldosteronism?

- A. Pituitary tumour
- B. Adrenocortical adenoma
- C. Adrenal carcinoma
- D. Ectopic secretion
- E. Bilateral idiopathic adrenal hyperplasia

Question 89 of 138

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- C. Adrenal carcinoma
- D. Ectopic secretion
- E. Bilateral idiopathic adrenal hyperplasia

bilateral idiopathic adrenal hyperplasia is the most common cause of primary hyperaldosteronism

Primary hyperaldosteronism

Primary hyperaldosteronism was previously thought to be most commonly caused by an adrenal adenoma, termed Conn's syndrome. However, recent studies have shown that bilateral idiopathic adrenal hyperplasia is the cause in up to 70% of cases. Differentiating between the two is important as this determines treatment. Adrenal carcinoma is an extremely rare cause of primary hyperaldosteronism

Features
- hypertension
- hypokalaemia (e.g. muscle weakness)
- alkalosis

Investigations
- high serum aldosterone
- low serum renin
- high-resolution CT abdomen

Management
- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

Question 90 of 138

A 24-year-old woman is found to have a blood pressure of 170/100 mmHg during a routine medical check. She is well and clinical examination is unremarkable. Blood tests show:

Na^+	140 mmol/l
K^+	2.6 mmol/l
Bicarbonate	31 mmol/l
Urea	3.4 mmol/l
Creatinine	77 µmol/l

Which one of the following investigations is most likely to be diagnostic?

- A. Renal ultrasound
- B. Overnight dexamethasone suppression test
- C. Renin:aldosterone ratio
- D. MR angiography
- E. 21-hydroxylase estimation

Question 90 of 138

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- C. Renin:aldosterone ratio
- D. MR angiography
- E. 21-hydroxylase estimation

Conn's syndrome is the likely diagnosis - a renin:aldosterone ratio would be an appropriate first-line investigation. A normal clinical examination makes a diagnosis of Cushing's syndrome less likely

Primary hyperaldosteronism

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- alkalosis

Investigations
- high serum aldosterone
- low serum renin
- high-resolution CT abdomen

Management
- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

Question 91 of 138

A 62-year-old man who had a myocardial infarction six months ago presents for review. What should his target cholesterol levels be?

- A. Total cholesterol < 3.5 mmol/l; LDL < 1.5 mmol/l
- B. Total cholesterol < 4.0 mmol/l; LDL < 2.0 mmol/l
- C. Total cholesterol:HDL ratio < 5.0 mmol/l
- D. Total cholesterol:HDL ratio < 4.0 mmol/l
- E. Total cholesterol < 5.0 mmol/l; LDL < 3.0 mmol/l

Question 91 of 138

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- D. Total cholesterol:HDL ratio < 4.0 mmol/l
- E. Total cholesterol < 5.0 mmol/l; LDL < 3.0 mmol/l

NICE adopted the JBS2 targets for secondary prevention in the 2008 guidelines

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 92 of 138

A 54-year-old man with type 2 diabetes mellitus is started on exenatide. Which one of the following statements regarding exenatide is incorrect?

- A. Typically results in weight loss
- B. May be combined with a sulfonylurea
- C. The major adverse effect is flu-like symptoms
- D. May be combined with a thiazolidinedione
- E. Must be given by subcutaneous injection

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- E. Must be given by subcutaneous injection

Exenatide causes vomiting

The major adverse effect is nausea and vomiting

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 93 of 138

A 35-year-old female is referred to the endocrine clinic due to weight loss and palpitations. The following results are obtained:

TSH < 0.05 mu/l

T4 178 mmol/l

Which one of the following features would most suggest a diagnosis of Grave's disease?

- A. Atrial fibrillation
- B. Lid lag
- C. Family history of radioiodine treatment
- D. Pretibial myxoedema
- E. Multinodular goitre

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- E. Multinodular goitre

Pretibial myxoedema is not seen in other causes of thyrotoxicosis and points towards a diagnosis of Graves'

Graves' disease: features

Features seen in Graves' but not in other causes of thyrotoxicosis
- eye signs: exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

Autoantibodies
- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

Question 94 of 138

A 52-year-old man has a set of fasting bloods as part of a work-up for hypertension. The fasting glucose comes back as 6.5 mmol/l. The test is repeated and reported as 6.7 mmol/l. He says he feels constantly tired but denies any polyuria or polydipsia. How should these results be interpreted?

- A. Impaired fasting glycaemia
- B. Suggestive of diabetes mellitus but not diagnostic
- C. Diabetes mellitus
- D. Normal
- E. Impaired glucose tolerance

Question 94 of 138

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- C. Diabetes mellitus
- D. Normal
- E. Impaired glucose tolerance

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 95 of 138

One of your patients is diagnosed with having the metabolic syndrome. Which one of the following is associated with this condition?

- A. Endometriosis
- B. Hypothyroidism
- C. Asymptomatic rise in amylase levels
- D. Elevated albumin levels
- E. Raised uric acid levels

Question 95 of 138

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Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 96 of 138

An 25-year-old male develops type 2 diabetes mellitus. Which one of the following genes is most likely to be responsible?

- A. Glucokinase
- B. HNF-1 alpha
- C. HNF-4 alpha
- D. HNF-1 beta
- E. IPF-1

Question 96 of 138

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- D. HNF-1 beta
- E. IPF-1

MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

MODY 3
- 60% of cases
- due to a defect in the HNF-1 alpha gene

MODY 2
- 20% of cases
- due to a defect in the glucokinase gene

Question 97 of 138

An 24-year-old woman is reviewed due to facial hirsuitism. You suspect a diagnosis of polycystic ovarian syndrome (PCOS). Which one of the following features would necessitate the need for further investigations before confidently making a diagnosis of PCOS?

- A. Clitoromegaly
- B. Acanthosis nigricans
- C. Obesity
- D. Amenorrhoea
- E. Acne

Question 97 of 138

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- B. Acanthosis nigricans
- C. Obesity
- D. Amenorrhoea
- E. Acne

Clitoromegaly is seen occasionally in PCOS but is normally associated with very high androgen levels. If clitoromegaly is found then further investigations to exclude an ovarian or adrenal androgen secreting tumour are required.

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome

Features

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsuitism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful is diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Question 98 of 138

Which one of the following drugs used in the management of type 2 diabetes mellitus has the Medicines and Healthcare products Regulatory Agency warned is associated with an increased risk of severe pancreatitis and renal impairment?

- A. Rosiglitazone
- B. Metformin
- C. Acarbose
- D. Exenatide
- E. Sitagliptin

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Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 99 of 138

A 52-year-old woman with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.9
2	8.4

How should these results be interpreted?

- A. Impaired fasting glucose and impaired glucose tolerance
- B. Normal
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Question 99 of 138

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2	8.4

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- A. Impaired fasting glucose and impaired glucose tolerance
- B. Normal
- C. Diabetes mellitus
- D. Impaired glucose tolerance
- E. Impaired fasting glucose

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 100 of 138

What is the most appropriate screening investigation to exclude a phaeochromocytoma?

- A. Ultrasound adrenals
- B. Phenoxybenzamine suppression test
- C. 24 hour urinary collection of vanillylmandelic acid
- D. 24 hour urinary collection of catecholamines
- E. Plasma adrenaline (morning)

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- D. 24 hour urinary collection of catecholamines
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Phaeochromocytoma: do 24 hr urinary catecholamines, not VMA etc

A 24 hr urinary collection of catecholamines is preferred to one of vanillylmandelic acid as it has a higher sensitivity. Three 24 hour collections are needed as some patients have intermittently raised levels

Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

Basics
- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

Tests
- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:
- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

Question 101 of 138

An obese man presents as he is concerned about his risk of developing cardiovascular disease. Which one of the following sets of results would suggest a diagnosis of the metabolic syndrome using the Scottish Intercollegiate Guidelines Network (SIGN) criteria?

- A. Waist circumference = 98 cm; fasting glucose = 7.2 mmol/l; HDL = 1.2 mmol/l
- B. Triglycerides = 2.0 mmol/l; HDL = 1.2 mmol/l; fasting glucose = 5.4 mmol/l
- C. Blood pressure = 140/90 mmHg; waist circumference = 90 cm; HDL = 1.4 mmol/l
- D. Waist circumference = 110 cm; fasting glucose = 5.8 mmol/l; HDL = 0.8 mmol/l
- E. LDL = 3.0 mmol/l; blood pressure = 130/80; fasting glucose = 6.4 mmol/l

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E. LDL = 3.0 mmol/l; blood pressure = 130/80; fasting glucose = 6.4 mmol/l

Whilst all the results contain at least one factor consistent with the metabolic syndrome only option D contains three of the criteria and would hence support a diagnosis.

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m2
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

Question 102 of 138

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

- A. Hypocalcaemia
- B. Sickle-cell anaemia
- C. Lithium
- D. Hypokalaemia
- E. Demeclocycline

Question 102 of 138

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- D. Hypokalaemia
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Diabetes insipidus

Causes of cranial DI
- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X

DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

Causes of nephrogenic DI
- genetic (primary)
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

Investigation
- high plasma osmolarity, low urine osmolarity
- water deprivation test

Question 103 of 138

A 25-year-old man with a family history of multiple endocrine neoplasia type 1 is reviewed in clinic. What is the single most useful investigation to monitor such patients?

- A. Short synacthen test
- B. Urinary catecholamines
- C. Serum calcium
- D. Thyroid function tests
- E. Serum prolactin

Question 103 of 138

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- C. Serum calcium
- D. Thyroid function tests
- E. Serum prolactin

The high incidence of parathyroid tumours and hypercalcaemia make serum calcium a useful indicator of MEN type 1 in suspected individuals

Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	**MEN type IIa**	**MEN type IIb**
Mnemonic 'three P's': • parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia • pituitary (70%) • pancreas (50%, e.g. insulinoma, gastrinoma) • also: adrenal and thyroid	• phaeochromocytoma (95%, e.g. Phaeochromocytoma) • medullary thyroid cancer (70%) • parathyroid (60%)	• medullary thyroid cancer • phaeochromocytoma • marfanoid body habitus • neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene

MEN is inherited as an autosomal dominant disorder

Question 104 of 138

Which one of the following statements regarding the management of diabetes mellitus during pregnancy is incorrect?

- A. A previous macrosomic baby is a risk factor for gestational diabetes
- B. Diabetes complicates around 1 in 40 pregnancies
- C. A higher dose of folic acid (5 mg/day) should be used
- D. Metformin is contraindicated
- E. Tight glycaemic control reduces complication rates

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- E. Tight glycaemic control reduces complication rates

There is increasing evidence that metformin is safe during pregnancy

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes
- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes
- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes
- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes
- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 105 of 138

Which one of the following regarding the management of thyroid problems during pregnancy is incorrect?

- A. Maternal free thyroxine levels should be kept in the upper third of the normal reference range when treating thyrotoxicosis
- B. Increased levels of thyroxine-binding globulin are seen in pregnancy
- C. Block-and-replace is preferable in pregnancy compared to antithyroid drug titration
- D. Breast feeding is safe whilst on thyroxine
- E. Untreated thyrotoxicosis increases the risk of premature labour

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- D. Breast feeding is safe whilst on thyroxine
- E. Untreated thyrotoxicosis increases the risk of premature labour

Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

Thyrotoxicosis

Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

Management

- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

Hypothyroidism

Key points

- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

Question 106 of 138

A 30-year-old female is started on carbimazole 20mg bd following a diagnosis of Grave's disease. What is the best biochemical marker to assess her response to treatment?

- A. Total T4
- B. TSH
- C. Free T4
- D. ESR
- E. Free T3

Question 106 of 138

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- C. Free T4
- D. ESR
- E. Free T3

The answer the College are looking for is TSH. There is however a significant proportion of patients for whom TSH monitoring alone is insufficient. TSH may remain suppressed for several weeks as continued production of thyroid stimulating immunoglobulins seen in Grave's disease reduces the need for the pituitary to secrete TSH

Thyrotoxicosis

Graves' disease accounts for around 50-60% of cases of thyrotoxicosis.

Causes

- Graves' disease
- toxic nodular goitre
- subacute (de Quervain's) thyroiditis
- post-partum thyroiditis
- acute phase of Hashimoto's thyroiditis (later results in hypothyroidism)
- toxic adenoma (Plummer's disease)
- amiodarone therapy

Investigation

- TSH down, T4 and T3 up
- thyroid autoantibodies
- other investigations are not routinely done but includes isotope scanning

Question 107 of 138

Which one of the following statements regarding NICE guidance on the primary prevention of cardiovascular disease is incorrect?

