HAEMATOLOGY/ONCOLOGY MCQs

Q-1

Which electrolyte disturbance is cisplatin most associated with?

A. Hypocalcaemia
B. Hyponatraemia
C. Hypomagnesaemia
D. Hypokalaemia
E. Hypercalcaemia

ANSWER:
Hypomagnesaemia

EXPLANATION:
Cisplatin is associated with hypomagnesaemia

CYTOTOXIC AGENTS
The tables below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents.

Alkylating agents

Cytotoxic	Mechanism of action	Adverse effects
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma

Cytotoxic antibodies

Cytotoxic	Mechanism of action	Adverse effects
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy

Antimetabolites

Cytotoxic	Mechanism of action	Adverse effects
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis, lung fibrosis
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis by blocking thymidylate synthase (works during S phase)	Myelosuppression, mucositis, dermatitis
6-mercaptopurine	Purine analogue that is activated by HGPRTase, decreasing purine synthesis	Myelosuppression
Cytarabine	Pyrimidine antagonist. Interferes with DNA synthesis specifically at the S-phase of the cell cycle and inhibits DNA polymerase	Myelosuppression, ataxia

Acts on microtubules

Cytotoxic	Mechanism of action	Adverse effects
Vincristine, vinblastine	Inhibits formation of microtubules	Vincristine: Peripheral neuropathy
		(reversible) , paralytic ileus Vinblastine: myelosuppression
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Other cytotoxic drugs

Cytotoxic	Mechanism of action	Adverse effects
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Hydroxyurea (hydroxycarbamide)	Inhibits ribonucleotide reductase, decreasing DNA synthesis	Myelosuppression

Q-2

What chemical mediator is mainly responsible for the tissue oedema seen in patients in hereditary angioedema?

A. Histamine
B. Serotonin
C. Neurokinin A
D. Bradykinin
E. Nitric oxide

ANSWER:
Bradykinin

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

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

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

Management

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

Q-3

A 62-year-old woman presents after being advised by the chemotherapy helpline to come to a hospital. She has a past medical history of neuroendocrine cancer of the cervix treated with carboplatin and etoposide. Her last treatment was eight days ago. She has been feeling generally unwell with temperatures measured at home at 38.1C. Blood cultures are taken and she is started on neutropenic sepsis protocol. What is gram-staining of the blood cultures most likely to show?

A. Gram-negative cocci
B. Gram-positive cocci
C. Gram-negative rods
D. Anaerobic bacteria
E. Spores

ANSWER:
Gram-positive cocci

EXPLANATION:
The correct answer is gram-positive cocci. Gram-negative bacilli used to be the most common pathogen isolated in neutropenic sepsis, but over time the most common pathogens are now gram-positive organisms. These accounts for a majority of the identified organisms, and are most commonly endogenous organisms. The most frequent cause is Staphylococcus epidermidis, and following this are other staphylococci and streptococci species.

NEUTROPENIC SEPSIS
Neutropenic sepsis is a relatively common complication of cancer therapy, usually as a consequence of chemotherapy. It most commonly occurs 7-14 days after chemotherapy. It may be defined as a neutrophil count of < 0.5 * 109 in a patient who is having anticancer treatment and has one of the following:

- a temperature higher than 38ºC or
- other signs or symptoms consistent with clinically significant sepsis

Prophylaxis

- if it is anticipated that patients are likely to have a neutrophil count of < 0.5 * 109 as a consequence of their treatment they should be offered a fluoroquinolone

Management

- antibiotics must be started immediately, do not wait for the WBC
- NICE recommend starting empirical antibiotic therapy with piperacillin with tazobactam (Tazocin) immediately
- many units add vancomycin if the patient has central venous access but NICE do not support this approach
- following this initial treatment patients are usually assessed by a specialist and risk-stratified to see if they may be able to have outpatient treatment
- if patients are still febrile and unwell after 48 hours an alternative antibiotic such as meropenem is often prescribed +/- vancomycin
- if patients are not responding after 4-6 days the Christie guidelines suggest ordering investigations for fungal infections (e.g. HRCT), rather than just starting therapy antifungal therapy blindly
- there may be a role for G-CSF in selected patients

Q-4

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 * 109/l**
WBC	**5.3 * 109/l**

Further tests were then ordered:

Reticulocytes	**5.2%l**
Direct antiglobulin test	**Positive, IgG only**
Film	**Spherocytes and reticulocytes**

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

ANSWER:
Non-Hodgkin's lymphoma

EXPLANATION:
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

Q-5

A 67-year-old woman is referred to the haematology clinic. Her GP has noted that her platelet count is persistently elevated and no reactive cause can be found. Bloods taken a week before clinic are as follows:

Hb	**15.4 g/dl**
Platelets	**784 * 109/l**
WBC	**5.3* 109/l**
JAK2 kinase (V617F mutation)	**Positive**

What is the treatment of choice?

A. Imatinib
B. Stem-cell transplantation
C. Hydroxycarbamide
D. Vincristine
E. Venesection

ANSWER:
Hydroxycarbamide

EXPLANATION:
THROMBOCYTOSIS
Thrombocytosis is an abnormally high platelet count, usually > 400 * 109/l.

Causes of thrombocytosis
- reactive: platelets are an acute phase reactant - platelet count can increase in response to stress such as a severe infection or surgery
- malignancy
- essential thrombocytosis (see below), or as part of another myeloproliferative disorder such as chronic myeloid leukaemia or polycythaemia rubra vera
- hyposplenism

Essential thrombocytosis
Essential thrombocytosis is one of the myeloproliferative disorders which overlaps with chronic myeloid leukaemia, polycythaemia rubra vera and myelofibrosis. Megakaryocyte proliferation results in an overproduction of platelets.

Features
- platelet count > 600 * 109/l
- both thrombosis (venous or arterial) and haemorrhage can be seen
- a characteristic symptom is a burning sensation in the hands
- a JAK2 mutation is found in around 50% of patients

Management
- hydroxyurea (hydroxycarbamide) is widely used to reduce the platelet count
- interferon-α is also used in younger patients
- low-dose aspirin may be used to reduce the thrombotic risk

Q-6

A 54-year-old woman is reviewed in oncology clinic following debulking surgery for primary peritoneal cancer. She is known to have two liver metastases. She underwent surgery one month ago and has come in for review prior to adjuvant chemotherapy. During her chemotherapy treatment, which tumour marker would be most appropriate to monitor disease progression?

A. CA 15-3
B. CA 19-9
C. CA 125
D. Human chorionic gonadotropin (hCG)
E. S-100

ANSWER:
CA 125

EXPLANATION:
CA 125 is the tumour marker most associated with primary peritoneal cancer as well as ovarian cancer and can be used to monitor response to chemotherapy, alongside regular CT scans. It can also be raised in various other cancers.

The other tumour markers are more appropriate for other cancers.

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
S-100	Melanoma, schwannomas
Bombesin	Small cell lung carcinoma, gastric cancer, neuroblastoma

Q-7

A 67-year-old man presents feeling 'generally unwell' and complaining of pain in his back and legs. His wife also reports that he has been slightly confused for the past two weeks. Basic blood tests are ordered:

Hb	**12.1 g/dl**
Platelets	**411 * 109/l**
WBC	**7.6 * 109/l**
Na+	**143 mmol/l**
K+	**5.3 mmol/l**
Urea	**15.7 mmol/l**
Creatinine	**208 µmol/l**
Bilirubin	**20 µmol/l**
ALP	**110 u/l**
ALT	**55 u/l**
γGT	**67 u/l**
Albumin	**31 g/l**
Total protein	**84 g/l**
Calcium	**3.10 mmol/l**
Phosphate	**0.79 mmol/l**

What is the most likely underlying diagnosis?

A. Multiple myeloma
B. Renal cancer with bony metastases
C. Sarcoidosis
D. Primary hyperparathyroidism
E. Prostate cancer with bony metastases

ANSWER:
Multiple myeloma

EXPLANATION:
Hypercalcaemia, renal failure, high total protein = myeloma
One of the stand out results is the high calcium level. This immediately narrows the differential diagnosis considerably. Remember the two most common causes of hypercalcaemia are malignancy and primary hyperparathyroidism. Neither of these alone would however explain the renal failure and high total protein, both common features of untreated myeloma.

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

Investigations
- monoclonal proteins (usually IgG or IgA) in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- historically a skeletal survey has been done to look for bone lesions. However, whole-body MRI is increasingly used and is now recommended in the 2016 NICE guidelines
- X-rays: 'rain-drop skull' (likened to the pattern rain forms after hitting a surface and splashing, where it leaves a random pattern of dark spots). Note that a very similar, but subtly different finding is found in primary hyperparathyroidism - 'pepperpot skull'

The diagnostic criteria for multiple myeloma requires one major and one minor criteria or three minor criteria in an individual who has signs or symptoms of multiple myeloma.

Major criteria
- Plasmacytoma (as demonstrated on evaluation of biopsy specimen)
- 30% plasma cells in a bone marrow sample
- Elevated levels of M protein in the blood or urine

Minor criteria
- 10% to 30% plasma cells in a bone marrow sample.
- Minor elevations in the level of M protein in the blood or urine.
- Osteolytic lesions (as demonstrated on imaging studies).

- Low levels of antibodies (not produced by the cancer cells) in the blood.

Hypercalcaemia in myeloma
- primary factor: due primarily to increased osteoclastic bone resorption caused by local cytokines (e.g. IL-1, tumour necrosis factor) released by the myeloma cells
- much less common contributing factors: impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Q-8

A 7-year-old male presents with generalised lymphadenopathy. Which one of the following is least likely to result in this presentation?

A. Kawasaki disease
B. Cytomegalovirus
C. Acute lymphoblastic leukaemia
D. Phenytoin therapy
E. Infectious mononucleosis

ANSWER:
Kawasaki disease

EXPLANATION:
Kawasaki disease causes only cervical lymphadenopathy

LYMPHADENOPATHY
There are many causes of generalised lymphadenopathy

Infective
- infectious mononucleosis
- HIV, including seroconversion illness
- eczema with secondary infection
- rubella
- toxoplasmosis
- CMV
- tuberculosis
- roseola infantum

Neoplastic
- leukaemia
- lymphoma

Others
- autoimmune conditions: SLE, rheumatoid arthritis
- graft versus host disease
- sarcoidosis
- drugs: phenytoin and to a lesser extent allopurinol, isoniazid

Q-9

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

ANSWER:
Nodes on both sides of diaphragm with night sweats

EXPLANATION:
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)

Q-10

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

A. Anabolic steroids
B. Oral contraceptive pill
C. ACE inhibitors
D. Beta-blockers
E. Aspirin

ANSWER:
Anabolic steroids

EXPLANATION:
Please see Q-2 for Hereditary Angioedema

Q-11

A 68-year-old man who has small cell lung cancer is admitted onto the ward for chemotherapy. He has experienced severe nausea and vomiting due to the chemotherapy in the past. The consultant asks you to prescribe a neurokinin 1 (NK1) receptor blocker.

What agent will you choose?

A. **Aprepitant**
B. **Dexamethasone**
C. **Metoclopramide**
D. **Domperidone**
E. **Haloperidol**

ANSWER:
Aprepitant

EXPLANATION:
Aprepitant is an anti-emetic which blocks the neurokinin 1 (NK1) receptor
Aprepitant is an anti-emetic which blocks the neurokinin 1 (NK1) receptor. It is a substance P antagonists (SPA). It is licensed for chemotherapy-induced nausea and vomiting (CINV) and for prevention of postoperative nausea and vomiting. It is also been shown to be effective in treating clinical depression.

Dexamethasone is a glucocorticoid. It is useful for preventing the delayed emesis phase of CINV.

Metoclopramide, domperidone, and haloperidol can all be used as anti-emetics due to their dopamine blocking effects.

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

Q-12

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**

ANSWER:
Myelofibrosis

EXPLANATION:
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

Q-13

You are reviewing a man who has metastatic small cell lung cancer. He has developed a progressively severe headache over the past week. As part of your differential diagnosis you consider superior vena cava obstruction. What is the most common feature of this condition?

A. **Nasal stuffiness**
B. **Visual disturbance**
C. **Arm swelling**
D. **Facial swelling**
E. **Dyspnoea**

ANSWER:
Dyspnoea

EXPLANATION:
SVC obstruction - dyspnoea is the most common symptom

SUPERIOR VENA CAVA OBSTRUCTION
Superior vena cava (SVC) obstruction is an oncological emergency caused by compression of the SVC. It is most commonly associated with lung cancer.

Features

- dyspnoea is the most common symptom
- swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
- headache: often worse in the mornings
- visual disturbance
- pulseless jugular venous distension

Causes

- common malignancies: non-small cell lung cancer, lymphoma
- other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
- aortic aneurysm
- mediastinal fibrosis
- goitre
- SVC thrombosis

Management

- general: dexamethasone, balloon venoplasty, stenting
- small cell: chemotherapy + radiotherapy
- non-small cell: radiotherapy

Q-14

Each one of the following is seen in Wiskott-Aldrich syndrome, except:

A. Thrombocytopenia
B. Recurrent chest infections
C. X-linked recessive inheritance
D. Mutation in the WASP gene
E. Psoriasis

ANSWER:
Psoriasis

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

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

Q-15

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 * 109/l**
WBC	**5.4 * 109/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

ANSWER:
1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months

EXPLANATION:
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
- metformin (rare)

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

Q-16

Which one of the following features is characteristic of acute intermittent porphyria?

A. Photosensitivity
B. Increased urinary porphobilinogen between acute attacks
C. Hypernatraemia during attacks
D. Autosomal recessive inheritance
E. Increased faecal protoporphyrin excretion

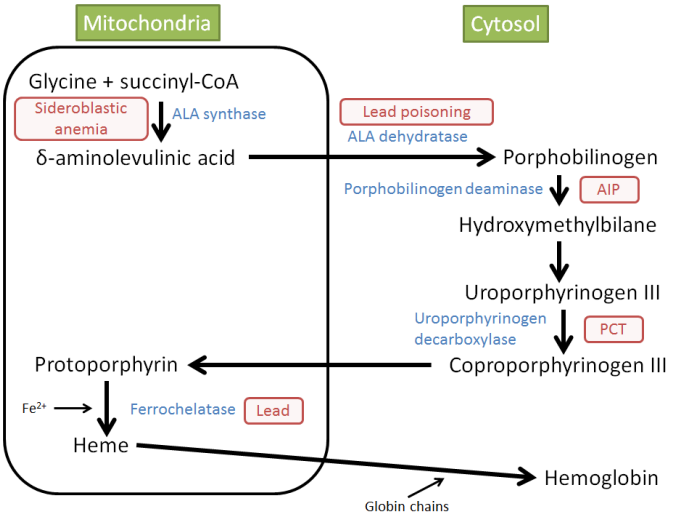
ANSWER:
Increased urinary porphobilinogen between acute attacks

EXPLANATION:
ACUTE INTERMITTENT PORPHYRIA
Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with

abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Features
- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

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



Q-17

A 40-year-old male patient is admitted with recurrent pancreatitis. A CT scan reveals no pancreatic mass, but evidence of widespread lymphadenopathy. Dedicated liver imaging reveals a stricture in the common bile duct but no stones. He also has a history of parotiditis. What is the most likely diagnosis?

A. Lymphoma
B. IgG4 disease
C. Pancreatic cancer
D. Biliary malignancy
E. Primary sclerosing cholangitis

ANSWER:
IgG4 disease

EXPLANATION:
IgG4-RELATED DISEASE
IgG4-related disease has been described in virtually every organ system: the biliary tree, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, and skin. The histopathological features are similar across organs, regardless of the site. IgG4-related disease is analogous to sarcoidosis, in which diverse organ manifestations are linked by similar histopathological characteristics. Raised concentrations of IgG4 in tissue and serum can be helpful in diagnosing IgG4 disease, but neither is a specific diagnostic marker.

Examples include:
- Riedel's Thyroiditis
- Autoimmune pancreatitis
- Mediastinal and Retroperitoneal Fibrosis
- Periaortitis/periarteritis/Inflammatory aortic aneurysm
- Kuttner's Tumour (submandibular glands) & Mikulicz Syndrome (salivary and lacrimal glands)
- Possibly sjogren's and primary biliary cirrhosis

Q-18

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

ANSWER:
Desmopressin

EXPLANATION:
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 2A VWD is caused by defective platelet adhesion due to decreased high molecular weight VWF multimers (i.e. the VWF protein is too small). Type 2B is characterised by a pathological increase of VWF-platelet interaction. Type 2M is caused by a decrease in VWF-platelet interaction (not related to loss of high molecular weight multimers). Type 2N is caused by abnormal binding of the VWF to Factor VIII. There is no clear correlation between symptomatic presentation and type of VWD however common themes amongst patients include excessive mucocutaneous bleeding, bruising in the absence of trauma and menorrhagia in females.

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

Q-19

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

ANSWER:
B2-microglobulin

EXPLANATION:
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

Q-20

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

ANSWER:
Parvovirus infection

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

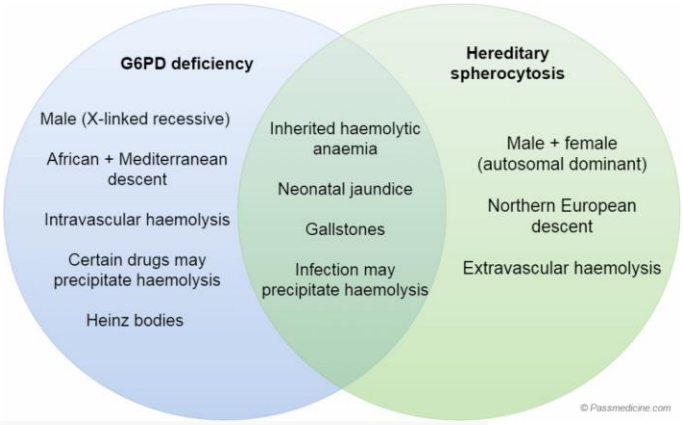
HEREDITARY SPHEROCYTOSIS
Basics
- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

Presentation
- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable
- MCHC elevated

Diagnosis
- the osmotic fragility test was previously the recommend investigation of choice. However, it is now deemed unreliable and is no longer recommended
- the British Journal of Haematology (BJH) guidelines state that 'patients with a family history of HS, typical clinical features and laboratory investigations (spherocytes, raised mean corpuscular haemoglobin concentration[MCHC], increase in reticulocytes) do not require any additional tests
- if the diagnosis is equivocal the BJH recommend the cryohaemolysis test and EMA binding
- for atypical presentations electrophoresis analysis of erythrocyte membranes is the method of choice

Management
- folate replacement
- splenectomy

Comparing G6PD deficiency to hereditary spherocytosis:



Comparison of G6PD deficiency to hereditary spherocytosis

	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	• Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones	• Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	Osmotic fragility test

Q-21

A 26-year-old female is diagnosed with an unprovoked DVT and a thrombophilia screen is performed.

What abnormality is most likely to be found?

A. Factor V Leiden
B. Lupus anticoagulant
C. Protein C deficiency
D. Protein S deficiency
E. Waldenstrom's macroglobulinaemia

ANSWER:
Factor V Leiden

EXPLANATION:
Factor V Leiden is the commonest inherited thrombophilia
Factor V Leiden is the commonest inherited thrombophilia in European populations (approximately 5% prevalence of a heterozygous mutation).

Protein C and S deficiency are possible answers but both are less common than Factor V Leiden. Lupus anticoagulant is another possible answer and features in antiphospholipid syndrome but this is again less common.

Waldenstrom's macroglobulinaemia typically presents in elderly males with symptoms of hyperviscosity.

FACTOR V LEIDEN
Factor V Leiden (activated protein C resistance) is the most common inherited thrombophilia, being present in around 5% of the UK population.

It is due to a gain of function mutation in the Factor V Leiden protein. The result of the mis-sense mutation is that activated factor V (a clotting factor) is inactivated 10 times more slowly by activated protein C than normal. This explains the alternative name for factor V Leiden of activated protein C resistance,

Heterozygotes have a 4-5 fold risk of venous thrombosis. Homozygotes have a 10 fold risk of venous thrombosis but the prevalence is much lower at 0.05%.

Screening for factor V Leiden is not recommended, even after a venous thromboembolism. The logic behind this is that a previous thromboembolism itself is a risk factor for further events and this should dictate specific management in the future, rather than the particular thrombophilia identified.

The table below shows the prevalence and relative risk of venous thromboembolism (VTE) of the different inherited thrombophilias:

Condition	Prevalence	Relative risk of VTE
Factor V Leiden (heterozygous)	5%	4
Factor V Leiden (homozygous)	0.05%	10
Prothrombin gene mutation (heterozygous)	1.5%	3
Protein C deficiency	0.3%	10
Protein S deficiency	0.1%	5-10
Antithrombin III deficiency	0.02	10-20

Q-22

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

ANSWER:
Paroxysmal nocturnal haemoglobinuria

EXPLANATION:
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

*strictly speaking there is an element of extravascular haemolysis in G6PD as well, although it is usually classified as a intravascular cause

Q-23

You are arranging a blood transfusion for a patient who has been admitted with an upper gastrointestinal haemorrhage as their haemoglobin is 59 g/l. They are concerned about the risks of contracting diseases from the transfusion and ask specifically about the risk of variant Creutzfeldt-Jakob Disease (vCJD) transmission. What is the most appropriate advice with respect to vCJD?

A. There was never any risk of vCJD being transmitted via blood transfusion
B. There had previously been a small risk of vCJD transmission but the risk has now been eliminated through screening
C. Measures are taken to reduce the risk of vCJD transmission but there remains a very small risk of transmission
D. There is a significant chance of vCJD transmission to patients who are between the ages of 40-60 years
E. There is a significant chance of vCJD transmission to patients who are between the ages of 60-90 years

ANSWER:
Measures are taken to reduce the risk of vCJD transmission but there remains a very small risk of transmission

EXPLANATION:
BLOOD PRODUCT TRANSFUSION COMPLICATIONS
Blood product transfusion complications may be broadly classified into the following:
- immunological: acute haemolytic, non-haemolytic febrile, allergic/anaphylaxis
- infective
- transfusion-related acute lung injury (TRALI)
- fluid overload
- other: hyperkalaemia, iron overload, clotting

Acute haemolytic transfusion reaction
Acute haemolytic transfusion reaction results from a mismatch of blood group (ABO) which causes massive intravascular haemolysis. Symptoms begin minutes after the transfusion is started and include a fever, abdominal and chest pain, agitation and hypotension.

Treatment should include immediate transfusion termination, generous fluid resuscitation with saline solution and informing the lab

Complications include disseminated intravascular coagulation, and renal failure

Non-haemolytic febrile reaction
Febrile reactions
- due to white blood cell HLA antibodies
- often the result of sensitization by previous pregnancies or transfusions

Allergic/anaphylaxis reaction
Allergic reactions to blood transfusions are caused by hypersensitivity reactions to components within the transfusion. Symptoms typically arise within minutes of starting the transfusion and severity can range from urticaria to anaphylaxis with hypotension, dyspnoea, wheezing, and stridor, or angioedema.

Simple urticaria should be treated by discontinuing the transfusion and with an antihistamine. Once the symptoms resolve, the transfusion may be continued with no need for further workup.

More severe allergic reaction or anaphylaxis should be treated urgently. The transfusion should be permanently discontinued, intramuscular adrenaline should be administered and supportive care. Antihistamine, corticosteroids and bronchodilators should also be considered for these patients.

Infective
Transmission of vCJD
- although the absolute risk is very small, vCJD may be transmitted via blood transfusion
- a number of steps have been taken to minimise this risk, including:
- → from late 1999 onward, all donations have undergone removal of white cells (leucodepletion) in order to reduce any vCJD infectivity present
- →from 1999, plasma derivatives have been fractionated from imported plasma rather than being sourced from UK donors. Fresh Frozen Plasma (FFP) used for children and certain groups of adults needing frequent transfusions is also imported
- → from 2004 onward, recipients of blood components have been excluded from donating blood

Q-24

A 48 year old nurse presents with a short history of epistaxis and bleeding gums. You request urgent bloods, the results of which are shown in the table below:

Haemoglobin	**86 g/L**
White cells	**2.3 x 10^9/L**
Platelets	**18 x 10^9/L**
Clotting	**deranged**
Blood film	**bilobed large mononuclear cells**

What is the most likely diagnosis?

A. Von Willebrand's disease
B. Acute lymphoblastic leukaemia
C. Lymphoma
D. Acute myeloid leukaemia
E. Surreptitious warfarin overdose

ANSWER:
Acute myeloid leukaemia

EXPLANATION:
This is a picture of bone marrow failure secondary to acute myeloid leukaemia.