- A. Premature coronary heart disease is defined as < 65 years in females
- B. A 10-year risk of 15% is used to identify patients who should be considered for lipid-lowering therapy
- C. Simvastatin 40mg on is the first line treatment in patients with a significant risk
- D. The 1991 Framingham equations are still recommended for calculating risk
- E. If a patient has a first degree relative with premature heart disease the risk should be multiplied by 1.5

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Primary prevention CVD: 10-year risk of 20% is cut-off

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 108 of 138

A 23-year-old woman is diagnosed with Graves' disease. Which one of the following statements regarding treatment is correct?

- A. Block-and-replace regimes are usually of a shorter duration than carbimazole titration therapy
- B. Concurrent administration of propranolol and carbimazole should be avoided
- C. Patients on block-and-replace regimes have fewer side-effects than those using titration therapy
- D. Carbimazole should be started at no higher than 10mg/day for patients commencing a titration regime
- E. In the block-and-replace regime levothyroxine should be started at the same time as carbimazole

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Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

Question 109 of 138

A 45-year-old woman presents with weight gain and recurrent 'dizzy' episodes. Over the past four months she has gained 20 kg. The episodes occur on an almost daily basis and are characterised by blurred vision, sweating, headaches and palpitations. Her GP checked a blood sugar during one of these episodes which was record as being 1.4 mmol/l. What is the single most useful test?

- A. Glucagon stimulation test
- B. Oral glucose tolerance test with growth hormone measurements
- C. Insulin + C-peptide levels during a hypoglycaemic episode
- D. Short ACTH test
- E. Insulin tolerance test

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- D. Short ACTH test
- E. Insulin tolerance test

This patient has symptoms typical of an insulinoma. Whilst supervised fasting is normally the investigation of choice if this option is not given then insulin + C-peptide levels during an acute hypoglycaemic episode are useful.

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics
- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features
- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis
- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management
- surgery
- diazoxide and somatostatin if patients are not *Candida*tes for surgery

Question 110 of 138

A 53-year-old heavy goods vehicle driver with a history of type II diabetes mellitus is reviewed in the diabetes clinic. Despite maximal oral hypoglycaemic therapy his HbA1c is 9.7%. If insulin therapy is started then which one of the following is most appropriate with regards to his job?

- A. Cannot continue to drive heavy goods vehicle
- B. Inform DVLA and recommence driving once stable insulin dose achieved
- C. Can only drive during daylight hours
- D. As under 55 years of age then no requirement to inform DVLA
- E. Needs annual screening to exclude retinopathy or neuropathy

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Patients on insulin cannot hold a HGV licence

DVLA: diabetes mellitus

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

Specific rules

- if on insulin then cannot hold HGV licence*
- if on insulin then patient can drive a car as long as they have hypoglycaemic awareness and no relevant visual impairment
- if on tablets, exenatide or gliptin no need to notify DVLA
- if diet controlled alone and no relevant complications (e.g. Maculopathy) then no requirement to inform DVLA

*there are complex exceptions to this rule, but these are not relevant for the purposes of the exam

Question 111 of 138

Each one of the following is associated with Pendred's syndrome, except:

- A. Goitre
- B. Short 4th and 5th metacarpals
- C. Autosomal recessive inheritance
- D. Sensorineural deafness
- E. Euthyroid status

Question 111 of 138

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- E. Euthyroid status

Pendred's syndrome

Autosomal recessive disorder of defective iodine uptake

Features
- sensorineural deafness
- goitre
- euthyroid or mild hypothyroidism

Question 112 of 138

Which one of the following combinations of treatments should be avoided in patients with type 2 diabetes mellitus?

- A. Metformin + insulin + exenatide
- B. Sulfonylurea + DPP-4 inhibitor
- C. Metformin + sulfonylurea + exenatide
- D. Metformin + DPP-4 inhibitor
- E. Insulin + metformin + sulfonylurea

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- C. Metformin + sulfonylurea + exenatide
- D. Metformin + DPP-4 inhibitor
- E. Insulin + metformin + sulfonylurea

Exenatide should only be used in combination with metformin, a sulfonylurea or both.

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 113 of 138

A 55-year-old woman with type 2 diabetes mellitus is reviewed. A decision is made to start thiazolidinedione therapy. Which one of the following points is it most relevant to consider before starting treatment?

- A. History of oesophageal problems
- B. Fracture risk
- C. History of depression
- D. History of cardiac arrhythmias
- E. Visual acuity

Question 113 of 138

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- A. History of oesophageal problems
- B. Fracture risk
- C. History of depression
- D. History of cardiac arrhythmias
- E. Visual acuity

There is increasing evidence thiazolidinediones increase the risk of fractures

Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 114 of 138

Which one of the following types of bariatric surgery is most likely to cause significant malabsorption?

- A. Laparoscopic-adjustable gastric banding
- B. Roux-en-Y gastric bypass surgery
- C. Biliopancreatic diversion with duodenal switch
- D. Sleeve gastrectomy
- E. Intragastric balloon

Question 114 of 138

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Biliopancreatic diversion with duodenal switch is a primarily malabsorptive procedure and reserved for patients who are very obese.

Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m2 in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m^2
- patients with a BMI > 40 kg/m^2 may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m^2)

Question 115 of 138

Which one of the following is most likely to be found in a patient with Hashimoto's thyroiditis?

- A. Raised ESR
- B. Anti-TSH receptor stimulating antibodies
- C. Anti-thyroid peroxidase antibodies
- D. Decreased TSH
- E. Co-existing type 2 diabetes mellitus

Question 115 of 138

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- E. Co-existing type 2 diabetes mellitus

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

Features

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

Question 116 of 138

A 20-year-old man presents with a nine month history of weight gain. Prior to this he was of a normal weight and cannot identify any obvious lifestyle changes that would account for his obesity. On examination he is noted to have abdominal striae and a degree of proximal myopathy. Blood pressure is 130/80 mmHg. Bloods show the following:

Na^+	141 mmol/l
K^+	3.3 mmol/l
Bicarbonate	26 mmol/l
Urea	3.3 mmol/l
Creatinine	72 µmol/l

What is the most appropriate test to confirm the diagnosis?

- A. High-dose dexamethasone suppression test
- B. Plasma ACTH
- C. Short ACTH test
- D. 24 hour urinary free cortisol
- E. Renin:aldosterone ratio

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The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

There is some debate as to whether a 24 hour urinary free cortisol or an overnight dexamethasone suppression test should be used to screen patients for Cushing's. The overnight (not high-dose) dexamethasone suppression test has however been shown to be more sensitive and is now much more commonly used in clinical practice. As this is not offered then 24 hour urinary free cortisol is the next best answer

For a review comparing diagnostic methods see 'Specificity of first-line tests for the diagnosis of Cushing's syndrome: assessment in a large series, J Clin Endocrinol Metab. 2007 Nov;92(11):4123-9'

The high-dose dexamethasone suppression test is used to help differentiate the cause of Cushing's syndrome

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test
- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation
- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Question 117 of 138

Each one of the following is associated with autoimmune polyendocrinopathy syndrome type 1, except:

A. Chronic mucocutaneous candidiasis

B. Addison's disease

C. Primary hyperparathyroidism

D. Autosomal recessive inheritance

E. A mutation of the AIRE1 gene on chromosome 21

Question 117 of 138

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Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

Question 118 of 138

A 62-year-old man is investigated for hypertension and proximal myopathy. On examination he is noted to have abdominal striae. Which one of the following is most associated with ectopic ACTH secretion?

- A. Carcinoid tumour
- B. Small cell lung cancer
- C. Cardiac myxoma
- D. Squamous cell lung cancer
- E. Adrenal carcinoma

Question 118 of 138

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- C. Cardiac myxoma
- D. Squamous cell lung cancer
- E. Adrenal carcinoma

Small cell lung cancer accounts 50-75% of case of ectopic ACTH

Adrenal carcinoma and cardiac myxoma are causes of ACTH independent Cushing's syndrome

Cushing's syndrome: causes

ACTH dependent causes
- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes
- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's
- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Question 119 of 138

Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

- A. Hypothyroidism
- B. Obesity
- C. Liver disease
- D. Bendrofluazide
- E. Chronic renal failure

Question 119 of 138

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- E. Chronic renal failure

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia
- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia
- nephrotic syndrome
- cholestasis
- hypothyroidism

Question 120 of 138

A 54-year-old man with type 2 diabetes mellitus is reviewed in clinic. He is currently taking rosiglitazone, aspirin and simvastatin. Which one of the following problems is most likely caused by rosiglitazone?

- A. Photosensitivity
- B. Thrombocytopaenia
- C. Myalgia
- D. Peripheral oedema
- E. Hyponatraemia

Question 120 of 138

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Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- rosiglitazone is not recommended for use in patients with ischaemic heart disease or peripheral arterial disease. The risk of complications may be increased if rosiglitazone is combined with insulin

NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 121 of 138

A 65-year-old man known to have a carcinoid tumour of the appendix is found to have hepatic metastases. If the patient develops carcinoid syndrome, which one of the following symptoms is most likely to occur first?

- A. Facial flushing
- B. Headache
- C. Vomiting
- D. Diarrhoea
- E. Palpitations

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Carcinoid tumours

Carcinoid syndrome
- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

Features
- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation
- urinary 5-HIAA
- plasma chromogranin A y

Management
- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help

Question 122 of 138

A 49-year-old woman with type 2 diabetes mellitus is being considered for exenatide therapy. Which one of the following is not part of the NICE criteria for starting or continuing this drug?

- A. BMI > 35 kg/m^2
- B. Greater than 1.0 percentage point HbA1c reduction after 6 months
- C. Has failed with insulin therapy
- D. Has type 2 diabetes mellitus
- E. Weight loss > 3% at 6 months

Question 122 of 138

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D. Has type 2 diabetes mellitus

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Patients do not need to have been on insulin prior to using exenatide

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)
- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide
- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:
- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)
- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 123 of 138

Which one of the following conditions may cause hypokalaemia in association with hypertension?

- A. Gitelman syndrome
- B. 21-hydroxylase deficiency
- C. Bartter's syndrome
- D. Phaeochromocytoma
- E. 11-beta hydroxylase deficiency

Question 123 of 138

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- E. 11-beta hydroxylase deficiency

21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension
- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2**)
- Bartter's syndrome
- Gitelman syndrome

*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

**type 4 renal tubular acidosis is associated with hyperkalaemia

Question 124 of 138

A 52-year-old has a fasting lipid profile checked as part of an annual occupational health check. Combined with his blood pressure and current smoking status his 10-year risk of cardiovascular disease is calculated to be 23% percent. Following appropriate counselling he chooses to start simvastatin 40mg on. What should his target cholesterol be?

- A. Total cholesterol:HDL ratio < 5
- B. Total cholesterol < 5 mmol/l
- C. Target cholesterol is inappropriate in this situation
- D. Total cholesterol < 4 mmol/l
- E. Total cholesterol:HDL ratio < 4

Question 124 of 138

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- E. Total cholesterol:HDL ratio < 4

In primary prevention of CVD, a target cholesterol is not appropriate

Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

The 1991 Framingham equations are still recommended to assess 10-year CVD risk. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing to simvastatin 80 mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained

Question 125 of 138

A 55-year-old female is reviewed in the diabetes clinic. The following results are obtained:
Urinalysis protein +
HbA1c 10.0%

What average blood glucose level for the past 2 months is this most likely to represent?

- A. 9
- B. 10
- C. 11
- D. 15
- E. There is no relation between HbA1c and average blood glucose

Question 125 of 138

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Glycosylated haemoglobin

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HBA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose = (2 * HbA1c) - 4.5

Question 126 of 138

Which one of the following increases the risk of developing peripheral oedema in a patient taking pioglitazone?

- A. Concomitant use with gliclazide
- B. Serum sodium < 140 mmol/l
- C. Concomitant use with insulin
- D. Concomitant use with metformin
- E. Serum potassium < 4.0 mmol/l

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- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
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NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Question 127 of 138

Which one of the following statements regarding dipeptidyl peptidase-4 inhibitors in the management of type 2 diabetes mellitus is correct?

- A. Metformin should always be co-prescribed
- B. Do not cause weight gain
- C. Is given via a subcutaneous injection
- D. An example is exenatide
- E. Patients should be warned that hypoglycaemia is the most common side-effect

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D. An example is exenatide

E. Patients should be warned that hypoglycaemia is the most common side-effect

Hypoglycaemia is rare in patients taking dipeptidyl peptidase-4 inhibitors.

Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

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NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Question 128 of 138

A middle-aged man with type 2 diabetes mellitus is reviewed. Despite weight loss, metformin and gliclazide his HbA1c is 8.4%. The patient agrees to start insulin therapy. According to NICE guidelines which type of insulin should be tried initially?

- A. Basal bolus regime
- B. Isophane
- C. Biphasic insulin
- D. Glargine
- E. Detemir

Question 128 of 138

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Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

Dietary advice
- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c
- the general target for patients is 6.5%. HbA1c levels below 6.5% should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

Blood pressure
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:
- NICE still suggest a trial of lifestyle interventions first*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 6.5%
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 7.5% then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m^2) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction in 6 months and weight loss > 5% at 1 year)

Starting insulin

- usually commenced if HbA1c > 7.5%
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Other risk factor modification

- aspirin to all patients > 50 years and to younger patients with other significant risk factors
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reach consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 129 of 138

Which one of the following is least associated with gynaecomastia?

- A. Klinefelter's syndrome
- B. Seminoma
- C. Liver disease
- D. Puberty
- E. Hypothyroidism

Question 129 of 138

Which one of the following is least associated with gynaecomastia?

- A. Klinefelter's syndrome
- B. Seminoma
- C. Liver disease
- D. Puberty
- E. Hypothyroidism

Gynaecomastia is seen in up to a third of men with thyrotoxicosis, but is not a feature of hypothyroidism

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia
- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

Drug causes of gynaecomastia
- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia
- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

Question 130 of 138

A 54-year-old man has a routine medical for work. He is asymptomatic and clinical examination is unremarkable. Which of the following results establishes a diagnosis of impaired fasting glucose?

- A. Fasting glucose 7.1 mmol/L on one occasion
- B. Fasting glucose 6.8 mmol/L on two occasions
- C. Glycosuria ++
- D. 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L
- E. HbA1c of 6.7%

Question 130 of 138

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- E. HbA1c of 6.7%

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

A 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L would imply impaired glucose tolerance rather than impaired fasting glucose

Diabetes mellitus: diagnosis

The following is based on the World Health Organisation 2006 guidelines.

Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Question 131 of 138

A 51-year-old woman is reviewed in the diabetes clinic. She was diagnosed with type 2 diabetes mellitus 12 months ago and still has poor glycaemic control. She has recently had to stop taking gliclazide due to repeated episodes of hypoglycaemia and is only taking maximum dose metformin. Her BMI is 26 kg/m^2. What is the most appropriate next step in management?

- A. Add either a thiazolidinedione or a DPP-4 inhibitor
- B. Refer her for a laparoscopic gastric band
- C. Refer her for insulin therapy
- D. Add either a thiazolidinedione or exenatide
- E. Add either a DPP-4 inhibitor or exenatide

Question 131 of 138

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The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

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- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

*many local protocols now recommend starting metformin upon diagnosis

Question 132 of 138

A 62-year-old male with a history of type 2 diabetes mellitus is investigated for lethargy. Blood tests are as follows:

Na^+	139 mmol/l
K^+	4.2 mmol/l
Bicarbonate	15 mmol/l
Chloride	105 mmol/l
Urea	15.2 mmol/l
Creatinine	267 µmol/l
Glucose	9.2 mmol/l

Which one of the following is most likely to be contributing to the low bicarbonate value?

- A. Vomiting due to gastroparesis
- B. Renal tubular acidosis
- C. Addison's disease
- D. Metformin
- E. Rosiglitazone

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- D. Metformin
- E. Rosiglitazone

Whilst the decreased bicarbonate value may be worsened by deteriorating renal function, it is important to exclude lactic acidosis secondary to metformin.

The raised anion gap is against a diagnosis of renal tubular acidosis.

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis* with severe liver disease or renal failure

Contraindications**

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

**metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Question 133 of 138

A 29-year-old woman has just found out she is pregnant for the second time. Her first pregnancy was complicated by gestational diabetes. Following her first pregnancy she was told she was no longer diabetic. What is the most appropriate management?

- A. Start insulin
- B. Start metformin and do oral glucose tolerance test at 12-14 weeks
- C. Do oral glucose tolerance test at booking visit
- D. Do oral glucose tolerance test at 16-18 weeks
- E. Do fasting glucose at booking visit

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- D. Do oral glucose tolerance test at 16-18 weeks
- E. Do fasting glucose at booking visit

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of > 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a women has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24–28 weeks

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of > 27 kg/m^2
- stop oral hypoglycaemic agents, apart from metformin*, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

Management of gestational diabetes

- responds to changes in diet and exercise in most women
- oral hypoglycaemic agents or insulin injections are needed if blood glucose control is poor or this is any evidence of complications (e.g. Macrosomia)
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

*there is increasing evidence that metformin is safe during pregnancy

Question 134 of 138

A 54-year-old obese man presents with lethargy and polyuria. A fasting blood sugar is requested:

Fasting glucose 8.4 mmol/l

He is given dietary advice and a decision is made to start metformin. What is the most appropriate prescription?

- A. Metformin 500mg od with food for 5 days then metformin 500mg bd for 5 days then metformin 500mg tds for 20 days then review
- B. Metformin 500mg tds with food
- C. Metformin 500mg od with food for 14 days then metformin 500mg bd for 14 days then review
- D. Metformin 1g tds with food
- E. Metformin 500mg tds taken at least 1 hour before meals

Question 134 of 138

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Metformin should be titrated slowly, leave at least 1 week before increasing dose

Gastrointestinal side-effects are more likely to occur if metformin is not slowly titrated up. The BNF advises leaving at least 1 week before increasing the dose.

Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

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Adverse effects

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Question 135 of 138

A 50-year-old man who is known to have obesity and hypertension comes for review. His current BMI is 38 kg/m^2 and blood pressure today is 154/92 mmHg despite ramipril and bendroflumethiazide. Lifestyle and a trial of orlistat have failed to reduce his weight. Which one of the following is the most suitable intervention?

- A. Biliopancreatic diversion with duodenal switch
- B. Laparoscopic-adjustable gastric banding
- C. Trial of sibutramine
- D. Referral for counselling to discuss his excessive eating
- E. Sleeve gastrectomy

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A trial of sibutramine would not be appropriate given his poorly controlled hypertension. Laparoscopic-adjustable gastric banding is the intervention of choice in patients with a BMI < 40 kg/m^2.

Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m2 in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m^2
- patients with a BMI > 40 kg/m^2 may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m^2)

Question 136 of 138

A 56-year-old Muslim man with a history of type 2 diabetes asks for advice. He is due to start fasting for Ramadan soon and is unsure what he should do with regards to his diabetes medications. He currently takes metformin 500mg tds. What is the most appropriate advice?

- A. Switch to subcutaneous biphasic insulin for the duration of Ramadan
- B. 500 mg at the predawn meal + 1000 mg at the sunset meal
- C. No change to the metformin dose
- D. 1000 mg at the predawn meal + 500 mg at the sunset meal
- E. Stop metformin for the duration of Ramadan

Question 136 of 138

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Please see the Diabetes Care link for more details.

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Question 137 of 138

Which one of the following features is least associated with primary hyperparathyroidism?

- A. Depression
- B. Polydipsia
- C. Sensory loss
- D. Peptic ulceration
- E. Hypertension

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Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism
- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'
- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations
- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations
- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment
- total parathyroidectomy

Question 138 of 138

A 7-year-old boy is being investigated for failure to thrive and generalised weakness. His blood pressure is normal. The following blood results are obtained:

Na^+	137 mmol/l
K^+	3.0 mmol/l
Urea	4.5 mmol/l
Creatinine	65 µmol/l
Bicarbonate	33 mmol/l

What is the most likely diagnosis?

- A. Conn's syndrome
- B. Bartter's syndrome
- C. Cushing's syndrome
- D. 21-hydroxylase deficiency
- E. Liddle's syndrome

Question 138 of 138

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Bartter's syndrome is associated with normotension

Bartter's syndrome is the most likely diagnosis. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency is associated with precocious puberty rather than failure to thrive in boys. Both Conn's and Cushing's are associated with hypertension and are not common in this age group.

Liddle's syndrome is a rare autosomal dominant condition that causes hypertension and hypokalaemic alkalosis. It is thought to be caused by disordered sodium channels in the distal tubules leading to increased reabsorption of sodium.

Bartter's syndrome

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na^+ K^+ 2Cl- cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension (unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome which are associated with hypertension)

Features

- usually presents in childhood, e.g. Failure to thrive
- polyuria, polydipsia
- hypokalaemia
- normotension
- weakness

Recommendations for Management of Diabetes During Ramadan

Before Ramadan	During Ramadan
Patients on diet and exercise control	No change needed (modify time and intensity of exercise), ensure adequate fluid intake
Patients on oral hypoglycemic agents	Ensure adequate fluid intake
Biguanide, metformin 500 mg three times a day, or sustained release metformin (glucophage R)	Metformin, 1,000 mg at the sunset meal (Iftar), 500 mg at the predawn meal (Suhur)
TZDs, pioglitazone or rosiglitazone once daily	No change needed
Sulfonylureas once a day, e.g., glimepiride 4 mg daily, gliclazide MR 60 mg daily	Dose should be given before the sunset meal (Iftar); adjust the dose based on the glycemic control and the risk of hypoglycemia
Sulfonylureas twice a day, e.g., glibenclamide 5 mg or gliclazide 80 mg, twice a day (morning and evening)	Use half the usual morning dose at the predawn meal (Suhur) and the full dose at the sunset meal (Iftar), e.g., glibenclamide 2.5 mg or gliclazide 40 mg in the morning, glibenclamide 5 mg or gliclazide 80 mg in evening
Patients on insulin	Ensure adequate fluid intake
70/30 premixed insulin twice daily, e.g., 30 units in morning and 20 units in evening	Use the usual morning dose at the sunset meal (Iftar) and half the usual evening dose at predawn (Suhur), e.g., 70/30 premixed insulin, 30 units in evening and 10 units in morning; also consider changing to glargine or detemir plus lispro or aspart

Question 1 of 142

A 54-year-old female presents with fatigue and xerostomia. Bloods tests reveal the following:

Hb	13.9 g/dl
WBC	6.1 *10^9/l
Platelets	246 *10^9/l
Bilirubin	33 µmol/l
ALP	292 u/l
ALT	47 u/l

What is the most likely diagnosis?

- A. Systemic lupus erythematous
- B. Infectious mononucleosis
- C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Sjogren's syndrome

Question 1 of 142

A 54-year-old female presents with fatigue and xerostomia. Bloods tests reveal the following:

Hb	13.9 g/dl
WBC	6.1 *10^9/l
Platelets	246 *10^9/l
Bilirubin	33 µmol/l
ALP	292 u/l
ALT	47 u/l

What is the most likely diagnosis?

- A. Systemic lupus erythematous
- B. Infectious mononucleosis
- ✓ C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Sjogren's syndrome

> Primary biliary cirrhosis - the **M** rule
> - Ig**M**
> - anti-**M**itochondrial antibodies, **M**2 subtype
> - **M**iddle aged females

The dry mouth is this patient is due to sicca syndrome, which occurs in 70% of cases of primary biliary cirrhosis. The cholestatic liver function tests point towards primary biliary cirrhosis rather than Sjogren's syndrome

Primary biliary cirrhosis: features

Primary biliary cirrhosis is chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis, which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

Clinical features
- early: may be asymptomatic (e.g. raised ALP on routine LFTs) or fatigue, pruritus
- cholestatic jaundice
- hyperpigmentation, especially over pressure points
- xanthelasmas, xanthomata
- also: clubbing, hepatosplenomegaly
- late: may progress to liver failure

Complications
- malabsorption: osteomalacia, coagulopathy
- sicca syndrome occurs in 70% of cases
- portal hypertension: ascites, variceal haemorrhage
- hepatocellular cancer (20-fold increased risk)

Question 2 of 142

A 24-year-old man presents with rectal bleeding and pain on defecation. This has been present for the past two weeks. He has a tendency towards constipation and notices that when he wipes himself fresh blood is often on the paper. Rectal examination is limited due to pain but no external abnormalities are seen. What is the most likely diagnosis?

- A. Internal haemorrhoids
- B. Anal carcinoma
- C. Rectal polyp
- D. Anogenital herpes
- E. Anal fissure

Question 2 of 142

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- C. Rectal polyp
- D. Anogenital herpes
- ✓ E. Anal fissure

Superficial anal fissures may be difficult to see on examination.

Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks)

- dietary advice: high-fibre diet with high fluid intake
- bulk-forming laxatives are first line - if not tolerated then lactulose should be tried
- lubricants such as petroleum jelly may be tried before defecation
- topical anaesthetics
- sitz baths: hip baths in hot water for 2–5 minutes followed by cold water for 1 minute
- topical steroids do not provide significant relief

Management of a chronic anal fissure (> 6 weeks)

- the above techniques should be continued
- topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure
- if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

Question 3 of 142

A 54-year-old man with a long history of heartburn has an endoscopy to investigate his symptoms. A biopsy is taken from an abnormal area of mucosa in the lower oesophagus and reported as follows:

Non-dysplastic columnar-lined oesophagus

What is the most suitable management?

- A. Reassure and discharge
- B. Fundoplication
- C. Laser ablation
- D. Ivor-Lewis oesophagectomy
- E. High-dose proton pump inhibitor and follow-up

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The 2005 British Society of Gastroenterology guidelines state that high-dose proton pump inhibitor therapy is first-line treatment in such patients. There is yet insufficient evidence to support the use of endoscopic ablation.

Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

Question 4 of 142

A 54-year-old woman presents with jaundice shortly after being discharged from hospital. Liver function tests are reported as follows:

Albumin	49 g/l
Bilirubin	89 µmol/l
Alanine transferase (ALT)	66 iu/l
Alkaline phosphatase (ALP)	245 µmol/l
Gamma glutamyl transferase (yGT)	529 u/l

Which of the following antibiotics is she most likely to have received?

- A. Flucloxacillin
- B. Gentamicin
- C. Ciprofloxacin
- D. Trimethoprim
- E. Ceftazidime

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- E. Ceftazidime

Flucloxacillin + co-amoxiclav are well recognised causes of cholestasis

Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 5 of 142

A 35-year-old man who is usually fit and well presents with a 2 month history of indigestion. His weight is stable and there is no history of dysphagia. Examination of the abdomen is unremarkable. Of the following options, what is the most suitable initial management?

- A. Urea breath testing and non-urgent referral for endoscopy
- B. H pylori eradication therapy and full-dose proton pump inhibitor for three months
- C. Full-dose Proton pump inhibitor and immediate referral for endoscopy
- D. Three month course of a standard-dose proton pump inhibitor
- E. One month course of a full-dose proton pump inhibitor

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- C. Full-dose Proton pump inhibitor and immediate referral for endoscopy
- D. Three month course of a standard-dose proton pump inhibitor
- ✓ E. One month course of a full-dose proton pump inhibitor

This question highlights the NICE guidelines for the management of dyspepsia.

There is no evidence currently to suggest whether a one month course of a PPI or 'test and treat' strategy should be adopted first line. Many clinicians prefer to test for H pylori first as this cannot be done within 2 weeks of acid-suppression therapy, as false-negative results may occur

Given the options available, only the answer is in line with current NICE guidelines

Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')

This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month*
- 4. 'Test and treat' using carbon-13 urea breath test

*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Question 6 of 142

A patient with upper gastrointestinal symptoms tests positive for *Helicobacter pylori* following a urea breath test. Which one of the following conditions is most strongly associated *Helicobacter pylori* infection?

- A. Gastric adenocarcinoma
- B. Gastro-oesophageal reflux disease
- C. Oesophageal cancer
- D. Duodenal ulceration
- E. Atrophic gastritis

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Helicobacter pylori infection is also associated with both gastric adenocarcinoma and atrophic gastritis but the strongest association is with duodenal ulceration.

Helicobacter pylori

Helicobacter pylori is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

Associations
- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of
- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

Question 7 of 142

Which one of the following is most suggestive of Wilson's disease?

- A. Reduced hepatic copper concentration
- B. Reduced 24hr urinary copper excretion
- C. Increased skin pigmentation
- D. Reduced serum caeruloplasmin
- E. Reduced serum copper

Question 7 of 142

Which one of the following is most suggestive of Wilson's disease?

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- B. Reduced 24hr urinary copper excretion
- C. Increased skin pigmentation
- ✓ D. Reduced serum caeruloplasmin
- E. Reduced serum copper

Wilson's disease - serum caeruloplasmin is **decreased**

Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Question 8 of 142

A 22-year-old male blood donor is noted to have the following blood results:

Bilirubin	41 µmol/L
ALP	84 U/L
ALT	23 U/L
Albumin	41 g/L

Dipstick urinalysis No bilirubinuria

He has recently complained of coryzal symptoms and a non-productive cough. What is the most likely diagnosis?

- A. Gilbert's syndrome
- B. Dubin-Johnson syndrome
- C. Rotor syndrome
- D. Hepatitis C infection
- E. Infectious mononucleosi

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- D. Hepatitis C infection
- E. Infectious mononucleosis

An isolated hyperbilirubinaemia in a 22-year-old male is likely to be secondary to Gilbert's syndrome. The normal dipstix urinalysis excludes Dubin-Johnson and Rotor syndrome as these both produce a conjugated bilirubinaemia. Viral infections are common triggers for a rise in the bilirubin in patients with Gilbert's

Gilbert's syndrome

Gilbert's syndrome is an autosomal recessive* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

Features

- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

Investigation and management

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

*the exact mode of inheritance is still a matter of debate

Question 9 of 142

A 49-year-old female is referred to the gastroenterology out-patient clinic with a 3 month history of epigastric pain and diarrhoea. Her GP initially prescribed lansoprazole 30mg od but this didn't alleviate her symptoms. The only past medical history of note is hyperparathyroidism.

Endoscopy revealed multiple duodenal ulcerations. What is the likely diagnosis?

- A. Multiple endocrine neoplasia type II a
- B. Coeliac disease
- C. Multiple endocrine neoplasia type I
- D. Autoimmune polyendocrinopathy syndrome
- E. Crohn's disease

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Zollinger-Ellison syndrome: epigastric pain and diarrhoea

Zollinger-Ellison syndrome typically presents with multiple gastroduodenal ulcers causing abdominal pain and diarrhoea. High-dose proton pump inhibitors are needed to control the symptoms. Around a third of patients may have multiple endocrine neoplasia type I (MEN-I), explaining the hyperparathyroidism in this patient.

MEN-I
- parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia
- pituitary (70%)
- pancreas (50%, e.g. Insulinoma, gastrinoma)
- also: adrenal and thyroid

Zollinger-Ellison syndrome

Zollinger-Ellison syndrome is condition characterised by excessive levels of gastrin, usually from a gastrin secreting tumour usually of the duodenum or pancreas. Around 30% occur as part of MEN type I syndrome

Features
- multiple gastroduodenal ulcers
- diarrhoea
- malabsorption

Diagnosis
- fasting gastrin levels: the single best screen test
- secretin stimulation test

Question 10 of 142

A 31-year-old man with a known history of alcoholic liver disease is reviewed following a suspected oesophageal variceal haemorrhage. He has been resuscitated and intravenous terlipressin has been given. His blood pressure is now 104/60 mmHg and his pulse is 84/min. What is the most appropriate intervention?

- A. Transjugular Intrahepatic Portosystemic Shunt
- B. Surgical referral
- C. Endoscopic variceal band ligation
- D. Sengstaken-Blakemore tube
- E. Endoscopic sclerotherapy

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Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 11 of 142

Which one of the following is the most likely presentation of *Staphylococcus aureus* food poisoning?

- A. Tenesmus
- B. Watery diarrhoea
- C. Dysentery
- D. Severe vomiting
- E. Presentation 24-48 hours after eating affected food

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Severe nausea and vomiting are caused by enterotoxins A-E

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 12 of 142

A 43-year-old man presents with diarrhoea and rectal bleeding for the past ten days. On examination he has brown pigmented lesions on his lips and palms but abdominal and rectal examination is unremarkable. What is the most likely cause for this presentation?

- A. Intussusception
- B. Angiodysplasia
- C. Meckel's Diverticulum
- D. Colon cancer
- E. Diverticular abscess

Question 12 of 142

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- B. Angiodysplasia
- C. Meckel's Diverticulum
- ✓ D. Colon cancer
- E. Diverticular abscess

This patient has Peutz-Jeghers syndrome. Intussusception would not normally cause rectal bleeding at this age. Colon cancer is the most common type of gastrointestinal cancer that patients with Peutz-Jeghers syndrome develop.

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 13 of 142

A 46-year-old man is being investigated for indigestion. Jejunal biopsy shows deposition of macrophages containing PAS-positive granules. What is the most likely diagnosis?

- A. Bacterial overgrowth
- B. Coeliac disease
- C. Tropical sprue
- D. Whipple's disease
- E. Small bowel lymphoma

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- ✓ D. Whipple's disease
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Whipple's disease: jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

Whipple's disease

Whipple's disease is a rare multi-system disorder caused by Tropheryma whippelii infection. It is more common in those who are HLA-B27 positive and in middle-aged men

\Features
- malabsorption: diarrhoea, weight loss
- large-joint arthralgia
- lymphadenopathy
- skin: hyperpigmentation and photosensitivity
- pleurisy, pericarditis
- neurological symptoms (rare): ophthalmoplegia, dementia, seizures, ataxia, myoclonus

Investigation
- jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

Management
- varies e.g. IV penicillin then oral co-trimoxazole for a year

Question 14 of 142

Of the following, which one is the most useful prognostic marker in paracetamol overdose?

- A. ALT
- B. Prothrombin time
- C. Paracetamol levels at presentation
- D. Paracetamol levels at 12 hours
- E. Paracetamol levels at 24 hours

Question 14 of 142

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- ✓ B. Prothrombin time
- C. Paracetamol levels at presentation
- D. Paracetamol levels at 12 hours
- E. Paracetamol levels at 24 hours

An elevated prothrombin time signifies liver failure in paracetamol overdose and is a marker of poor prognosis. However, arterial pH, creatinine and encephalopathy are also markers of a need for liver transplantation \

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300 µmol/l
- grade III or IV encephalopathy

Question 15 of 142

A 54-year-old female presents with a 3 month history of dysphagia affecting both food and liquids from the start, along with occasional symptoms of heartburn. What is the most likely underlying diagnosis?

- A. Pharyngeal pouch
- B. Gastric adenocarcinoma
- C. Benign stricture
- D. Oesophageal cancer
- E. Achalasia

Question 15 of 142

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- D. Oesophageal cancer
- ✓ E. Achalasia

Dysphagia affecting both solids and liquids from the start - think achalasia

This is a classic history of achalasia with dysphagia affecting both solids and liquids from the start.

Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is more common in women

Clinical features

- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

Investigations

- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

Treatment

- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Question 16 of 142

A 25-year-old man presents with lethargy and increased skin pigmentation. Blood test reveal deranged liver function tests and impaired glucose tolerance. Given the likely diagnosis of haemochromatosis, what is the most appropriate initial investigation strategy?

- A. Transferrin saturation + ferritin
- B. Haematocrit + ferritin
- C. Liver biopsy with Perl's stain
- D. Serum iron + ferritin
- E. Serum iron + haematocrit

Question 16 of 142

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- E. Serum iron + haematocrit

Screening for haemochromatosis
- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

The British Committee for Standards in Haematology (BCSH) guidelines recommend measuring the transferrin saturation first as this is the most specific and sensitive test for iron accumulation. They also recommend that serum ferritin is measured but this marker is not usually abnormal in the early stages of iron accumulation

Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:
- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

Diagnostic tests
- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis
- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection
- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Question 17 of 142

Crohn's disease is associated with each one of the following findings, except:

- A. Inflammation confined to the mucosa and submucosa
- B. Non-caseating granulomas
- C. Rose-thorn ulcers
- D. Cobblestone pattern
- E. Fistulas

Question 17 of 142

Crohn's disease is associated with each one of the following findings, except:

- ✓ A. Inflammation confined to the mucosa and submucosa
- B. Non-caseating granulomas
- C. Rose-thorn ulcers
- D. Cobblestone pattern
- E. Fistulas

IBD: histology

This histological differences between ulcerative colitis and Crohn's are summarised below:

Ulcerative colitis

- inflammation in mucosa and submucosa only (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

Crohn's

- inflammation occurs in all layers, down to the serosa. This predisposes to strictures, fistulas and adhesions
- oedema of mucosa and submucosa, combined with deep fissured ulcers ('rose-thorn') leads to a 'cobblestone' pattern
- lymphoid aggregates
- non-caseating granulomas

Question 18 of 142

A 34-year-old female with a history of alcoholic liver disease is admitted with frank haematemesis. She was discharged three months ago following treatment for bleeding oesophageal varices. Following resuscitation, what is the most appropriate treatment whilst awaiting endoscopy?