In acute leukaemia a malignant expansion abnormal white cells accumulate in the bone marrow, replacing normal haemopoietic cells.

Acute expansion of the myeloid stem line (acute myeloid leukaemia) is more common over the age of 45, in comparison with acute lymphoblastic leukaemia which is mostly seen in children.

Lymphoma does not tend to present in this way, but more so with rubbery enlargement of lymph nodes.

Von Willebrand's disease may present with epistaxis and bleeding gums in severe cases, but it is rare that there are abnormalities on blood results.

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.

Features are largely related to bone marrow failure:
- anaemia: pallor, lethargy, weakness
- neutropenia: whilst white cell counts may be very high, functioning neutrophil levels may be low leading to frequent infections etc
- thrombocytopenia: bleeding
- splenomegaly
- bone pain

Poor prognostic features
- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: 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)
- Auer rods (seen with myeloperoxidase stain)
- 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

Q-25

What are the most common types of transformations seen in patients with polycythaemia vera?

A. Myelodysplasia + chronic myeloid leukaemia
B. Myelofibrosis + chronic myeloid leukaemia
C. Myelodysplasia + myelofibrosis
D. Myelofibrosis + acute myeloid leukaemia
E. Myelodysplasia + acute myeloid leukaemia

ANSWER:
Myelofibrosis + acute myeloid leukaemia

EXPLANATION:
Polycythaemia rubra vera - around 5-15% progress to myelofibrosis or AML

POLYCYTHAEMIA VERA: MANAGEMENT
Polycythaemia 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
- aspirin
- 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
- 5-15% of patients progress to myelofibrosis
- 5-15% of patients progress to acute leukaemia (risk increased with chemotherapy treatment)

Q-26

A 72-year-old man is referred to haematology with a raised haemoglobin. A diagnosis of polycythaemia vera is suspected. Which other abnormality of the blood would be most consistent with this diagnosis?

A. Raised alkaline phosphatase
B. Hypokalaemia
C. Thrombocytopaenia
D. Raised ferritin level
E. Neutrophilia

ANSWER:
Neutrophilia

EXPLANATION:
POLYCYTHAEMIA VERA: FEATURES
Polycythaemia vera (previously called 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 recently been established that a mutation in JAK2 is present in approximately 95% of patients with polycythaemia vera and this has resulted in significant changes to the diagnostic criteria. The incidence of polycythaemia vera 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 polycythaemia vera have recently been updated by the BCSH. This replaces the previous polycythaemia vera Study Group criteria.

JAK2-positive polycythaemia vera - diagnosis requires both criteria to be present

Criteria	Notes
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

Criteria	Notes
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

Q-27

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

A. Factor V Leiden gene mutation
B. Polycystic ovarian syndrome
C. Hyperprolactinaemia
D. Antithrombin III deficiency
E. Antiphospholipid syndrome

ANSWER:
Antiphospholipid syndrome

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

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

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

Q-28

A 67-year-old man with lung cancer is currently taking MST 30mg bd for pain relief. What dose of oral morphine solution should he be prescribed for breakthrough pain?

A. 5 mg
B. 10 mg
C. 15 mg
D. 20 mg
E. 30 mg

ANSWER:
10 mg

EXPLANATION:
Breakthrough dose = 1/6th of daily morphine dose
The total daily morphine dose is 30 * 2 = 60 mg, therefore the breakthrough dose should be one-sixth of this, 10 mg

PALLIATIVE CARE PRESCRIBING: PAIN
NICE guidelines
In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered
- drowsiness is usually transient - if it does not settle then adjustment of the dose should be considered

SIGN guidelines
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 strong opioids, bisphosphonates or radiotherapy. The assertion that NSAIDs are particularly effective for metastatic bone pain is not supported by studies. Strong opioids have the lowest number needed to treat for relieving the pain and can provide quick relief, in contrast to radiotherapy and bisphosphonates*. All patients, however, should be considered for referral to a clinical oncologist for consideration of further treatments such as radiotherapy

Other points
When increasing the dose of opioids the next dose should be increased by 30-50%.

Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

Conversion between opioids

From	To	Conversion factor
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 10**

Oxycodone generally causes less sedation, vomiting and pruritis than morphine but more constipation.

From	To	Conversion factor
Oral morphine	Oral oxycodone	Divide by 1.5-2***

The current BNF gives the following conversion factors for transdermal perparations

- a transdermal fentanyl 12 microgram patch equates to approximately 30 mg oral morphine daily
- a transdermal buprenorphine 10 microgram patch equates to approximately 24 mg oral morphine daily.

From	To	Conversion factor
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

*BMJ 2015;350:h315 Cancer induced bone pain

**this has previously been stated as 5 but the current version of the BNF states a conversion of 10

***historically a conversion factor of 2 has been used (i.e. oral oxycodone is twice as strong as oral morphine). The current BNF however uses a conversion rate of 1.5

Q-29

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

ANSWER:
Nodular sclerosing

EXPLANATION:
Hodgkin's lymphoma - most common type = nodular sclerosing

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

Type	Frequency	Prognosis	Notes
Nodular sclerosing	Most common (around 70%)	Good prognosis	More common in women. Associated with lacunar cells
Mixed cellularity	Around 20%	Good prognosis	Associated with a large number of Reed-Sternberg cells
Lymphocyte predominant	A*round 5%	Best prognosis	
Lymphocyte depleted	Rare	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

*Reed-Sternberg cells with nuclei surrounded by a clear space

Q-30

A 72-year-old woman is admitted with confusion and pallor. Her daughter reports that she has been getting more confused and tired for the past three months. Blood tests are reported as follows:

Hb 89 g/l
MCV 125 fl
Plt 148 * 109/l
WBC 4.4 * 109/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

ANSWER:
Intramuscular vitamin B12 + start oral folic acid when vitamin B12 levels are normal

EXPLANATION:
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	• alcohol • liver disease • hypothyroidism • pregnancy • reticulocytosis • myelodysplasia • drugs: cytotoxics

Q-31

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

ANSWER:
Ovarian fibroma

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

Please see Q-6 for Tumour Markers

Q-32

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

ANSWER:
Mycoplasma infection

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

Please see Q-4 for Autoimmune Haemolytic Anaemia

Q-33

A 66-year-old woman with lung cancer develops a deep vein thrombosis. She is reviewed in the hospital clinic and started on treatment dose low-molecular weight heparin (LMWH). What is the most appropriate treatment plan?

A. Switch to warfarin, continue for 6 months
B. Switch to warfarin, continue for 3 months
C. Continue on LMWH for 6 months
D. Continue on LMWH for 6 weeks
E. Continue on LMWH for 3 months

ANSWER:
Continue on LMWH for 6 months

EXPLANATION:
Cancer patients with VTE - 6 months of LMWH
Patients with active cancer are at continued risk of thrombosis. For this reason a 6 month course of anticoagulation is recommended. Low-molecular weight heparin has the advantage of being more easy to reverse and stop if a cancer-related bleed occurs, for example massive haemoptysis in a patient with lung cancer.

DEEP VEIN THROMBOSIS: DIAGNOSIS AND MANAGEMENT

Diagnosis
NICE published guidelines in 2012 relating to the investigation and management of deep vein thrombosis (DVT).

If a patient is suspected of having a DVT a two-level DVT Wells score should be performed:

Two-level DVT Wells score

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	-2

Clinical probability simplified score
DVT likely: 2 points or more
DVT unlikely: 1 point or less

If a DVT is 'likely' (2 points or more)

- a proximal leg vein ultrasound scan should be carried out within 4 hours and, if the result is negative, a D-dimer test
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours a D-dimer test should be performed and low-molecular weight heparin administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

If a DVT is 'unlikely' (1 point or less)

- perform a D-dimer test and if it is positive arrange:
- a proximal leg vein ultrasound scan within 4 hours
- if a proximal leg vein ultrasound scan cannot be carried out within 4 hours low-molecular weight heparin should be administered whilst waiting for the proximal leg vein ultrasound scan (which should be performed within 24 hours)

Management
Low molecular weight heparin (LMWH) or fondaparinux should be given initially after a DVT is diagnosed.
- a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE add 'consider extending warfarin beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding'. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months. In practice most clinicians give 6 months of warfarin for patients with an unprovoked DVT/PE
- for patients with active cancer NICE recommend using LMWH for 6 months

Further investigations and thrombophilia screening
As both malignancy and thrombophilia are obvious risk factors for deep vein thrombosis NICE make recommendations on how to investigate patients with unprovoked clots.

Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
- a physical examination (guided by the patient's full history) and
- a chest X-ray and
- blood tests (full blood count, serum calcium and liver function tests) and urinalysis.

Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE

Thrombophilia screening
- not offered if patients will be on lifelong warfarin (i.e. won't alter management)
- consider testing for antiphospholipid antibodies if unprovoked DVT or PE
- consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE

Q-34

A 69-year-old man with terminal lung cancer is reviewed. He currently takes MST 60mg bd for pain. He has become unable to take oral medications and a decision is made to set-up a syringe driver. What dose of diamorphine should be prescribed for the syringe driver?

A. 60 mg
B. 40 mg
C. 120 mg
D. 30 mg
E. 20 mg

ANSWER:
40 mg

EXPLANATION:
To convert from oral morphine to diamorphine the total daily morphine dose (60 * 2 = 120mg) should be divided by 3 (120 / 3 = 40mg)

Please see Q-28 for Palliative Care Prescribing: Pain

Q-35

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

A. Cellular proliferation
B. Apoptotic activity
C. Glucose uptake
D. Vascular supply
E. Tyrosine kinase activity

ANSWER:
Glucose uptake

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

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

Q-36

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

ANSWER:
Oral dexamethasone + urgent MRI

EXPLANATION:
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. Extradural compression accounts for the majority of cases, usually due to vertebral body metastases. It is more common in patients with lung, breast and prostate cancer

Features
- back pain - the earliest and most common symptom - may be worse on lying down and coughing
- lower limb weakness
- sensory changes: sensory loss and numbness
- neurological signs depend on the level of the lesion. Lesions above L1 usually result in upper motor neuron signs in the legs and a sensory level. Lesions below L1 usually cause lower motor neuron signs in the legs and perianal numbness. 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

Q-37

A patient with testicular cancer is started on cisplatin therapy. Which of the following side-effects is most characteristically associated with cisplatin?

A. Liver cirrhosis
B. Alopecia
C. Peripheral neuropathy
D. Haemorrhagic cystitis
E. Cardiomyopathy

ANSWER:
Peripheral neuropathy

EXPLANATION:
Cisplatin may cause peripheral neuropathy

Please see Q-1 for Cytotoxic Agents

Q-38

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

ANSWER:
Glycoprotein IIb/IIIa complex

EXPLANATION:
IMMUNE THROMBOCYTOPENIA (ITP) IN ADULTS
Immune (or idiopathic) thrombocytopenic purpura (ITP) is an immune-mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb/IIIa or Ib-V-IX 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)

Q-39

A 38-year-old Pakistani female was admitted with shortness of breath and a syncopal episode. She describes a 2 week history of lethargy, malaise and dizziness. The patient had recently started anti-tuberculous therapy. History revealed she was not a vegetarian.

Hb	**8.5g/dl**
MCV	**72fl**
WCC	**11 * 10^9/l**
Platelets	**225 * 10^9/l**
TSAT	**33%**
Ferritin	**600ng/ml**
Haemoglobin electrophoresis	**normal**

Which stain should be applied to a blood film?

A. Giemsa
B. Gram
C. Ziehl Neelsen
D. Perl's
E. India ink

ANSWER:
Perl's

EXPLANATION:
This 38 year old Pakistani female has presented with symptomatic anaemia. Blood tests reveal a microcytic anaemia, the causes of which can be broadly categorised into: 1, iron deficiency, 2, thalassaemia trait 3, sideroblastic anaemia.

Interpreting the iron studies shows a normal transferrin saturation and normal ferritin, ruling out iron deficiency anaemia. Normal haemoglobin electrophoresis rules out thalassaemia, therefore the likely cause is sideroblastic anaemia. This is also hinted at by the recent commencement of Isoniazid (anti tuberculous therapy) a cause of sideroblastic anaemia.

Sideroblastic anaemia when stained with Perl's stain shows ring sideroblasts. The disease is characterised by ineffective erythropoiesis leading to poor incorporation of iron into the nucleus of erythroblasts.

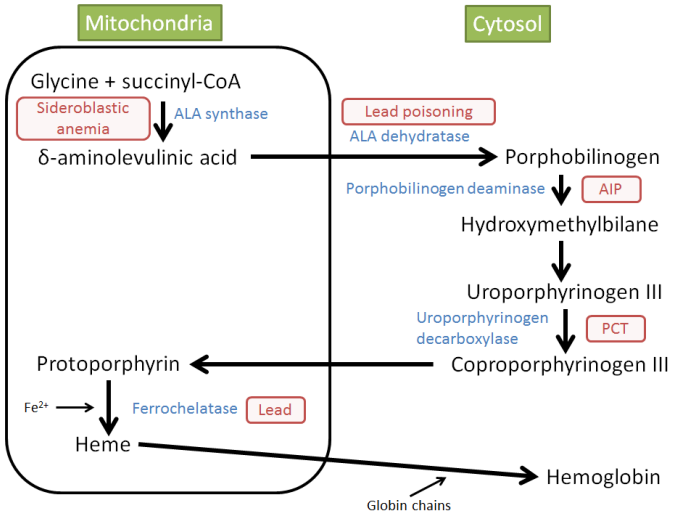
SIDEROBLASTIC ANAEMIA
Sideroblastic anaemia is a condition where red cells fail to completely form haem, whose biosynthesis takes place partly in the mitochondrion. This leads to deposits of iron in the mitochondria that form a ring around the nucleus called a ring sideroblast. It may be congenital or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



Q-40

A 34-year-old female presents due to the development of a purpuric rash on the back of her legs. Her only regular medication is Microgynon 30. She also reports frequent nose bleeds and menorrhagia. A full blood count is requested:

Hb	**11.7 g/dl**
Platelets	**62 * 109/l**
WCC	**5.3 * 109/l**
PT	**11 secs**
APTT	**30 secs**

Factor VIIIc activity **Normal**

What is the most likely diagnosis?

A. Drug-induced thrombocytopenia
B. Henoch-Schonlein purpura
C. Thrombotic thrombocytopenic purpura
D. Idiopathic thrombocytopenic purpura
E. Antiphospholipid syndrome

ANSWER:
Idiopathic thrombocytopenic purpura

EXPLANATION:
The isolated thrombocytopenia in a well patient points to a diagnosis of ITP. The combined oral contraceptive pill does not commonly cause blood dyscrasias

Please see Q-38 for Immune Thrombocytopenia (ITP) in Adults

Q-41

A 40-year-old female is referred to medical assessment unit by her physician for querying thrombotic thrombocytopenic purpura (TTP) after she presented with a temperature of 38.9ºC. Her subsequent urea and electrolytes showed deteriorating renal function with a creatinine 3 times greater than her baseline.

What is the underlying pathophysiology of TTP?

A. Autoimmune destruction of red blood cells
B. Failure to cleave von Willebrand factor normally
C. Anti-bodies against von Willebrand factor
D. Autoimmune destruction of platelets
E. A deficiency of von Willebrand factor

ANSWER:
Failure to cleave von Willebrand factor normally

EXPLANATION:
TTP is caused by the failure to cleave vWF normally Patients with TTP have unusually large multimers of von Willebrand factor (vWF) in their plasma. Patients with TTP lack a plasma protease that is responsible for the breakdown of these ultra-large vWF multimers. See notes below.

Autoimmune destruction of red blood cells is a form of autoimmune hemolytic anaemia and is not the correct answer in this scenario.

Autoimmune destruction of platelets is seen in idiopathic thrombocytopenic purpura (ITP).

A deficiency of von Willebrand factor (vWF) is seen in von Willebrand disease, a genetic disorder.

Anti-bodies against vWF is incorrect.

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 ADAMTS13 (a metalloprotease enzyme) 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

Q-42

Which one of the following is least associated with thymomas?

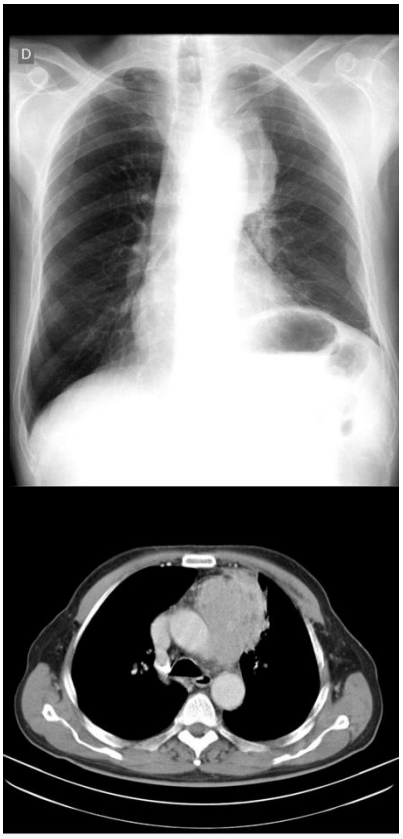
A. Syndrome inappropriate ADH
B. Myasthenia gravis
C. Red cell aplasia
D. Dermatomyositis
E. Motor neurone disease

ANSWER:
Motor neurone disease

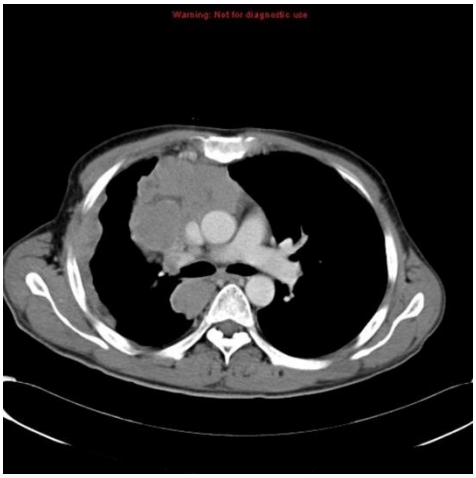
EXPLANATION:
THYMOMA
Thymomas are the most common tumour of the anterior mediastinum and is usually detected between the sixth and seventh decades of life.

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



Chest x-ray and accompanying CT scan of a patient with a thymoma. In the chest x-ray there is a partially delineated mediastinal mass (anterior mediastinum) with regular borders, bulging the left upper mediastinal contour.



CT slice at the bifurcation of the main bronchus showing an invasive thymoma presenting as an anterior mediastinal mass

Q-43

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 vera?

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

ANSWER:
JAK2 mutation screen

EXPLANATION:
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 vera

Please see Q-26 for Polycythaemia: Features

Q-44

A 17-year-old man is investigated after he bled excessively following a tooth extraction. The following results are obtained:

Plt	**173 * 109/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

ANSWER:
Factor VIII

EXPLANATION:
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

Q-45

A 45-year-old woman attends the acute medical unit with her second DVT this year. Her background is notable for COPD, hypertension and chronic kidney disease stage 4 secondary to membranous glomerulonephritis.

In chronic kidney disease, which of the following contributes most to the increased risk of VTE?

A. Immobility
B. Loss of protein C
C. Loss of antithrombin III
D. Concurrent cancer
E. Lupus anticoagulant

ANSWER:
Loss of antithrombin III

EXPLANATION:
CKD is the most common cause of antithrombin III deficiency
Antithrombin III is an important regulatory molecule that reduces the activity of the intrinsic pathway of the clotting cascade. Loss of antithrombin III, thus, increases coagulability.

Whilst there are hereditary causes of antithrombin III, it is a particularly small protein and is easily lost through the nephron in CKD.

CKD does also increase the risk of concurrent cancers, but not as significantly as the protein loss. Lupus anticoagulant is indeed highly prothrombotic and is associated with antiphospholipid syndrome.

ANTITHROMBIN III DEFICIENCY

Antithrombin III deficiency is an inherited cause of thrombophilia occurring in approximately 1:3,000 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 are uncommon

Management

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

The table below shows the prevalence and relative risk of venous thromboembolism (VTE) of the different inherited thrombophilias:

Condition	Prevalence	Relative risk of VTE
Factor V Leiden (heterozygous)	5%	4
Prothrombin gene mutation (heterozygous)	1.5%	3
Protein C deficiency	0.3%	10
Protein S deficiency	0.1%	5-10
Antithrombin III deficiency	0.03	10-20

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

Q-46

A 79-year-old female with a history of COPD and metastatic lung cancer is admitted with increasing shortness of breath. Following discussion with family it is decided to withdraw active treatment, including fluids and antibiotics, as the admission likely represents a terminal event. Two days after admission she becomes agitated and restless. What is the most appropriate management?

A. Subcutaneous midazolam
B. Intramuscular haloperidol
C. Oral lormetazepam
D. Oral haloperidol
E. Recommence fluids and antibiotics

ANSWER:

Subcutaneous midazolam

EXPLANATION:

PALLIATIVE CARE PRESCRIBING: AGITATION AND CONFUSION

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness then agitation or restlessness is best treated with midazolam

Q-47

A 46-year-old woman presents to her GP with a 2-month history of increasing tiredness and fatigue. She has also noticed that she has been getting more short of breath recently. Her past medical history includes two urinary tract infections in the past year and lower back pain for which she takes paracetamol. She does not take any other medications. On examination, she is pale. The GP orders some baseline blood tests:

Hb	**101 g/l (115–165 g/L)**
MCV	**88.1 fL (80-100 fL)**
Platelets	**129 * 109/l (140-400 * 109/l)**
ESR	**114 mm/h (3–9 mm/h)**
WBC	**3.2 * 109/l (4.0-11.0 * 109/l)**
Na+	**137 mmol/l (135-145mmol/l)**
K+	**4.9 mmol/l (3.5-5mmol/l)**
Urea	**10 mmol/l (2.5-6.7mmol/l)**
Creatinine	**108 µmol/l (45-90µmol/l)**
eGFR	**50 ml/min/1.73m2 (>90 ml/min/1.73m2)**
Ca2+	**2.9 mmol/L (2.12-2.65mmol/L)**

What is the next most appropriate investigation?

A. Renal ultrasound scan
B. Cervical lymph node biopsy
C. PTH levels
D. CT KUB
E. Serum electrophoresis

ANSWER:

Serum electrophoresis

EXPLANATION:

'CRAB' features of multiple myeloma = hyperCalcaemia, Renal failure, Anaemia (and thrombocytopenia) and Bone fractures/lytic lesions

The combination of the history, examination findings and blood test results point towards a diagnosis of multiple

myeloma. This patient is demonstrating evidence of all four features of multiple myeloma:

- *C - hypercalcaemia*
- *R - renal insufficiency (suggested by the U&Es and complicated by the recurrent UTIs - patients are susceptible to infections as the production of antibodies by normal plasma cells is impaired)*
- *A - this patient is short of breath due to her anaemia (and the FBC shows evidence of pancytopenia - typically due to plasma cells infiltrating the bone marrow)*
- *B - bone pain (albeit subtle in the form of a vague history of lower back pain)*

The immunoglobulin produced by dysplastic plasma cells shows up as a monoclonal band on serum electrophoresis.

Renal ultrasound scan will not aid diagnosis of multiple myeloma.

Cervical lymph node biopsy may be helpful in lymphoma but not myeloma (a bone marrow biopsy would be more helpful in multiple myeloma).

PTH levels can help identify the cause of hypercalcaemia but this patient has enough features suggestive of multiple myeloma to justify investigating for myeloma first.

CT scan of the kidneys, ureters and bladder is unlikely to be helpful in identifying multiple myeloma (although whole-body CT scanning is often used to detect osteolytic lesions).

Please see Q-7 for Myeloma: Features

Q-48

You are working on a geriatric post when you notice that a 93-year-old man on your ward has had consistently high white blood cells, despite several courses of antibiotics. His bloods today show:

Hb	**91 g/l**
Platelets	**250 * 109/l**
WBC	**32.2 * 109/l**
Neutrophils	**28.1 * 109/l**

Despite this he has at no point shown signs of any infection. Your consultant suggests contacting haematology with regards to ascertaining the leucocyte alkaline phosphatase score.

Which of the following conditions would have a high leucocyte alkaline phosphatase score?

A. Chronic myeloid leukaemia (CML)
B. Acute myeloid leukaemia (AML)
C. Paroxysmal nocturnal haemoglobinuria (PNH)
D. Leukemoid reaction
E. Pregnancy

ANSWER:
Leukemoid reaction

EXPLANATION:
Leukemoid reaction has a high leucocyte alkaline phosphatase score
The answer is leukemoid reaction. Leucocyte ALP is one of types of alkaline phosphatase. It has a diagnostic value in differentiating causes of high number of white blood cells, seen on manual differentials.