- A. Octreotide
- B. Omeprazole
- C. Propranolol
- D. Tranexamic acid
- E. Terlipressin

Question 18 of 142

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- B. Omeprazole
- C. Propranolol
- D. Tranexamic acid
- ✓ E. Terlipressin

Terlipressin is the only licensed vasoactive agent for variceal haemorrhage in the UK

Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 19 of 142

A 25-year-old man with a history of Crohn's disease is reviewed in clinic. Over the past week he has developed painful perianal ulcers. On examination numerous shallow ulcers can be seen with a small number of skin tags. What is the most appropriate first-line treatment?

- A. Topical mesalazine
- B. Oral metronidazole
- C. Barrier creams + laxatives
- D. Oral prednisolone
- E. Oral mesalazine

Question 19 of 142

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- C. Barrier creams + laxatives
- D. Oral prednisolone
- E. Oral mesalazine

Please see the British Society of Gastroenterology guidelines for more details.

Crohn's disease: management

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

General points
- patients should be strongly advised to stop smoking
- some studies suggest an increased risk of relapse secondary to NSAIDs and the combined oral contraceptive pill but the evidence is patchy

Active disease
- mesalazine: whilst evidence base is limited widely used in active disease
- steroids (oral, topical or intravenous)
- azathioprine is used as a second-line treatment in active disease
- methotrexate is used in patients intolerant of azathioprine or refractory disease. Usually given intramuscularly
- infliximab is useful in refractory disease and fistulating Crohn's. Patients typically continue on azathioprine or methotrexate

Perianal disease
- metronidazole is first-line

Enteral feeding with an elemental diet
- may be used in addition to or instead of other measures to induce remission

Surgery
- around 80% of patients with Crohn's disease will eventually have surgery

Question 20 of 142

A 44-year-old man is diagnosed with a duodenal ulcer. CLO testing performed during the gastroscopy is positive for *Helicobacter pylori*. What is the most appropriate management to eradicate *Helicobacter pylori*?

- A. Lansoprazole + clindamycin + metronidazole
- B. Lansoprazole + amoxicillin + clindamycin
- C. Lansoprazole + amoxicillin + clarithromycin
- D. Omeprazole + amoxicillin + clindamycin
- E. Omeprazole + penicillin + metronidazole

Question 20 of 142

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B. Lansoprazole + amoxicillin + clindamycin

✓ C. Lansoprazole + amoxicillin + clarithromycin

D. Omeprazole + amoxicillin + clindamycin

E. Omeprazole + penicillin + metronidazole

H. pylori eradication:
- PPI + amoxicillin + clarithromycin, or
- PPI + metronidazole + clarithromycin

The BNF recommends a regimen containing amoxicillin and clarithromycin as first-line therapy

Helicobacter pylori

Helicobacter pylori is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

Associations
- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of
- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

Question 21 of 142

Which one of the following is true regarding bacterial exotoxins?

- A. They are mainly produced by Gram positive bacteria
- B. Cholera toxin inhibits cAMP release in intestinal cells
- C. Diphtheria toxin necrosis is limited to the pharynx, nasopharynx and tonsils
- D. *Staph. aureus* exotoxins are not known to cause gastroenteritis
- E. 'Lockjaw' seen in tetanus is secondary to blockade of the neuromuscular junction by Botulinus toxin

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Exotoxins

Exotoxins are generally released by Gram positive bacteria with the notable exceptions of Vibrio cholerae and some strains of *E. coli*

Diphtheria toxin commonly causes a 'diphtheric membrane' on tonsils caused by necrotic mucosal cells. Systemic distribution may produce necrosis of myocardial, neural and renal tissue.

Staph. aureus exotoxins lead to acute gastroenteritis, toxic shock syndrome and Staphylococcal scalded skin syndrome

Lockjaw is caused by *Clostridium tetani* neurotoxin (tetanospasmin)

Cholera toxin causes activation of adenylate cyclase leading to increases in cAMP levels, which in turn leads to increased chloride secretion.

Question 22 of 142

A 54-year-old female with a history of scleroderma presents with chronic diarrhoea and bloating. Blood tests show a mild macrocytic anaemia. A diagnosis of small bowel bacterial overgrowth is suspected. Which one of the following tests is most likely to confirm the diagnosis?

- A. Jejunal biopsy
- B. Small bowel aspiration and culture
- C. 14C-xylose breath test
- D. Small bowel meal
- E. 14C-glycocholate breath test

Question 22 of 142

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- C. 14C-xylose breath test
- D. Small bowel meal
- E. 14C-glycocholate breath test

Whilst small bowel aspiration and culture is the gold standard investigation in this situation, its use is often limited due to resource limitations. Please see the British Society of Gastroenterology guidelines

The hydrogen breath test is another option. It has low sensitivity but high specificity

Bacterial overgrowth: investigation

The gold standard investigation of bacterial overgrowth is small bowel aspiration and culture

Other possible investigations include:

- hydrogen breath test
- 14C-xylose breath test
- 14C-glycocholate breath test: used increasingly less due to low specificity

In practice many clinicians give an empirical course of antibiotics as a trial

Question 23 of 142

A 38-year-old female with a long history of alcohol excess presents with abdominal pain, weight loss and bulky stools. What is the most suitable investigation to confirm the diagnosis?

- A. Endoscopic ultrasound
- B. Endoscopic retrograde cholangiopancreatography
- C. Ultrasound abdomen
- D. CT abdomen
- E. Endoscopy with D2 biopsy

Question 23 of 142

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- A. Endoscopic ultrasound
- B. Endoscopic retrograde cholangiopancreatography
- C. Ultrasound abdomen
- ✓ D. CT abdomen
- E. Endoscopy with D2 biopsy

This patient has chronic pancreatitis. CT is the most sensitive method to detect the characteristic pancreatic calcification which is associated with the condition

Chronic pancreatitis

Chronic pancreatitis is an inflammatory condition which can ultimately affect both the exocrine and endocrine functions of the pancreas. Around 80% of cases are due to alcohol excess with up to 20% of cases being unexplained

Features
- pain is typically worse 15 to 30 minutes following a meal
- steatorrhoea: symptoms of pancreatic insufficiency usually develop between 5 and 25 years after the onset of pain
- diabetes mellitus develops in the majority of patients. It typically occurs more than 20 years after symptom begin

Investigation
- abdominal x-ray shows pancreatic calcification in 30% of cases
- CT is more sensitive at detecting pancreatic calcification
- functional tests: pancreolauryl and Lundh tests may be used to assess exocrine function if imaging inconclusive

Management
- pancreatic enzyme supplements
- analgesia
- antioxidants: limited evidence base - one study suggests benefit in early disease

Question 24 of 142

A 31-year-old female is admitted to the Emergency Department following a paracetamol overdose. The paracetamol level comes back as elevated but the doctor is unsure which treatment line to use. Which one of the following features in the medical history would classify the patient as high risk?

- A. Hypothyroidism
- B. Anorexia nervosa
- C. Previous paracetamol overdose
- D. Combined overdose with codeine
- E. Long-term sodium valproate use

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- D. Combined overdose with codeine
- E. Long-term sodium valproate use

Paracetamol overdose - high risk if chronic alcohol, HIV, anorexia or P450 inducers

Paracetamol overdose: risk factors

The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose:

- chronic alcohol excess
- patients on P450 enzyme inducers (rifampicin, phenytoin, carbamazepine)
- anorexia nervosa: decreased glutathione stores
- HIV

Question 25 of 142

A 54-year-old man is investigated for dyspepsia. An endoscopy shows a gastric ulcer and a CLO test done during the procedure demonstrates *H. pylori* infection. A course of *H. pylori* eradication therapy is given. What is the most appropriate test to confirm eradication?

- A. Culture of gastric biopsy
- B. *H. pylori* serology
- C. Hydrogen breath test
- D. Urea breath test
- E. Stool culture

Question 25 of 142

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- C. Hydrogen breath test
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- E. Stool culture

It is important to remember that *H. pylori* serology remains positive following eradication

***Helicobacter pylori*: tests**

Urea breath test
- patients consume a drink containing carbon isotope 13 (13C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of 13C CO2
- sensitivity 95-98%, specificity 97-98%

Rapid urease test (e.g. CLO test)
- biopsy sample is mixed with urea and pH indicator
- colour change if H pylori urease activity
- sensitivity 90-95%, specificity 95-98%

Serum antibody
- remains positive after eradication
- sensitivity 85%, specificity 80%

Culture of gastric biopsy
- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

Gastric biopsy
- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

Stool antigen test
- sensitivity 90%, specificity 95%

Question 26 of 142

A 25-year-old woman develops deranged liver function tests following the introduction of a new drug. Alb 40, Bilirubin 46, ALT 576, ALP 95, yGT 150. Which of the following drugs is the most likely cause?

- A. Oral contraceptive pill
- B. Sodium valproate
- C. Flucloxacillin
- D. Chlorpromazine
- E. Tetracycline

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- C. Flucloxacillin
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- E. Tetracycline

The liver function tests suggest a hepatitis rather than cholestasis. Sodium valproate may be associated with such a picture

Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin*, nitrofurantoin
- anabolic steroids, testosterones
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

*risk may be reduced with erythromycin stearate

Question 27 of 142

Primary sclerosing cholangitis is most associated with:

- A. Primary biliary cirrhosis
- B. Crohn's disease
- C. Hepatitis C infection
- D. Ulcerative colitis
- E. Coeliac disease

Question 27 of 142

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Primary sclerosing cholangitis

Primary sclerosing cholangitis is a biliary disease of unknown aetiology characterised by inflammation and fibrosis of intra and extra-hepatic bile ducts

Associations
- ulcerative colitis: 4% of patients with UC have PSC, 80% of patients with PSC have UC
- Crohn's (much less common association than UC)
- HIV

Features
- cholestasis

Investigation
- ERCP is the standard diagnostic tool, showing multiple biliary strictures giving a 'beaded' appearance
- ANCA may be positive
- there is a limited role for liver biopsy, which may show fibrous, obliterative cholangitis often described as 'onion skin'

Complications
- cholangiocarcinoma (in 10%)
- increased risk of colorectal cancer

Question 28 of 142

A patient presents with gastrointestinal symptoms. Which one of the following features in the history would be least consistent with making a diagnosis of irritable bowel syndrome?

- A. Past medical history of epilepsy
- B. Symptoms made worse by eating
- C. 62-year-old female
- D. Passage of mucous with stool
- E. Bladder symptoms

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- ✓ C. 62-year-old female
- D. Passage of mucous with stool
- E. Bladder symptoms

Onset after 60 years of age is considered a red flag in the new NICE guidelines. A history of epilepsy has no bearing on whether a patient is diagnosed with irritable bowel syndrome

Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Question 29 of 142

A 26-year-old woman who is known to have type 1 diabetes mellitus presents with a three-month history of diarrhoea, fatigue and weight loss. She has tried excluding gluten from her diet for the past 4 weeks and feels much better. She requests to be tested so that a diagnosis of coeliac disease is confirmed. What is the most appropriate next step?

- A. Check her HbA1c
- B. No need for further investigation as the clinical response is diagnostic
- C. Check anti-endomysial antibodies
- D. Arrange a jejunal biopsy
- E. Ask her to reintroduce gluten for the next 6 weeks before further testing

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Serological tests and jejunal biopsy may be negative if the patient is following a gluten-free diet. The patient should eat some gluten in more than one meal every day for at least 6 weeks before further testing.

Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

Immunology
- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

Jejunal biopsy
- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

Question 30 of 142

A 52-year-old woman is diagnosed with non-alcoholic steatohepatitis following a liver biopsy. What is the single most important step to help prevent the progression of her disease?

- A. Stop smoking
- B. Start statin therapy
- C. Eat more omega-3 fatty acids
- D. Start sulfonylurea therapy
- E. Weight loss

Question 30 of 142

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- ✓ E. Weight loss

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and though to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

Question 31 of 142

Which of the following statements is true regarding the genetics of colon cancer?

- A. Hereditary non-polyposis colorectal carcinoma is a autosomal recessive condition
- B. The adenomatous polyposis coli gene is located on chromosome 12
- C. Around 50% of patients with familial adenomatous polyposis develop colon cancer
- D. Both hereditary and non-hereditary colon cancers typically present at 60-70 yrs of age
- E. Non-inherited colon cancer often involves mutation of the adenomatous polyposis coli gene

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Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are often poorly differentiated and highly aggressive. Currently four gene mutations have been identified (including in the hMLH1 and hMSH2 genes). The Amsterdam criteria are sometimes used to aid diagnosis:

Amsterdam criteria for HNPCC

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Question 32 of 142

A 23-year-old man develops watery diarrhoea 5 days after arriving in Mexico. Which one of the following is the most likely responsible organism?