The leukemoid reaction refers to the 'left-shift' of immature white blood cells that occurs in underlying infections. On a blood film, this could mistakenly be thought to be a malignant process (like CML). Leukocyte ALP can differentiate the two - a low score indicates undeveloped leukocytes, like those found in CML and AML. PNH also causes a low score.

Placental ALP found in pregnancy is a distractor.

Please see Q-12 for Leucocyte Alkaline Phosphatase

Q-49

A 7-year-old boy who recently emigrated from Nigeria was seen in emergency department with a 6 week history of progressive swelling of his jaw, fevers, night sweats and weight loss. He had no past medical history but his mother describes a sore throat in the past, which was treated with antibiotics, but unfortunately developed a rash subsequently. On examination there was a painless 4x3cm mass that was fixed and hard. The only other examination findings of note was rubbery symmetrical cervical lymphadenopathy.

What translocation would most likely to found on biopsy karyotyping?

A. T9:22
B. T15:17
C. T8:14
D. T14:18
E. T11:14

ANSWER:
T8:14

EXPLANATION:
Burkitt's lymphoma is an uncommon, very high grade non Hodgkin's lymphoma endemic to west Africa and the mosquito belt. There is a close association with contraction of Epstein Barr virus (EBV). Burkitt's lymphoma often presents with symmetrical painless lymphadenopathy, systemic B symptoms (fever, sweats and weight loss), central nervous system involvement and bone marrow infiltration. Classically in the textbooks the patient also develops a large jaw tumour.

T9:22 - Chronic myeloid leukaemia - 9 ABL (oncogene - an aberrant tyrosine kinase) + 22 B cell receptor

T15:17 - Acute pro-myelocytic leukaemia - 15 Promyelocytic gene + 17 Retinoid acid receptor alpha (Fusion protein binds retinoid acid receptor and promotes transcription).

T8:14 - Burkitt's Lymphoma - 8 c-myc (oncogene) + 14 Ig heavy constant region

T14:18 - Follicular Lymphoma - 14 Ig heavy constant region + 18 Bcl2 (anti-apoptotic gene)

T11:14 - Mantle Cell Lymphoma - 11 - Cyclin D (oncogene) + 14 Ig heavy constant region

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 of Burkitt's lymphoma and to a lesser extent the sporadic form.

Microscopy findings

- 'starry sky' appearance: lymphocyte sheets interspersed with macrophages containing dead apoptotic tumour cells

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Rasburicase (a recombinant version of urate oxidase, an enzyme which catalyses the conversion of uric acid to allantoin*) is often given before the chemotherapy to reduce the risk of this occurring. Complications of tumour lysis syndrome include:

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

*allantoin is 5-10 times more soluble than uric acid, so renal excretion is more effective

Q-50

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

ANSWER:
Breast cancer

EXPLANATION:
Please see Q-6 for Tumour Markers

Q-51

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

ANSWER:
Pyridoxine

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

Please see Q-39 for Sideroblastic Anaemia

Q-52

You are an SHO on an acute oncology ward. You are asked to speak to a 56-year-old man with colorectal cancer. He was diagnosed 1 month ago after participating in screening. Following a positive faecal occult blood test, colonoscopy demonstrated a malignant lesion in the descending colon. CT staging showed lymph node involvement but no distant metastases. He has undergone a left-hemicolectomy and is due to start adjuvant chemotherapy with a combination of 5-FU and oxaliplatin. During his work-up, his consultant explained that he would need to be monitored for disease recurrence.

Which of the following has a role in monitoring disease activity in colorectal cancer?

A. Alpha-Fetoprotein (AFP)
B. Mesorectal MRI
C. Ca-19-9
D. Carcinoembryonic Antigen (CEA)
E. Ca-15-3

ANSWER:
Carcinoembryonic Antigen (CEA)

EXPLANATION:
Carcinoembryonic Antigen (CEA) is a tumour marker in colorectal cancer and has a role in monitoring disease activity
The correct answer is carcinoembryonic antigen (CEA). CEA is a known tumour marker for colorectal cancer. It is not used diagnostically, but in patient's with a known diagnosis of colorectal cancer associated with raised CEA levels, it can be used to monitor disease activity and help with early identification of disease recurrence.

Please see Q-6 for Tumour Markers

Q-53

Burkitt's lymphoma is associated with which one of the following genetic changes:

A. Cyclin D1-IGH gene translocation
B. TEL-JAK2 gene translocation
C. Bcl-2 gene translocation
D. C-myc gene translocation
E. BCR-Abl1 gene translocation

ANSWER:
C-myc gene translocation

EXPLANATION:
Burkitt's lymphoma - c-myc gene translocation

Please see Q-49 for Burkitt's Lymphoma

Q-54

Each one of the following is associated with polycythaemia vera, except:

A. Splenomegaly
B. Hyperviscosity
C. Raised ESR
D. Hypertension
E. Pruritus

ANSWER:
Raised ESR

EXPLANATION:
Polycythaemia rubra vera is associated with a low ESR

Please see Q-26 for Polycythaemia: Features

Q-55

You review a 65-year-old woman in oncology clinic. She has known metastatic breast cancer, and has received a mastectomy, chemotherapy and radiotherapy.

She has complained of headaches and nausea for the last 7 days, which are worse in the mornings. A CT head showed multiple brain metastases, with compression of the ventricles and sulci.

Your patient declines further chemotherapy or radiotherapy. She is currently taking opioid painkillers.

Which of the following medications can be used as an adjunct to further relieve her symptoms?

A. Ondansetron
B. Cyclizine
C. Dexamethasone
D. Haloperidol
E. Sumatriptan

ANSWER:
Dexamethasone

EXPLANATION:
Headache caused by raised intracranial pressure due to brain cancer (or metastases) can be palliated with dexamethasone
Dexamethasone is used to reduce oedema around brain metastases, to palliate symptoms of raised intracranial pressure.

Ondansetron, cyclizine and haloperidol are all effective agents for nausea, but would not treat the root cause.

Sumatriptan is a treatment for migraines and has no role here.

Please see Q-28 for Palliative Care Prescribing: Pain

Q-56

A patient is investigated for leukocytosis. Cytogenetic analysis shows the presence of the following translocation: t(9;22)(q34;q11). Which haematological malignancy is most strongly associated with this translocation?

A. Chronic myeloid leukaemia
B. Acute promyelocytic leukaemia
C. Acute lymphoblastic leukaemia
D. Burkitt's lymphoma
E. Mantle cell lymphoma

ANSWER:
Chronic myeloid leukaemia

EXPLANATION:
CML - Philadelphia chromosome - t(9:22)
The Philadelphia translocation is seen in around 95% of patients with chronic myeloid leukaemia. Around 25% of adult acute lymphoblastic leukaemia cases also have this translocation.

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

Q-57

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

ANSWER:

Plasma exchange

EXPLANATION:

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

Q-58

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

ANSWER:

Antithrombin III deficiency

EXPLANATION:

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

Please see Q-45 for Antithrombin III Deficiency

Q-59

A 24-year-old female presents to the acute medical take with several lumps in her neck and under her arms, weight loss, vomiting and low mood. She is found to have several areas of suspicious lymphadenopathy, including in the neck, both axillae and mediastinum. She also has multiple lesions in her liver. All lesions are confirmed to be manifestations of Hodgkin's lymphoma after biopsy and discussion at the oncology MDT. Which stage of disease does she have?

A. I
B. II
C. III
D. IV
E. V

ANSWER:

IV

EXPLANATION:

Spread into the liver, bone marrow, lungs or other organs would be classified as stage IV on the Ann Arbor staging system for Hodgkin's lymphoma
This patient has stage IV disease as per the Ann Arbor scale. She has spread of disease beyond the lymph nodes into the liver.

Stage I consists of disease in one lymph node area only. Stage II consists of disease in two lymph node areas, but both on the same side of the diaphragm. Stage III consists of disease in two lymph node areas on different sides of the diaphragm. Stage IV consists of the spread of disease beyond the lymph nodes, into the liver, lungs or bone marrow. Stage V is not included in the scale.

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)

Q-60

A patient with glucose-6-phosphate dehydrogenase (G6PD) deficiency presents for advice about malaria prophylaxis. He is about to go on a 'gap year' during which he will be travelling abroad for 12 months. Which one of the following medications is it most important that he avoids?

A. Artemether with lumefantrine
B. Mefloquine
C. Proguanil
D. Doxycyline
E. Primaquine

ANSWER:

Primaquine

EXPLANATION:

G6PD DEFICIENCY

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in an X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

Pathophysiology

↓ G6PD → ↓ glutathione → increased red cell susceptibility to oxidative stress

Features

- neonatal jaundice is often seen
- intravascular haemolysis
- gallstones are common
- splenomegaly may be present
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

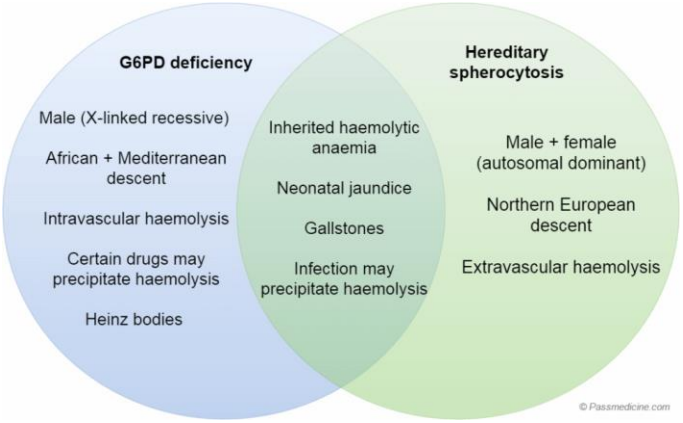
Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulph- group drugs: sulphonamides, sulphasalazine, sulfonylureas

Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Comparing G6PD deficiency to hereditary spherocytosis:



	G6PD deficiency	Hereditary spherocytosis
Gender	Male (X-linked recessive)	Male + female (autosomal dominant)
Ethnicity	African + Mediterranean descent	Northern European descent
Typical history	• Neonatal jaundice • Infection/drugs precipitate haemolysis • Gallstones	• Neonatal jaundice • Chronic symptoms although haemolytic crises may be precipitated by infection • Gallstones • Splenomegaly is common
Blood film	Heinz bodies	Spherocytes (round, lack of central pallor)
Diagnostic test	Measure enzyme activity of G6PD	Osmotic fragility test

Q-61

A 39-year-old woman presents with a strange collection of symptoms over the past six months. She has been seen by multiple specialists, none of whom have been able to find a cause for her symptoms.

Her symptoms include worsening headaches, memory loss, low mood, lethargy, abdominal pain causing paroxysms of intermittent generalised pain, nausea, an unusual taste in her mouth and paraesthesia in her extremities.

She is irritable during your consultation and at times tearful complaining that no one is taking her seriously and confiding that her General Practitioner had referred her for counselling.

Routine blood tests show:

Hb	**101g/L**
WBC	**5.6 10*9/L**
Platelets	**350 10*9/L**
MCV	**77fL**
Na	**136mmol/L**
K	**4.3mmol/L**
Urea	**18.2mmol/L**
Creatinine	**408umol/L**

What is the likely cause of her symptoms?

A. Pick's disease
B. Hepatic encephalopathy
C. Lead poisoning
D. Early-onset Alzheimer's
E. Viral encephalitis

ANSWER:
Lead poisoning

EXPLANATION:
It is important to keep lead poisoning in mind as a differential, particularly in someone for whom routine investigations are not providing an answer and who clearly has abnormal pathology (demonstrated by her kidney failure and microcytic anaemia).

It can cause a varied and often non-specific array of symptoms. Some more 'classical' features include an unusual taste in the mouth and paraesthesia of the extremities.

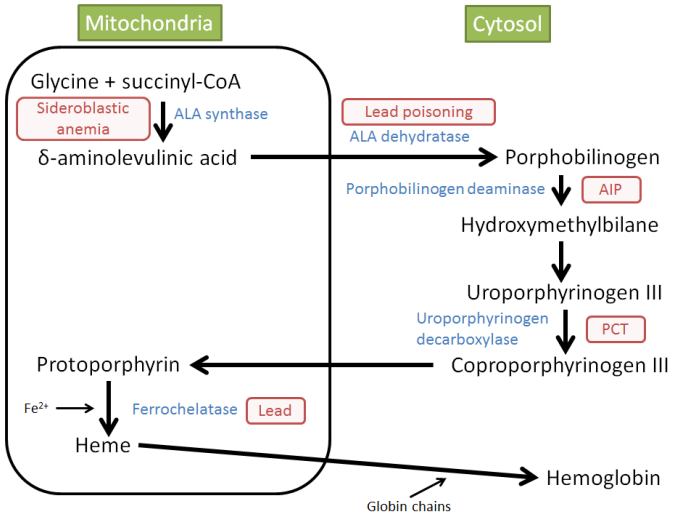
Questions may more obviously point to the route of exposure through industrial exposure or contact with lead-based products such as paint or contaminated water.

LEAD POISONING
Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs

Features
- abdominal pain
- peripheral neuropathy (mainly motor)
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

Investigations
- the blood lead level is usually used for diagnosis. Levels greater than 10 mcg/dl are considered significant
- full blood count: microcytic anaemia. Blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)

Management - various chelating agents are currently used:
- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- Dimercaprol



Q-62

A 60-year-old woman develops a deep vein thrombosis (DVT) 10 days after having a hip replacement despite taking prophylactic dose low-molecular weight heparin (LMWH). She has no significant past medical history of note other than osteoarthritis. After being diagnosed she is started on treatment dose LMWH. What is the most appropriate anticoagulation strategy?

A. Continue on treatment dose LMWH for 6 weeks
B. Continue on treatment dose LMWH for 3 months
C. Continue on treatment dose LMWH for 6 months
D. Switch to warfarin for 3 months
E. Switch to warfarin for 6 months

ANSWER:
Switch to warfarin for 3 months

EXPLANATION:
Venous thromoboembolism - length of warfarin treatment
- ***provoked (e.g. recent surgery): 3 months***
- ***unprovoked: 6 months***

The recent surgery is an obvious 'provoking' factor for the DVT. She should therefore be anticoagulated for 3 months.

Please see Q-33 for Deep Venous Thrombosis: Diagnosis and Management

Q-63

A 49-year-old woman 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 * 109/l
WCC 6.6 * 109/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

ANSWER:
Oral prednisolone

EXPLANATION:
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

Please see Q-57 for ITP: Investigation and Management

Q-64

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

ANSWER:
Night sweats

EXPLANATION:
Night sweats are a 'B' symptom and imply a poor prognosis

Please see Q-29 for Hodgkin's Lymphoma: Histological Classification and Prognosis

Q-65

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

ANSWER:
Increased osteoclastic activation

EXPLANATION:
Please see Q-7 for Myeloma: Features

Q-66

A 54-year-old man is investigated for recurrent episodes of abdominal pain associated with weakness of his arms and legs. Which one of the following urine tests would best indicate lead toxicity?

A. Haemoglobinuria
B. Coproporphyrin
C. Porphobilinogen
D. Uroporphyrin
E. Ham's test

ANSWER:
Coproporphyrin

EXPLANATION:
Please see Q-61 for Lead Poisoning

Q-67

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

ANSWER:
Adult T-cell leukaemia

EXPLANATION:
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

Q-68

A 54-year-old lady presents with shortness of breath, distended neck veins, and a swollen and red face. She had She undergoes a CT scan of her chest demonstrating obstruction of the superior vena cava (SVC). What is the most likely cause?

A. Fibrosing mediastinitis
B. Thrombosis
C. Syphilitic thoracic aortic aneurysm
D. Primary malignancy
E. Metastatic malignancy

ANSWER:
Primary malignancy

EXPLANATION:
The correct answer is a primary malignancy. Intrathoracic malignancy is responsible for up to 60-85% of SVC obstruction cases. Most common is non-small cell lung cancer, small cell lung cancer and non-Hodgkin lymphoma. Together these malignancies represent 95% of SVC syndromes caused by malignancy. This can be the presenting feature of a undiagnosed tumour. Thrombosis can occur following pacemaker wire insertion and central line placement. Syphilitic thoracic aortic aneurysm and fibrosing mediastinitis used to be common causes prior to widespread antibiotic use.

Please see Q-13 for Superior Vena Cava Obstruction

Q-69

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

ANSWER:
Sequestration crisis

EXPLANATION:
During a sequestration crisis, the sickle cells cause the spleen to become grossly enlarged causing the abdominal pain as present in this case. This is more common in early childhood as repeated sequestration and infarction of the spleen during childhood gradually results in an auto-splenectomy. A sequestration crisis may result in severe anaemia, marked pallor and cardiovascular collapse due to loss of effective circulating volume.

SICKLE-CELL CRISES
Sickle cell anaemia is characterised by periods of good health with intervening crises

A number of types of crises are recognised:
- thrombotic, 'painful crises'
- sequestration
- acute chest syndrome
- 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

Q-70

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

ANSWER:
Add a 5HT3 antagonist

EXPLANATION:
Please see Q-11 for Chemotherapy Side-Effects: Nausea and Vomiting

Q-71

A 32-year-old female is noted to have a mild microcytic anaemia on routine blood tests. She is otherwise well with no major past medical history. She is originally from Turkey. You suspect that she might have a haemoglobin abnormality. Which of the following blood results is most likely to be elevated above the normal range?

A. **Total haemoglobin**
B. **Haemoglobin A2**
C. **Haemoglobin H**
D. **Haptoglobin**
E. **White cell count**

ANSWER:
Haemoglobin A2

EXPLANATION:
HbA2 is raised in patients with beta thalassaemia major The correct answer is HbA2. This patient is most likely to have beta thalassaemia minor. She has no symptoms of disease other than a mild asymptomatic anaemia and is from an area of higher prevalence for this genetic condition. HbA2 levels are elevated in beta thalassaemia major and minor. It is a variant of haemoglobin A with two delta chains replacing the normal two beta chains. It is found in small amounts in healthy adults at around 1.5 – 3% of total haemoglobin. It is increased in beta thalassaemia because of reduced production of haemoglobin beta chains.

Total haemoglobin would be reduced because of low level haemolysis, leading to a mild anaemia. Haptoglobin would be normal or mildly reduced, as it binds to free haemoglobin released from erythrocytes after haemolysis. Haemoglobin H is found in severe alpha thalassaemia and consists of four beta chains. The white cell count would not be affected in thalassaemia.

BETA-THALASSAEMIA MAJOR
Overview
- absence of beta chains
- chromosome 11

Features
- presents in first year of life with failure to thrive and hepatosplenomegaly
- microcytic anaemia
- HbA2 & HbF raised
- HbA absent

Management
- repeated transfusion → iron overload
- s/c infusion of desferrioxamine

Q-72

A 58-year-old man is reviewed in clinic. Six months ago he had a Whipple procedure for pancreatic cancer and is currently undergoing chemotherapy. Which one of the following blood tests is most useful in monitoring his disease?

A. **CA 15-3 levels**
B. **Faecal elastase**
C. **CA 125 levels**
D. **Amylase levels**
E. **CA 19-9 levels**

ANSWER:
CA 19-9 levels

EXPLANATION:
Please see Q-6 for Tumour Markers

Q-73

A 25-year-old woman with primary antiphospholipid syndrome is reviewed. She has just had a booking ultrasound at 11 weeks gestation 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**

ANSWER:
Aspirin + low-molecular weight heparin

EXPLANATION:
Antiphospholipid syndrome in pregnancy: aspirin + LMWH The ultrasound at 11 weeks gestation would show a fetal heart if the pregnancy was viable. This patient should therefore be taking both aspirin and low-molecular weight heparin.

Please see Q-27 for Antiphospholipid Syndrome: Pregnancy

Q-74

A 68-year-old man presents to the acute medical ward following a referral from his general practitioner. The patient has experienced a 3 month history of weight loss, lethargy and malaise, accompanied by headaches and blurred vision. On examination the patient has mild splenomegaly and some minor cervical lymphadenopathy.

Initial investigations are as follows:

Hb	**110 g/l**
Platelets	**95 * 109/l**
WBC	**14 * 109/l**
Bilirubin	**11 µmol/l**
ALP	**70 u/l**
ALT	**17 u/l**
γGT	**52 u/l**
Albumin	**20 g/l**

Urinary Bence Jones protein **Positive**
Skeletal survey X-rays **No lesions observed**

Given these initial results and the patient's presenting symptoms, what is the most likely diagnosis?

A. **Acute myeloid leukaemia**
B. **Multiple myeloma**
C. **Burkitt's lymphoma**
D. **Waldenstrom's macroglobulinaemia**
E. **Myelodysplasia**

ANSWER:
Waldenstrom's macroglobulinaemia

EXPLANATION:
Waldenstrom's macroglobulinaemia - Organomegaly with no bone lesions

Multiple myeloma - Bone lesions with no organomegaly
Differentiating between multiple myeloma and Waldenstrom's macroglobulinaemia can be difficult due to the considerable overlap seen in their presenting symptoms. However, key differences do exist.

In cases of multiple myeloma, bone pain in the hips, back or shoulders is present in the majority of patients. This kind of pain is absent in Waldenstrom's macroglobulinaemia, who usually will complain of pain secondary to hyperviscosity e.g. persistent headaches

Organomegaly is also more commonly seen in Waldenstrom's macroglobulinaemia.

Bence Jones protein, although classically associated with multiple myeloma, can be present in patients with Waldenstrom's macroglobulinaemia or patients with chronic B cell lymphocytic leukaemia.

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

Q-75

A 45-year-old woman is diagnosed with non-Hodgkin's lymphoma. She is a recovering alcoholic and has been left with significant alcohol-related peripheral neuropathy. Which one of the following chemotherapy agents should be avoided if possible, given her past history?

A. **Doxorubicin**
B. **Vincristine**
C. **Chlorambucil**
D. **Docetaxel**
E. **Cyclophosphamide**

ANSWER:
Vincristine

EXPLANATION:
Vincristine - peripheral neuropathy

Please see Q-1 for Cytotoxic Agents

Q-76

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**

ANSWER:
Onycholysis

EXPLANATION:
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

Q-77

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**

ANSWER:
Mantle cell lymphoma

EXPLANATION:
Please see Q-56 for Haematological Malignancies: Genetics

Q-78

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**

ANSWER:
Histoplasmosis

EXPLANATION:
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)

Q-79

A 72-year-old man with metastatic small cell lung cancer is admitted to the local hospice for symptom control. His main problem at the moment is intractable hiccups. What is the most appropriate management?

A. **Chlorpromazine**
B. **Codeine phosphate**
C. **Diazepam**
D. **Methadone**
E. **Phenytoin**

ANSWER:
Chlorpromazine

EXPLANATION:
Hiccups in palliative care - chlorpromazine or haloperidol
Haloperidol may also be used

PALLIATIVE CARE PRESCRIBING: HICCUPS
Management of hiccups
- chlorpromazine is licensed for the treatment of intractable hiccups
- haloperidol, gabapentin are also used
- dexamethasone is also used, particularly if there are hepatic lesions

Q-80

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**

ANSWER:
Hairy cell leukaemia

EXPLANATION:
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

Q-81

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**

ANSWER:
Resistance to action of protein C

EXPLANATION:

Factor V Leiden mutation results in activated protein C resistance

Please see Q-21 for Factor V Leiden

Q-82

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

A. C1-INH
B. C3
C. Heat shock protein type 1
D. C6
E. Histamine degradation protein (HDP)

ANSWER:
C1-INH

EXPLANATION:

Hereditary angioedema - C1-INH deficiency

Please see Q-2 for Hereditary Angioedema

Q-83

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 * 109/l
WCC 24.0 * 109/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

ANSWER:
Warm autoimmune haemolytic anaemia

EXPLANATION:

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%). It is the most common form of leukaemia seen in adults.