- A. *Salmonella*
- B. *Shigella*
- C. *Campylobacter*
- D. *Escherichia coli*
- E. *Bacillus cereus*

Question 32 of 142

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- C. *Campylobacter*
- ✓ D. *Escherichia coli*
- E. *Bacillus cereus*

E. coli is the most common cause of travellers' diarrhoea

Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Escherichia coli	Common amongst travellers Watery stools Abdominal cramps and nausea
Giardiasis	Prolonged, non-bloody diarrhoea
Cholera	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
Shigella	Bloody diarrhoea Vomiting and abdominal pain
Staphylococcus aureus	Severe vomiting Short incubation period
Campylobacter	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody Complications include Guillain-Barre syndrome
Bacillus cereus	Two types of illness are seen • vomiting within 6 hours, stereotypically due to rice • diarrhoeal illness occurring after 6 hours
Amoebiasis	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus**
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Question 33 of 142

Each one of the following is a risk factor for gastric cancer, except:

- A. Smoking
- B. Blood group O
- C. Nitrates in diet
- D. Pernicious anaemia
- E. *H. pylori* infection

Question 33 of 142

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Gastric cancer

Epidemiology
- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Colombia than the West
- more common in males, 2:1

Associations
- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

Investigation
- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Question 34 of 142

Which one of the following is most associated with the development of acute pancreatitis?

- A. Hyperchylomicronaemia
- B. Amyloidosis
- C. Hypogammaglobulinaemia
- D. Hypercholesterolaemia
- E. Hypotriglyceridaemia

Question 34 of 142

Which one of the following is most associated with the development of acute pancreatitis?

- ✓ A. Hyperchylomicronaemia
- B. Amyloidosis
- C. Hypogammaglobulinaemia
- D. Hypercholesterolaemia
- E. Hypotriglyceridaemia

Hyperchylomicronaemia may be caused by hereditary lipoprotein lipase deficiency and apolipoprotein CII deficiency. It predisposes to recurrent attacks of acute pancreatitis

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 35 of 142

A 25-year-old female currently under investigation for secondary amenorrhoea presents with jaundiced sclera. On examination spider naevi are present along with tender hepatomegaly. Blood tests show:

Hb	11.6 g/dl
Plt	145 * 10^9/l
WCC	6.4 * 10^9/l
Albumin	33 g/l
Bilirubin	78 µmol/l
ALT	245 iu/l

What is the most likely diagnosis?

- A. Haemochromatosis
- B. Wilson's disease
- C. Primary biliary cirrhosis
- D. Autoimmune hepatitis
- E. Primary sclerosing cholangitis

Question 35 of 142

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- E. Primary sclerosing cholangitis

The combination of deranged LFTs combined with secondary amenorrhoea in a young female strongly suggest autoimmune hepatitis

Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	**Type II**	**Type III**
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA) Affects both adults and children	Anti-liver/kidney microsomal type 1 antibodies (LKM1) Affects children only	Soluble liver-kidney antigen Affects adults in middle-age

Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Question 36 of 142

What is the most common cause of hepatocellular carcinoma in the United Kingdom?

- A. Haemochromatosis
- B. Hepatitis B
- C. Alcohol excess
- D. Aflatoxin
- E. Hepatitis C

Question 36 of 142

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Hepatocellular carcinoma
• hepatitis B most common cause worldwide • hepatitis C most common cause in Europe

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

*Wilson's disease is an exception

Question 37 of 142

A 34-year-old HIV positive man is referred to gastroenterology due to jaundiced sclera. Liver function tests are as follows:

Albumin 34 g/l

ALP 540 iu/l

Bilirubin 67 µmol/l

ALT 45 iu/l

What is the most likely diagnosis?

- A. Hepatic abscess
- B. Fungal obstruction of the bile duct
- C. Duodenal adenoma
- D. Primary biliary cirrhosis
- E. Sclerosing cholangitis

Question 37 of 142

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Albumin 34 g/l

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What is the most likely diagnosis?

- A. Hepatic abscess
- B. Fungal obstruction of the bile duct
- C. Duodenal adenoma
- D. Primary biliary cirrhosis
- ✓ E. Sclerosing cholangitis

The LFTs clearly show a cholestatic picture. Given the background of HIV the most likely cause is sclerosing cholangitis

HIV: biliary and pancreatic disease

The most common cause of biliary disease in patients with HIV is sclerosing cholangitis due to infections such as CMV, Cryptosporidium and Microsporidia

Pancreatitis in the context of HIV infection may be secondary to anti-retroviral treatment (especially didanosine) or by opportunistic infections e.g. CMV

Question 38 of 142

A 65-year-old man with a history of dyspepsia is found to have a gastric MALT lymphoma on biopsy. What treatment should be offered?

- A. Gastrectomy
- B. Laser ablation
- C. None
- D. CHOP chemotherapy
- E. *H. pylori* eradication

Question 38 of 142

A 65-year-old man with a history of dyspepsia is found to have a gastric MALT lymphoma on biopsy. What treatment should be offered?

- A. Gastrectomy
- B. Laser ablation
- C. None
- D. CHOP chemotherapy
- ✓ E. *H. pylori* eradication

Gastric MALT lymphoma

Overview
- associated with *H. pylori* infection in 95% of cases
- good prognosis
- if low grade then 80% respond to *H. pylori* eradication

Features
- paraproteinaemia may be present

Question 39 of 142

A 42-year-old dentist is reviewed in the medical clinic complaining of persistent lethargy. Routine bloods show abnormal liver function tests so a hepatitis screen is sent. The results are shown below:

Anti-HAV IgG	negative
HBsAg	negative
Anti-HBs	positive
Anti-HBc	negative
Anti-HCV	positive

What do these results most likely demonstrate?

- A. Hepatitis B infection
- B. Hepatitis C infection
- C. Previous vaccination to hepatitis B and C
- D. Hepatitis C infection with previous hepatitis B vaccination
- E. Hepatitis B and C infection

Question 39 of 142

A 42-year-old dentist is reviewed in the medical clinic complaining of persistent lethargy. Routine bloods show abnormal liver function tests so a hepatitis screen is sent. The results are shown below:

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HBsAg	negative
Anti-HBs	positive
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What do these results most likely demonstrate?

- A. Hepatitis B infection
- B. Hepatitis C infection
- C. Previous vaccination to hepatitis B and C
- ✓ D. Hepatitis C infection with previous hepatitis B vaccination
- E. Hepatitis B and C infection

Given the deranged liver function tests these results most likely indicate previous hepatitis B vaccination with active hepatitis C infection. However, around 15% of patients exposed to the hepatitis C virus clear the infection. It would therefore be necessary to perform a HCV PCR to see if the virus is still present

There is currently no vaccination for hepatitis C

Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 40 of 142

You wish to screen a patient for hepatitis B infection. Which one of the following is the most suitable test to perform?

- A. HBcAg
- B. HBsAg
- C. Hepatitis B viral load
- D. anti-HBs
- E. HBeAg

Question 40 of 142

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- A. HBcAg
- ✓ B. HBsAg
- C. Hepatitis B viral load
- D. anti-HBs
- E. HBeAg

A positive anti-HBs would imply immunity through either previous immunisation or disease. A positive HBsAg implies either acute or chronic hepatitis B.

Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Question 41 of 142

A 76-year-old woman with a history of atrial fibrillation presents with abdominal pain and bloody diarrhoea. On examination her temperature is 37.8ºC, pulse 102 / min and respiratory rate 30 / min. Her abdomen is tender with generalised guarding. Blood tests reveal the following:

Hb	10.9 g/dl
MCV	76 fl
Plt	348 * 10^9/l
WBC	23.4 * 10^9/l
Na^+	141 mmol/l
K^+	5.0 mmol/l
Bicarbonate	14 mmol/l
Urea	8.0 mmol/l
Creatinine	118 µmol/l

What is the most likely diagnosis?

- A. Diverticulitis
- B. Mesenteric ischaemia
- C. *Campylobacter* infection
- D. Ruptured abdominal aortic aneurysm
- E. Ulcerative colitis

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WBC 23.4 * 10^9/l

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Bicarbonate 14 mmol/l

Urea 8.0 mmol/l

Creatinine 118 µmol/l

What is the most likely diagnosis?

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- ✓ B. Mesenteric ischaemia
- C. *Campylobacter* infection
- D. Ruptured abdominal aortic aneurysm
- E. Ulcerative colitis

The low bicarbonate points to a metabolic acidosis - highly suggestive of mesenteric ischaemia.

Mesenteric ischaemia

Mesenteric ischaemia is primarily caused by arterial embolism resulting in infarction of the colon. It is more likely to occur in areas such as the splenic flexure that are located at the borders of the territory supplied by the superior and inferior mesenteric arteries.

Predisposing factors

- increasing age
- atrial fibrillation
- other causes of emboli: endocarditis
- cardiovascular disease risk factors: smoking, hypertension, diabetes

Features

- abdominal pain
- rectal bleeding
- diarrhoea
- fever
- bloods typically show an elevated WBC associated with acidosis

Management

- supportive care
- laparotomy and bowel resection

Question 42 of 142

Which one of the following medications is least associated with dyspepsia?

- A. Isosorbide mononitrate
- B. Prednisolone
- C. Aminophylline
- D. Atenolol
- E. Amlodipine

Question 42 of 142

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Drugs causing dyspepsia

Causes
- NSAIDs
- bisphosphonates
- steroids

The following drugs may cause reflux by reducing lower oesophageal sphincter (LOS) pressure
- calcium channel blockers*
- nitrates*
- theophyllines

*calcium channel blockers and nitrates are occasionally used in the management of achalasia, itself a cause of dyspepsia, because of their effect on the LOS.

Question 43 of 142

A 31-year-old man with ulcerative colitis presents with a worsening of his symptoms. He is passing around four loose stools a day which do not contain blood. He has also experienced some urgency and tenesmus but is otherwise systemically well. What is the most appropriate management?

- A. Rectal mesalazine
- B. Oral metronidazole
- C. Rectal corticoteroids
- D. Observe with review in 7 days time
- E. Oral loperamide

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- C. Rectal corticoteroids
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- E. Oral loperamide

Ulcerative colitis: management

Treatment can be divided into inducing and maintaining remission

Inducing remission

- treatment depends on the extent and severity of disease
- rectal aminosalicylates or steroids: for distal colitis rectal mesalazine has been shown to be superior to rectal steroids
- oral aminosalicylates or steroids
- severe colitis should be referred to hospital

Maintaining remission

- oral aminosalicylates e.g. Mesalazine
- azathioprine and mercaptopurine
- methotrexate is not recommended for the management of ulcerative colitis (in contrast to Crohn's disease)
- there is some evidence that probiotics may prevent relapse in patients with mild to moderate disease

Question 44 of 142

A 23-year-old nurse is reviewed in occupational health following a needle stick injury from a man known to be a carrier of hepatitis B. Which one of the following would appear first during acute hepatitis B infection?

- A. HBsAg
- B. HBeAg
- C. anti-HBg
- D. anti-HBs
- E. HBcAg

Question 44 of 142

A 23-year-old nurse is reviewed in occupational health following a needle stick injury from a man known to be a carrier of hepatitis B. Which one of the following would appear first during acute hepatitis B infection?

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- B. HBeAg
- C. anti-HBg
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- E. HBcAg

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Question 45 of 142

The increased risk of oesophageal malignancy in patients with Barrett's oesophagus is approximately:

- A. No increased risk
- B. Twice risk
- C. 5 times risk
- D. 50 - 100 times risk
- E. 500 - 1,000 times risk

Question 45 of 142

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- E. 500 - 1,000 times risk

Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

Question 46 of 142

A 59-year-old woman presents with dysphagia. There is no history of heartburn, weight loss or change in bowel habit. During endoscopy there is some difficulty passing through the lower oesophageal sphincter but no other abnormality is noted. Which one of the following tests is most likely to reveal the diagnosis?

- A. Oesophageal biopsy
- B. Oesophageal manometry
- C. Plain chest x-ray
- D. Endoscopy ultrasound
- E. CT thorax

Question 46 of 142

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- ✓ B. Oesophageal manometry
- C. Plain chest x-ray
- D. Endoscopy ultrasound
- E. CT thorax

The gold standard test for achalasia is oesophageal manometry

Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is more common in women

Clinical features
- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

Investigations
- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

Treatment
- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Question 47 of 142

The most common type of inherited colorectal cancer:

- A. Familial adenomatous polyposis
- B. Li-Fraumeni syndrome
- C. Hereditary non-polyposis colorectal carcinoma
- D. Fanconi syndrome
- E. Peutz-Jeghers syndrome

Question 47 of 142

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Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are often poorly differentiated and highly aggressive. Currently four gene mutations have been identified (including in the hMLH1 and hMSH2 genes). The Amsterdam criteria are sometimes used to aid diagnosis:

Amsterdam criteria for HNPCC

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Question 48 of 142

Which one of the following statements best describes the prevention and treatment of hepatitis C?

- A. No vaccine is available and treatment is only successful in around 10-15% of patients
- B. No vaccine and no treatment is available
- C. A vaccine is available and treatment is successful in around 50% of patients
- D. A vaccine is available but no treatment has been shown to be effective
- E. No vaccine is available but treatment is successful in around 50% of patients

Question 48 of 142

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Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 49 of 142

A 36-year-old man is reviewed in clinic. He has recently been started on mesalazine 400mg tds for ulcerative colitis. Which one of the following adverse effects is least likely to be attributable to mesalazine?

- A. Interstitial nephritis
- B. Headaches
- C. Acute pancreatitis
- D. Agranulocytosis
- E. Infertility

Question 49 of 142

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- C. Acute pancreatitis
- D. Agranulocytosis
- ✓ E. Infertility

Oligospermia is seen in patients taking sulphasalazine due to the sulphapyridine moiety, which is not present in mesalazine

Aminosalicylate drugs

5-aminosalicyclic acid (5-ASA) is released in the colon and is not absorbed. It acts locally as an anti-inflammatory. The mechanism of action is not fully understood but 5-ASA may inhibit prostaglandin synthesis

Sulphasalazine

- a combination of sulphapyridine (a sulphonamide) and 5-ASA
- many side-effects are due to the sulphapyridine moiety: rashes, oligospermia, headache, Heinz body anaemia
- other side-effects are common to 5-ASA drugs (see mesalazine)

Mesalazine

- a delayed release form of 5-ASA
- sulphapyridine side-effects seen in patients taking sulphasalazine are avoided
- mesalazine is still however associated with side-effects such as GI upset, headache, agranulocytosis, pancreatitis*, interstitial nephritis

Olsalazine

- two molecules of 5-ASA linked by a diazo bond, which is broken by colonic bacteria

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 50 of 142

A 59-year-old female presents with a two month history of indigestion. She is otherwise well, has not had a similar episode before and takes no regular medication. Of note there is no recent weight loss or vomiting and abdominal examination is unremarkable. What is the most appropriate initial management?

- A. Long-term course of a H2 receptor antagonist
- B. Lifestyle advice with follow-up appointment in one month
- C. Urgent referral for endoscopy
- D. One month course of a full-dose proton pump inhibitor
- E. Urea breath testing and treat for H pylori if positive

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- D. One month course of a full-dose proton pump inhibitor
- E. Urea breath testing and treat for H pylori if positive

This patient meets the criteria for urgent referral for endoscopy as she is older than 55 years, has recent onset, persistent and unexplained symptoms

Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')
This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month*
- 4. 'Test and treat' using carbon-13 urea breath test

*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Question 51 of 142

A 27-year-old man with multiple pigmented freckles on his lips and face is investigated for iron-deficiency anaemia. A diagnosis of Peutz-Jeghers syndrome is suspected. What is the mode of inheritance?

- A. Autosomal recessive
- B. Mitochondrial inheritance
- C. X-linked dominant
- D. Autosomal dominant
- E. X-linked recessive

Question 51 of 142

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- E. X-linked recessive

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

Genetics
- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

Features
- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

Management
- conservative unless complications develop

Question 52 of 142

Where do the majority of VIPomas arise from?

- A. Small intestine
- B. Pituitary
- C. Pancreas
- D. Antrum of stomach
- E. Pylorus of stomach

Question 52 of 142

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VIPoma

VIP (vasoactive intestinal peptide)
- source: small intestine, pancreas
- stimulation: neural
- actions: stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion

VIPoma
- 90% arise from pancreas
- large volume diarrhoea
- weight loss
- dehydration
- hypokalaemia, hypochlorhydia

Question 53 of 142

A 34-year-old male is admitted with central abdominal pain radiating through to the back and vomiting. The following results are obtained:

Amylase 1,245 u/dl

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

- A. Phenytoin
- B. Sodium valproate
- C. Metoclopramide
- D. Sumatriptan
- E. Pizotifen

Question 53 of 142

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- D. Sumatriptan
- E. Pizotifen

Sodium valproate induced pancreatitis is more common in young adults and tends to occur within the first few months of treatment. Asymptomatic elevation of the amylase level is seen in up to 10% of patients

Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Question 54 of 142

Which one of the following investigations is considered the gold standard for the diagnosis of gastro-oesophageal reflux disease?

- A. Endoscopy
- B. 24hr oesophageal pH monitoring
- C. Oesophageal manometry
- D. Barium swallow
- E. CT thorax

Question 54 of 142

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- C. Oesophageal manometry
- D. Barium swallow
- E. CT thorax

24hr oesophageal pH monitoring is gold standard investigation in GORD

GORD: investigation

Overview
- poor correlation between symptoms and endoscopy appearance

Indications for upper GI endoscopy:
- age > 55 years
- symptoms > 4 weeks or persistent symptoms despite treatment
- dysphagia
- relapsing symptoms
- weight loss

If endoscopy is negative consider 24-hr oesophageal pH monitoring (the gold standard test for diagnosis)

Question 55 of 142

A 30-year-old woman presents with a three month history of indigestion. There is no history of weight less, anorexia, dysphagia, vomiting or change in bowel habit and abdominal examination is unremarkable. Which one of the following may decrease the accuracy of a 13C-urea breath test?

- A. Use of Gaviscon around 10 days ago
- B. Use of ranitidine stopping 4 weeks ago
- C. Course of amoxicillin stopping 3 weeks ago
- D. Use of lansoprazole stopping 6 weeks ago
- E. Current use of the combined oral contraceptive pill

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✓ C. Course of amoxicillin stopping 3 weeks ago

D. Use of lansoprazole stopping 6 weeks ago

E. Current use of the combined oral contraceptive pill

Urea breath test - no antibiotics in past 4 weeks, no antisecretory drugs (e.g. PPI) in past 2 weeks

***Helicobacter pylori*: tests**

Urea breath test
- patients consume a drink containing carbon isotope 13 (13C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of 13C CO2
- sensitivity 95-98%, specificity 97-98%

Rapid urease test (e.g. CLO test)
- biopsy sample is mixed with urea and pH indicator
- colour change if H pylori urease activity
- sensitivity 90-95%, specificity 95-98%

Serum antibody
- remains positive after eradication
- sensitivity 85%, specificity 80%

Culture of gastric biopsy
- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

Gastric biopsy
- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

Stool antigen test
- sensitivity 90%, specificity 95%

Question 56 of 142

A 40-year-old man is investigated for abnormal liver function tests. It is decided to perform a liver biopsy. Which one of the following is a contraindication to liver biopsy?

- A. ALT of 2,212 iu/l
- B. Aspirin therapy
- C. Platelet count of 100 * 10^9/l
- D. Body mass index of 33 kg/m^2
- E. Bile duct dilatation

Question 56 of 142

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- B. Aspirin therapy
- C. Platelet count of 100 * 10^9/l
- D. Body mass index of 33 kg/m^2
- ✓ E. Bile duct dilatation

With modern techniques such as ERCP and MRI cholangiography the risks of liver biopsy when there is extra-hepatic biliary obstruction are rarely justified.

Liver biopsy

Contraindications to percutaneous liver biopsy

- deranged clotting (e.g. INR > 1.4)
- low platelets (e.g. < 60 * 10^9/l)
- anaemia
- bile duct obstruction
- hydatid cyst
- haemoangioma
- uncooperative patient
- ascites

Question 57 of 142

A 45-year-old man with a history of alcohol excess is diagnosed as having grade 3 oesophageal varices during an outpatient endoscopy. Of the following options, what is the most appropriate management to prevent variceal bleeding?

- A. Propranolol
- B. Isosorbide mononitrate
- C. Endoscopic sclerotherapy
- D. Terlipressin
- E. Lansoprazole

Question 57 of 142

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- B. Isosorbide mononitrate
- C. Endoscopic sclerotherapy
- D. Terlipressin
- E. Lansoprazole

Endoscopic sclerotherapy now has little role in the prophylaxis of variceal haemorrhage.

Oesophageal varices

Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

Question 58 of 142

A 27-year-old female is referred to the medical outpatient clinic due to a long history of fatigue and joint pains. An autoimmune screen is done which is positive for smooth muscle antibodies. What is the most appropriate next investigation?

- A. Liver function tests
- B. Thyroid function tests
- C. Creatine kinase
- D. Serum glucose
- E. Electrocardiogram

Question 58 of 142

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- ✓ A. Liver function tests
- B. Thyroid function tests
- C. Creatine kinase
- D. Serum glucose
- E. Electrocardiogram

Smooth muscle antibodies are associated with autoimmune hepatitis. Presentation is usually insidious and extrahepatic clinical features are common

Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	**Type II**	**Type III**
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA) Affects both adults and children	Anti-liver/kidney microsomal type 1 antibodies (LKM1) Affects children only	Soluble liver-kidney antigen Affects adults in middle-age

Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Question 59 of 142

Which one of the following statements is incorrect regarding Dubin-Johnson syndrome?

- A. Runs a benign course
- B. Due to a defect in the canillicular multispecific organic anion transporter
- C. Causes defective hepatic bilirubin excretion
- D. It is an autosomal recessive disorder
- E. Results in an unconjugated hyperbilirubinaem

Question 59 of 142

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- B. Due to a defect in the canillicular multispecific organic anion transporter
- C. Causes defective hepatic bilirubin excretion
- D. It is an autosomal recessive disorder
- ✓ E. Results in an unconjugated hyperbilirubinaemia

Dubin-Johnson syndrome

Dubin-Johnson syndrome is a benign autosomal recessive disorder resulting in hyperbilirubinaemia (conjugated, therefore present in urine). It is due to a defect in the canillicular multispecific organic anion transporter (cMOAT) protein. This causes defective hepatic bilirubin excretion

Question 60 of 142

Which one of the following is least likely to cause malabsorption?

- A. Systemic sclerosis
- B. Cystic fibrosis
- C. Primary biliary cirrhosis
- D. Whipple's disease
- E. Haemochromatosis

Question 60 of 142

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- ✓ E. Haemochromatosis

Malabsorption

Malabsorption is characterised by diarrhoea, steatorrhoea and weight loss. Causes may be broadly divided into intestinal (e.g. villous atrophy), pancreatic (deficiency of pancreatic enzyme production or secretion) and biliary (deficiency of bile-salts needed for emulsification of fats)

Intestinal causes of malabsorption
- coeliac disease
- Crohn's disease
- tropical sprue
- Whipple's disease
- Giardiasis
- brush border enzyme deficiencies (e.g. lactase insufficiency)

Pancreatic causes of malabsorption
- chronic pancreatitis
- cystic fibrosis
- pancreatic cancer

Biliary causes of malabsorption
- biliary obstruction
- primary biliary cirrhosis

Other causes
- bacterial overgrowth (e.g. systemic sclerosis, diverticulae, blind loop)
- short bowel syndrome
- lymphoma

Question 61 of 142

A 27-year-old woman with a history of depression presents to the Emergency Department. She reports taking 50 paracetamol tablets yesterday. Bloods are taken on admission. Which one of the following would most strongly indicate the need for a liver transplant?

- A. Blood glucose 2.2 mmol/l
- B. ALT 2364 iu/l
- C. INR 4.1
- D. Creatinine 230 µmol/l
- E. Arterial pH 7.27

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- C. INR 4.1
- D. Creatinine 230 µmol/l
- ✓ E. Arterial pH 7.27

The arterial pH is the single most important factor according to the King's College Hospital criteria for liver transplantation.

Paracetamol overdose: management

King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300 µmol/l
- grade III or IV encephalopathy

Question 62 of 142

According to recent NICE guidelines, which one of the following may have a role in the management of irritable bowel syndrome?

- A. Reflexology
- B. Acupuncture
- C. Aloe vera
- D. Homeopathy
- E. Hypnotherapy

Question 62 of 142

A 64-year-old female with a history of COPD and hypertension presents with pain on swallowing. Current medication includes a salbutamol and becotide inhaler, bendrofluazide and amlodipine. What is the most likely cause of the presentation?