Features

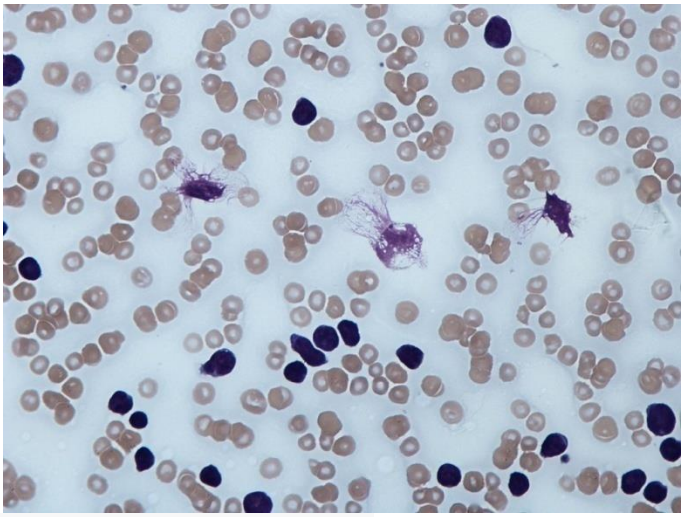
- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications

- anaemia
- 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 (also known as smear cells)
- immunophenotyping



Peripheral blood film showing smudge B cells

Q-84

A 23-year-old woman presents with lethargy. The following blood results are obtained:

Hb 10.4 g/dl
Plt 278 * 109/l
WCC 6.3 * 109/l
MCV 68 fl
Blood film Microcytic hypochromic RBCs, marked anisocytosis and basophilic stippling noted
HbA2 3.9%

What is the most likely diagnosis?

A. Lead poisoning
B. Sickle cell anaemia
C. Beta-thalassaemia trait
D. Hereditary spherocytosis
E. Sideroblastic anaemia

ANSWER:
Beta-thalassaemia trait

EXPLANATION:

Disproportionate microcytic anaemia - think beta-thalassaemia trait
A microcytic anaemia in a female should raise the possibility of either gastrointestinal blood loss or menorrhagia. However, there is no history to suggest this and the microcytosis is disproportionately low for the haemoglobin level. This combined with a raised HbA2 points to a diagnosis of beta-thalassaemia trait.

Basophilic stippling is also seen in lead poisoning but would not explain the raised HbA2 levels.

BETA-THALASSAEMIA TRAIT

The thalassaemias are a group of genetic disorders characterised by a reduced production rate of either alpha or beta chains. Beta-thalassaemia trait is an autosomal recessive condition characterised by a mild hypochromic, microcytic anaemia. It is usually asymptomatic

Features

- mild hypochromic, microcytic anaemia - microcytosis is characteristically disproportionate to the anaemia
- HbA2 raised (> 3.5%)

Q-85

nystagmus. CT head demonstrated a 4cm left cerebellar haematoma. She is discussed with the local neurosurgical unit and urgently transferred for intervention. She is repatriated a week later for further rehabilitation. Routine blood tests are notable for a platelet count of 1,700 * 109/l . Initially, you attribute this to a post-surgical rise. However, on closer examination of her results you realise that on initial presentation her platelet count was 1,300 * 109/l. What gene mutation is likely to be discovered in this lady?

A. JAK2
B. HFE
C. CFTR
D. WASP
E. BCR-ABL

ANSWER:
JAK2

EXPLANATION:

This lady has presented with a stroke at a young age, on a background of raised platelets. This is very suggestive of essential thrombocythaemia which is known to be a rare cause of stroke and is associated with a mutation in the JAK2 gene.

HFE mutation is seen in haemochromatosis, CFTR in cystic fibrosis and WASP in Wiskott-Aldrich. Mutations in BCR-ABL are associated with chronic myeloid leukaemia, and is known as the Philadelphia translocation.

<u>Please see Q-5 for Thrombocytosis</u>

Q-86

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

A. Di George syndrome
B. Chronic granulomatous disease
C. Bruton's congenital agammaglobulinaemia
D. Leukocyte adhesion deficiency
E. Ataxic telangiectasia

ANSWER:
Ataxic telangiectasia

EXPLANATION:

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

PRIMARY IMMUNODEFICIENCY

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

Neutrophil disorders

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

B-cell disorders

Disorder	Underlying defect	Notes
Common variable immunodeficiency	Many varying causes	Hypogammaglobulinemia is seen. May predispose to autoimmune disorders and lymphona
Bruton's (x-linked) congenital	Defect in Bruton's tyrosine kinase (BTK)	X-linked recessive. Recurrent bacterial

Disorder	Underlying defect	Notes
agammaglobulinaemia	gene that leads to a severe block in B cell development	infections are seen Absence of B-cells with reduced immunoglogulins of all classes
Selective immunoglobulin A deficiency	Maturation defect in B cells	Most common primary antibody deficiency. Recurrent sinus and respiratory infections Associated with coeliac disease and may cause false negative coeliac antibody screen Severe reactions to blood transfusions may occur (anti-IgA antibodies → analphylaxis)

T-cell disorders

Disorder	Underlying defect	Notes
DiGeorge syndrome	22q11.2 deletion, failure to develop 3rd and 4th pharyngeal pouches	Common features include congenital heart disease (e.g. tetralogy of Fallot), learning difficulties, hypocalcaemia, recurrent viral/fungal diseases, cleft palate

Combined B- and T-cell disorders

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

Q-87

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

ANSWER:
Subcutaneous low molecular weight heparin

EXPLANATION:
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)

Q-88

A 17-year-old man is reviewed in the haemato-oncology multi-disciplinary meeting with a diagnosis of Acute lymphoblastic leukaemia, (ALL). The results of bone marrow testing, immunophenotyping, and chromosomal analysis are reviewed.

Which of the following features is associated with a poor prognosis?

A. Hypodiploidy
B. Translocation t(12:21)
C. Precursor B ALL
D. Translocation t(1:19)
E. Trisomy 4

ANSWER:
Hypodiploidy

EXPLANATION:

Hypodiploidy is seen as an unfavourable feature in ALL, with the opposite, hyper diploidy associated with a good prognostic outcome.

Trisomy 4, 10 and 17 is associated with a good prognostic outcome in ALL.

The t(12;21) translocation associated with a fusion protein formerly known as TEL-AML1 is associated with a good prognostic outcome in ALL, The t(1:19) translocation is associated with low levels of resistance to chemotherapy intervention in ALL, and thus a good prognostic outcome. The t(9:22) or Philadelphia translocation, is associated with a poor prognosis.

Precursor B-ALL is more responsive to chemotherapy than that involving more mature B lymphocytes.

ACUTE LYMPHOBLASTIC LEUKAEMIA: PROGNOSTIC FEATURES

Acute lymphoblastic leukaemia is malignancy of lymphoid progenitor cells affecting B or T cell lineage resulting in arresting of lymphoid cell maturation and proliferation of immature blast (lymphoblast) cells that leads to bone marrow and tissue infiltration.

Basics

- most common childhood cancer
- peak age = 2-5yrs
- 80% of childhood leukaemia

Good prognostic factors

- French-American-British (FAB) L1 type
- common ALL
- pre-B phenotype
- low initial WBC
- del(9p)

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 * 109/l)
- non-Caucasian

Q-89

A 54-year-old man is diagnosed as having acute myeloid leukaemia. What is the single most important test in determining his prognosis?

A. Gene-expression profiling
B. White cell count at diagnosis
C. Immunophenotyping
D. Lactate dehydrogenase
E. Cytogenetics

ANSWER:

Cytogenetics

EXPLANATION:

All of the above may be important but chromosomal abnormalities detected by cytogenetics are the single most important prognostic factor.

Please see Q-24 for Acute Myeloid Leukaemia

Q-90

A 71-year-old woman with metastatic breast cancer comes to surgery with her husband. She is known to have bone metastases in her pelvis and ribs but her 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

ANSWER:

Increase MST + refer for radiotherapy

EXPLANATION:

Metastatic bone pain may respond to analgesia, bisphosphonates or radiotherapy
Dexamethasone should be considered if the metastatic spinal cord compression, but this is not a feature given the location of the lesions.

Please see Q-28 for Palliative Care Prescribing: Pain

Q-91

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

ANSWER:

Haemochromatosis

EXPLANATION:

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

Q-92

A 48-year-old who was initially investigated for having an abdominal mass is diagnosed as having Burkitt's lymphoma. He is due to start chemotherapy today. Which one of the following should be given to prior to his chemotherapy to reduce the risk of tumour lysis syndrome?

A. Rasburicase
B. Allopurinol
C. Sodium bicarbonate
D. Albumin
E. Calcium gluconate

ANSWER:
Rasburicase

EXPLANATION:
Please see Q-49 for Burkitt's Lymphoma

Q-93

A 69-year-old man with metastatic prostate cancer presents with worsening pain. He currently takes oral modified-release morphine sulphate 60mg bd but it is decided to convert this to subcutaneous administration as he is frequently vomiting. What is the most appropriate dose of morphine to give over a 24 hour period using a continuous subcutaneous infusion?

A. 20mg
B. 30mg
C. 40mg
D. 60mg
E. 120mg

ANSWER:
60 mg

EXPLANATION:
The BNF recommend half the oral dose of morphine in this situation:

The equivalent parenteral dose of morphine (subcutaneous, intramuscular, or intravenous) is about half of the oral dose. If the patient becomes unable to swallow, generally morphine is administered as a continuous subcutaneous infusion

This patient is on 60mg bd = 120mg. Divided by 2 = 60mg of subcutaneous morphine.

Please see Q-28 for Palliative Care Prescribing: Pain

Q-94

A 35-year-old woman who is 16 weeks pregnant has attended the acute medical unit after her first seizure. Her pregnancy has been uncomplicated thus far. Her temperature is 39.4ºC, pulse rate 86, blood pressure 125/86 mmHg. Bloods are as follows:

Hb	**69 g/l**
Platelets	**43 * 109/l**
WBC	**7.4 * 109/l**
Na+	**137 mmol/l**
K+	**4.9 mmol/l**
Urea	**18 mmol/l**
Creatinine	**278 µmol/l**

Urine dip was negative for protein and ketones. The laboratory phone you to inform you schistocytes have been seen on the blood film.

Which of these best describes the pathogenesis of this condition?

A. Dysregulation of coagulation and fibrinolysis, resulting in widespread clotting
B. An acquired inhibition of ADAMTS13, preventing the cleavage of von Willebrand Factor multimers
C. Bacterial toxin initiation of apoptosis and thrombogenesis
D. Abnormal placental perfusion and vascularisation
E. Parasitic infiltration of red blood cells

ANSWER:
An acquired inhibition of ADAMTS13, preventing the cleavage of von Willebrand Factor multimers

EXPLANATION:

Acquired inhibition of the protein ADAMTS13 which cleaves vWF multimers is the most common cause of TTP
This woman has presented with the classical pentad of thrombotic thrombocytopenic purpura - fever, neurological dysfunction, evidence of haemolysis (blood film), renal injury and thrombocytopenia.

Acquired inability to cleave vWF multimers is the most common cause of TTP. This can occasionally be prompted by pregnancy. This results in platelet deposition and widespread coagulation. ADAMTS13 is the protein responsible for this cleavage and can be inhibited by numerous causes. A congenital deficiency in this protein is a rare cause (Upshaw-Schulman Syndrome).

1 - Describes disseminated intravascular coagulation. This has a similar haemolytic picture, but fever, neurological dysfunction and AKI are less common.

3 - Describes haemolytic-uraemic syndrome which is classically associated with E coli O:157; however no prodromal history of diarrhoea is mentioned. The blood results would however be rather similar.

4 - Describes pre-eclampsia. This can cause both seizures (eclampsia) and a microangiopathic haemolytic anaemia. However, it would be uncommon to occur so early in pregnancy. a negative urine dip also suggests this is not the diagnosis.

5 - This is malaria. Whilst it can also cause haemolysis, it is uncommon for it to do so with this history. For malaria to be severe enough to cause seizures, one would expect the blood film to show some parasites and not just schistocytes.

Please see Q-41 for Thrombotic Thrombocytopenic Purpura

Q-95

A 67-year-old with chronic kidney disease stage 4 and metastatic prostate cancer presents as his pain is not controlled with co-codamol. Which one of the following opioids is it most appropriate to use given his impaired renal function?

A. Buprenorphine
B. Morphine
C. Hydromorphone
D. Diamorphine
E. Tramadol

ANSWER:
Buprenorphine

EXPLANATION:

Alfentanil, buprenorphine and fentanyl are the preferred opioids in patients with chronic kidney disease.
Please see Q-28 for Palliative Care Prescribing: Pain

Q-96

Which one of the following may be associated with an increased risk of venous thromboembolism?