- A. Myasthenia gravis precipitated by bendrofluazide
- B. Oesophageal web
- C. Achalasia secondary to amlodipine
- ✓ D. Oesophageal candidiasis
- E. Oesophageal cancer

Pain on swallowing (odynophagia) is a typical of oesophageal candidiasis, a well documented complication of inhaled steroid therapy

Dysphagia

The table below gives characteristic exam question features for conditions causing dysphagia:

Oesophageal cancer	Dysphagia may be associated with weight loss, anorexia or vomiting during eating Past history may include Barrett's oesophagus, GORD, excessive smoking or alcohol use
Oesophagitis	May be history of heartburn Odynophagia but no weight loss and systemically well
Oesophageal candidiasis	There may be a history of HIV or other risk factors such as steroid inhaler use
Achalasia	Dysphagia of both liquids and solids from the start Heartburn Regurgitation of food - may lead to cough, aspiration pneumonia etc
Pharyngeal pouch	More common in older men Represents a posteromedial herniation between thyropharyngeus and cricopharyngeus muscles Usually not seen but if large then a midline lump in the neck that gurgles on palpation Typical symptoms are dysphagia, regurgitation, aspiration and chronic cough. Halitosis may occasionally be seen
Systemic sclerosis	Other features of CREST syndrome may be present, namely Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia
Myasthenia gravis	Other symptoms may include extraocular muscle weakness or ptosis Dysphagia with liquids as well as solids
Globus hystericus	May be history of anxiety Symptoms are often intermittent

Question 63 of 142

A 45-year-old man is admitted to the Emergency Department with severe abdominal pain. He smokes 20 cigarettes a day and drinks approximately 50 units of alcohol per week. He also complains of sudden deterioration in vision. Fundoscopy reveals shows multiple micro infarcts (cotton wool spots). Which investigation would best confirm the most likely diagnosis?

- A. Gastroscopy
- B. Serum glucose
- C. Amylase
- D. Biliary USS
- E. ECG

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- A. Gastroscopy
- B. Serum glucose
- ✓ C. Amylase
- D. Biliary USS
- E. ECG

The cotton wool spots seen on fundoscopy represents Purtscher retinopathy. This condition may be seen following head trauma and in conditions such as acute pancreatitis, fat embolisation, amniotic fluid embolisation, and vasculitic diseases

Acute pancreatitis: features

Rare features associated with pancreatitis include:

- ischaemic (Purtscher) retinopathy - may cause temporary or permanent blindness

Question 64 of 142

Which of the following is not a recognised complication of coeliac disease?

- A. Hypersplenism
- B. Osteoporosis
- C. Lactose intolerance
- D. Oesophageal cancer
- E. Subfertility

Question 64 of 142

Which of the following is not a recognised complication of coeliac disease?

- ✓ A. Hypersplenism
- B. Osteoporosis
- C. Lactose intolerance
- D. Oesophageal cancer
- E. Subfertility

Hypo-, not hypersplenism is seen in coeliac disease

Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
? Chronic or intermittent diarrhoea ? Failure to thrive or faltering growth (in children) ? Persistent or unexplained gastrointestinal symptoms including nausea and vomiting ? Prolonged fatigue ('tired all the time') ? Recurrent abdominal pain, cramping or distension ? Sudden or unexpected weight loss ? Unexplained iron-deficiency anaemia, or other unspecified anaemia	? Autoimmune thyroid disease ? Dermatitis herpetiformis ? Irritable bowel syndrome ? Type 1 diabetes ? First-degree relatives (parents, siblings or children) with coeliac disease

Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

Question 65 of 142

A 19-year-old man is referred to the general medical clinic. For the past six months his family have noted increasing behavioural and speech problems. He himself has noticed that he is more clumsy than normal and reports excessive salivation. His older brother died of liver disease. Given the likely underlying condition what is the most appropriate therapy?

- A. Vitamin B6 supplements
- B. Venesection
- C. Ribavirin + interferon alpha
- D. Pulsed methylprednisolone
- E. Penicillamine

Question 65 of 142

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- A. Vitamin B6 supplements
- B. Venesection
- C. Ribavirin + interferon alpha
- D. Pulsed methylprednisolone
- ✓ E. Penicillamine

This man is likely to have Wilson's disease.

Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Question 66 of 142

Which one of the following is not associated with villous atrophy on jejunal biopsy?

- A. Tropical sprue
- B. Coeliac disease
- C. Hypogammaglobulinaemia
- D. Familial Mediterranean Fever
- E. Whipple's disease

Question 66 of 142

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- A. Tropical sprue
- B. Coeliac disease
- C. Hypogammaglobulinaemia
- ✓ D. Familial Mediterranean Fever
- E. Whipple's disease

Causes of villous atrophy (other than coeliacs): tropical sprue, Whipple's, lymphoma, hypogammaglobulinaemia

Jejunal villous atrophy

Whilst coeliac disease is the classic cause of jejunal villous atrophy there are a number of other causes you need to be aware of

Causes

- coeliac disease
- tropical sprue
- hypogammaglobulinaemia
- gastrointestinal lymphoma
- Whipple's disease
- cow's milk intolerance

Question 67 of 142

A 45-year-old man is noted to have non-tender, smooth hepatomegaly associated Dupuytren's contracture and parotid enlargement. He recently returned from a holiday in Thailand. What is the likely diagnosis?

- A. Primary hepatoma
- B. Hydatid disease
- C. Alcoholic liver disease
- D. Viral hepatitis
- E. Tricuspid regurgitation

Question 67 of 142

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- A. Primary hepatoma
- B. Hydatid disease
- ✓ C. Alcoholic liver disease
- D. Viral hepatitis
- E. Tricuspid regurgitation

Both Dupuytren's contracture and parotitis are associated with alcoholic liver disease. Whilst a history of alcohol excess would normally be volunteered it should be remembered many patients will lie about their alcohol intake.

The recent holiday in Thailand is a distractor.

Hepatomegaly

Common causes of hepatomegaly

- Cirrhosis: if early disease, later liver decreases in size. Associated with a non-tender, firm liver
- Malignancy: metastatic spread or primary hepatoma. Associated with a hard, irregular. liver edge
- Right heart failure: firm, smooth, tender liver edge. May be pulsatile

Other causes

- viral hepatitis
- glandular fever
- malaria
- abscess: pyogenic, amoebic
- hydatid disease
- haematological malignancies
- haemochromatosis
- primary biliary cirrhosis
- sarcoidosis, amyloidosis

Question 68 of 142

A 42-year-old woman is investigated for lethargy and diarrhoea. Investigations reveal positive anti-endomysial antibodies. Each of the following food stuffs should be avoided, except:

- A. Beer
- B. Rye
- C. Maize
- D. Bread
- E. Pasta

Question 68 of 142

A 42-year-old woman is investigated for lethargy and diarrhoea. Investigations reveal positive anti-endomysial antibodies. Each of the following food stuffs should be avoided, except:

- A. Beer
- B. Rye
- ✓ C. Maize
- D. Bread
- E. Pasta

Coeliac disease: management

The management of coeliac disease involves a gluten-free diet. Gluten containing cereals include:

- wheat: bread, pasta, pastry
- barley*: beer
- rye
- oats**

Some notable foods which are gluten-free include:

- rice
- potatoes
- corn (maize)

*whisky is made using malted barley. Proteins such as gluten are however removed during the distillation process making it safe to drink for patients with coeliac disease

**some patients with coeliac disease appear able to tolerate oats

Question 69 of 142

A 17-year-old girl presents with a 6 week history of nausea and abdominal discomfort. Routine blood tests reveal the following.

Hb	10.9 g/dl
WBC	6.7 *10^9/l
Platelets	346 *10^9/l
Calcium	2.33 mmol/l
Bilirubin	7 µmol/l
ALP	262 u/l
ALT	35 u/l

What is the most likely diagnosis?

- A. Alcoholic liver disease
- B. Cholangiocarcinoma
- C. Pregnancy
- D. Gallstones
- E. Primary biliary cirrhosis

Question 69 of 142

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WBC 6.7 *10^9/l

Platelets 346 *10^9/l

Calcium 2.33 mmol/l

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ALT 35 u/l

What is the most likely diagnosis?

- A. Alcoholic liver disease
- B. Cholangiocarcinoma
- ✓ C. Pregnancy
- D. Gallstones
- E. Primary biliary cirrhosis

Alkaline phosphatase is significantly elevated in pregnancy. This would also explain the borderline anaemia

Alkaline phosphatase

Causes of raised alkaline phosphatase (ALP)

- liver: cholestasis, hepatitis, fatty liver, neoplasia
- Paget's
- osteomalacia
- bone metastases
- hyperparathyroidism
- renal failure
- physiological: pregnancy, growing children, healing fractures

The table below splits the causes according to the calcium level

Raised ALP and raised calcium	Raised ALP and low calcium
• Bone metastases • Hyperparathyroidism	• Osteomalacia • Renal failure

Question 70 of 142

Which one of the following statements regarding hepatitis C is correct?

- A. Cannot be transmitted vertically from mother to child
- B. Interferon-alpha and ribavirin are the treatments of choice
- C. It is more infectious than hepatitis B following a needle stick injury
- D. Breast feeding is contraindicated in mothers with hepatitis C
- E. HCV RNA is the initial investigation of choice for at-risk groups

Question 70 of 142

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Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

Transmission
- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

Features
- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

Complications
- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

Management of chronic infection
- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

Complications of treatment
- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Question 71 of 142

Which one of the following is not associated with oesophageal cancer?

- A. Achalasia
- B. Smoking
- C. Gastro-oesophageal reflux disease
- D. *Helicobacter pylori*
- E. Alcohol

Question 71 of 142

Which one of the following is not associated with oesophageal cancer?

- A. Achalasia
- B. Smoking
- C. Gastro-oesophageal reflux disease
- ✓ D. *Helicobacter pylori*
- E. Alcohol

Helicobacter pylori may actually be protective against oesophageal cancer

Oesophageal cancer

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

Risk factors

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

Question 72 of 142

A 43-year-old man with type 2 diabetes mellitus presents with lethargy. His current medications include metformin and gliclazide, although the gliclazide may soon be stopped due to his obesity. A number of blood tests are ordered which reveal the following:

HbA1c 8.2%

Ferritin 204 ng/ml

Bilirubin 23 µmol/l

ALP 162 u/l

ALT 120 u/l

AST 109 u/l

On discussing these results he states that he does not drink alcohol. What is the most likely cause of these abnormal results?

- A. Metformin-induced steatohepatitis
- B. Haemochromatosis
- C. Acute hepatitis secondary to gliclazide
- D. Cryptogenic cirrhosis
- E. Non-alcoholic fatty liver disease

Question 72 of 142

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Obese T2DM with abnormal LFTs - ? non-alcoholic fatty liver disease

By far the most likely diagnosis in an obese type 2 diabetic is non-alcoholic fatty liver disease. This patient will require a liver screen, ultrasound and liver biopsy to confirm the diagnosis.

A normal ferritin makes a diagnosis of haemochromatosis unlikely, although it should always be considered in patients with both abnormal LFTs and diabetes.

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and though to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

Question 73 of 142

Which one of the following conditions is least likely to develop following hepatitis B infection?

- A. Glomerulonephritis
- B. Hepatocellular carcinoma
- C. Acute pancreatitis
- D. Chronic infection
- E. Polyarteritis nodosa

Question 73 of 142

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- D. Chronic infection
- E. Polyarteritis nodosa

Deterioration in patient with hepatitis B - ? hepatocellular carcinoma

Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	**Response**
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for past or previous infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in d dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

Question 74 of 142

Which one of the following patients is most likely to require screening for hepatocellular carcinoma?

- A. A 45-year-old man with liver cirrhosis secondary to hepatitis C
- B. A 33-year-old man with HIV. He is taking antiretroviral therapy
- C. A 22-year-old man with alpha-1 antitrypsin deficiency. He has no evidence of current liver disease
- D. A 52-year-old woman with alcohol-related liver cirrhosis who is still drinking
- E. A 75-year-old man who drinks 100 units / week. He has no current signs of liver disease

Question 74 of 142

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Patients with liver cirrhosis secondary to hepatitis C have a 3-5% annual incidence of hepatocellular carcinoma.

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

*Wilson's disease is an exception

Question 75 of 142

Which one the following disorders is most strongly associated with primary biliary cirrhosis?

- A. Systemic sclerosis
- B. Thyroid disease
- C. Sjogren's syndrome
- D. Rheumatoid arthritis
- E. Systemic lupus erythematous