A. Fluoxetine
B. Selegiline
C. Diazepam
D. Amitriptyline
E. Olanzapine

ANSWER:
Olanzapine

EXPLANATION:

VENOUS THROMBOEMBOLISM: RISK FACTORS
Common predisposing factors include malignancy, pregnancy and the period following an operation. The comprehensive list below is partly based on the 2010 SIGN venous thromboembolism (VTE) guidelines:

General
- increased risk with advancing age
- obesity
- family history of VTE
- pregnancy (especially puerperium)
- immobility
- hospitalisation
- anaesthesia
- central venous catheter: femoral >> subclavian

Underlying conditions
- malignancy
- thrombophilia: e.g. Activated protein C resistance, protein C and S deficiency
- heart failure
- antiphospholipid syndrome
- Behcet's
- polycythaemia
- nephrotic syndrome
- sickle cell disease
- paroxysmal nocturnal haemoglobinuria
- hyperviscosity syndrome
- homocystinuria

Medication
- combined oral contraceptive pill: 3rd generation more than 2nd generation
- hormone replacement therapy: the risk of VTE is higher in women taking oestrogen + progestogen preparations compared to those taking oestrogen only preparations
- raloxifene and tamoxifen
- antipsychotics (especially olanzapine) have recently been shown to be a risk factor

It should be remembered however that around 40% of patients diagnosed with a PE have no major risk factors.

Q-97

A 30-year-old male with sickle cell disease presents to the Emergency Department (ED) with fever, tachypnoea and rib pain. On examination, they have a low grade fever of 37.9ºC, oxygen saturations of 95% on air, and on auscultation there are bilateral vesicular breath sounds. A chest X-ray shows opacification in the right middle zone. Which of these statements most accurately describes the management of this patient?

A. Bronchodilators are indicated
B. The patient should undergo a simple transfusion to a target Hb > 8g/L
C. The patient should undergo an exchange transfusion to a target Hb > 8g/L
D. Incentive spirometry is indicated
E. Empirical antibiotic therapy is not indicated

ANSWER:
The patient should undergo an exchange transfusion to a target Hb > 8g/L

EXPLANATION:
This question requires the candidate first of all to diagnose this presentation as an acute chest syndrome. The British Committee for Standards in Haematology (BCSH) defines this as 'an acute illness characterized by fever and/or respiratory symptoms, accompanied by a new pulmonary infiltrate on chest X-ray'.

The fundamentals of initial management are as follows:

- ***Oxygen therapy to maintain saturations > 95%***
- ***Intravenous fluids to ensure euvolaemia***
- ***Adequate pain relief***
- ***Incentive spirometry in all patients presenting with rib or chest pain***
- ***Antibiotics with cover for atypical organisms***
- ***Early consultation with the critical care team and haematology***

A senior haematologist will make a decision as to whether a simple or exchange transfusion is necessary, and guidelines suggest an Hb target of 100-110g/L in either instance. On presentation, patients with acute chest syndrome should be fully cross matched and a history of red cell antibodies sought.

Bronchodilators are indicated if asthma co-exists with acute chest syndrome, or if there is evidence of acute bronchospasm on auscultation.

Please see Q-69 for Sickle-Cell Crises

Q-98

A 34-year-old intravenous drug user is admitted with a purpuric rash affecting her legs. Blood tests reveal the following:

Hb	**11.4g/dl**
Platelets	**489 * 109/l**
WCC	**12.3 * 109/l**
HCV PCR	**positive**
HBsAg	**negative**
Rheumatoid factor	**positive**
C3/C4	**reduced**

What is the most likely diagnosis?

A. Polyarteritis nodosa
B. Henoch-Schonlein purpura
C. Wegener's granulomatosis
D. Cryoglobulinaemia
E. Systemic lupus erythematous

ANSWER:
Cryoglobulinaemia

EXPLANATION:
Hepatitis C infection is associated with type II (mixed) cryoglobulinaemia, suggested by the purpuric rash, positive rheumatoid factor and reduced complement levels

CRYOGLOBULINAEMIA
Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One-third of cases are idiopathic

Three types
- type I (25%): monoclonal
- type II (25%): mixed monoclonal and polyclonal: usually with rheumatoid factor (RF)
- type III (50%): polyclonal: usually with RF

Type I
- monoclonal - IgG or IgM
- associations: multiple myeloma, Waldenstrom macroglobulinaemia

Type II
- mixed monoclonal and polyclonal: usually with RF
- associations: hepatitis C, RA, Sjogren's, lymphoma

Type III
- polyclonal: usually with RF
- associations: rheumatoid arthritis, Sjogren's

Symptoms (if present in high concentrations)
- Raynaud's only seen in type I
- cutaneous: vascular purpura, distal ulceration, ulceration
- arthralgia
- renal involvement (diffuse glomerulonephritis)

Tests
- low complement (esp. C4)
- high ESR

Treatment
- immunosuppression
- plasmapheresis

Q-99

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

ANSWER:
Red cell aplasia

EXPLANATION:
Please see Q-42 for Thymoma

Q-100

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 * 109/l**
PT	**11 secs**
APTT	**76 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

ANSWER:
Haemophilia B

EXPLANATION:
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

Please see Q-44 for Haemophilia

Q-101

An 80-year-old man is reviewed in the haematology clinic. He has been referred due to weight loss, lethargy and a significantly elevated IgM level. Recent bloods show the following:

Hb	**13.8 g/dl**
Platelets	**127 * 109/l**
IgM	**2150 mg/dl (range 50-330 mg/dl)**
ESR	**45 mm/hr**

Given the likely diagnosis, which one of the following complications is he most likely to develop?

A. Renal failure
B. Chronic lymphocytic leukaemia
C. Anaemia
D. Hyperviscosity syndrome
E. Hypercalcemia

ANSWER:
Hyperviscosity syndrome

EXPLANATION:
IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia
This patient has Waldenstrom's macroglobulinaemia. Hyperviscosity syndrome is present in around 10-15% of patients. Other common complications include hepatosplenomegaly.

Please see Q-74 for Waldenstrom's Macroglobulinaemia

Q-102

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

ANSWER:
Hypogammaglobulinaemia

EXPLANATION:
Please see Q-83 for Chronic Lymphocytic Leukaemia

Q-103

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 * 109/l
WBC 7.9 * 109/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

ANSWER:
Von Willebrand's disease

EXPLANATION:
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

Please see Q-18 for Von Willebrand's Disease

Q-104

A 65-year-old male patient presents to the oncology clinic with 6-months history of weight loss and anorexia. A tumour marker profile shows an elevated level of bombesin.

What is the most likely cancer to account for this result?

A. Rectal carcinoma
B. Prostate carcinoma
C. Breast carcinoma
D. Small cell lung carcinoma
E. Lymphoma

ANSWER:
Small cell lung carcinoma

EXPLANATION:
Bombesin is a tumour marker in small cell lung carcinomas Small cell lung carcinomas are the only option which could cause a raised level of bombesin. Bombesin is a tumour marker in small cell lung carcinomas, along with gastric carcinomas and retinoblastomas.

Carcinoembryonic antigen(CEA) is a tumour marker of colorectal cancer.

Prostate-specific antigen(PSA) is a tumour marker of prostate carcinomas.

CA 15-3 is a tumour marker for breast cancer.

There is no specific tumour marker for lymphoma.

Please see Q-6 for Tumour Markers

Q-105

A 50-year-old woman is investigated for weight loss and anaemia. She has no past medical history of note. Clinical examination reveals splenomegaly associated with pale conjunctivae. A full blood count is reported as follows:

Hb 10.9 g/dl
Platelets 702 * 109/l
WCC 56.6 * 109/l
Film Leucocytosis noted. All stages of granulocyte maturation seen

Given the likely diagnosis, what is the most appropriate treatment?

A. Chlorambucil
B. Stem cell transplantation
C. Rituximab
D. Repeat full blood count in 3 months
E. Imatinib

ANSWER:
Imatinib

EXPLANATION:
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 (60-70 years)
- anaemia: lethargy
- weight loss and sweating are common
- splenomegaly may be marked → abdo discomfort
- spectrum of myeloid cells seen in peripheral blood
- decreased leukocyte alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management
- imatinib is now considered first-line treatment
- hydroxyurea
- interferon-alpha
- allogenic bone marrow transplant

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

Q-106

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

ANSWER:
Tyrosine kinase inhibitor

EXPLANATION:
Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor
Imatinib is an inhibitor of the tyrosine kinase associated with the BCR-ABL defect

Please see Q-105 for Chronic Myeloid Leukaemia

Q-107

A 69-year-old male patient of yours is found to have an elevated serum paraprotein level of 35g/L. Bone marrow aspirate reveals 32% monoclonal plasma cell infiltrate. He has no evidence of anaemia, renal impairment, hypercalcaemia or lytic lesions. What is the next step in management?

A. Observe and monitor
B. Arrange for autologous stem cell transplantation
C. Commence thalidomide
D. Commence dexamethasone
E. Commence combined therapy with prednisolone and thalidomide / bortezomib

ANSWER:
Observe and monitor

EXPLANATION:
This question is asking about the diagnostic criteria for multiple myeloma and it's subsequent management. Here, because the patient is asymptomatic but has the criteria for multiple myeloma, the underlying diagnosis of this stem is smoldering multiple myeloma. The treatment of smoldering multiple myeloma is typically to watch and wait.

This decision to delay therapy in patients with smoldering multiple myeloma is supported by a 2003 Cochrane meta-analysis that compared chemotherapy at diagnosis versus deferral of chemotherapy until progression. Early treatment delayed progression of the disease but did not have significant effects on mortality or response rate, and early treatment may have increased the risk of acute leukaemia.

Please see Q-7 for Myeloma: Features

Q-108

Chronic lymphocytic leukaemia is mostly due to a:

A. Polyclonal proliferation of B-cell lymphocytes
B. Monoclonal proliferation of B-cell lymphocytes
C. Monoclonal proliferation of large granular lymphocytes
D. Monoclonal proliferation of T-cell lymphocytes
E. Polyclonal proliferation of T-cell lymphocytes

ANSWER:
Monoclonal proliferation of B-cell lymphocytes

EXPLANATION:
CLL is caused by a monoclonal proliferation of B-cell lymphocytes

Please see Q-83 for Chronic Lymphocytic Leukaemia

Q-109

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

A. Prevents renal excretion of von Willebrand's factor
B. Induces release of factor VIII from endothelial cells
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

ANSWER:
Induces release of von Willebrand's factor from endothelial cells

EXPLANATION:
Desmopressiin - induces release of von Willebrand's factor from endothelial cells

Please see Q-18 for Von Willebrand's Disease

Q-110

Which one of the following is least associated with lead poisoning?

A. Peripheral neuropathy
B. Acute glomerulonephritis
C. Blue lines on gum margin
D. Abdominal pain
E. Microcytic anaemia

ANSWER:
Acute glomerulonephritis

EXPLANATION:
Please see Q-61 for Lead Poisoning

Q-111

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

Hb	**14.1 g/dl**
Plt	**82 * 109/l**
WBC	**5.9 * 109/l**
Neuts	**4.4 * 109/l**

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

A. **Bruton's congenital agammaglobulinaemia**
B. **Wiskott-Aldrich syndrome**
C. **Ataxic telangiectasia**
D. **Chediak-Higashi syndrome**
E. **DiGeorge syndrome**

ANSWER:
Wiskott-Aldrich syndrome

EXPLANATION:
Wiskott-Aldrich syndrome

- ***recurrent bacterial infections (e.g. Chest)***
- ***eczema***
- ***thrombocytopaenia***

Please see Q-14 for Wiskott-Aldrich Syndrome

Q-112

Which one of the following is least likely to precipitate haemolysis in a patient with G6PD deficiency?

A. **Broad beans**
B. **Sepsis**
C. **Ciprofloxacin**
D. **Primaquine**
E. **Penicillin**

ANSWER:
Penicillin

EXPLANATION:
Please see Q-60 for G6PD Deficiency

Q-113

A 72-year-old man with metastatic colon cancer is reviewed. He currently takes co-codamol 30/500 2 tablets qds for pain relief. Unfortunately this is not controlling his pain. What is the most appropriate change to his medication?

A. **Switch to MST 15mg bd + paracetamol 1g qds**
B. **Switch to MST 35mg bd + paracetamol 1g qds**
C. **Add tramadol 50-100mg 1-2 qds**
D. **Switch to MST 25mg bd**
E. **Switch to MST 15mg bd**

ANSWER:
Switch to MST 15mg bd + paracetamol 1g qds

EXPLANATION:
His total codeine dose is 30 * 2 * 4 = 240 mg/day. Converting this to oral morphine = 24 mg/day. It is therefore reasonable to start MST 15mg bd as his pain is not currently controlled. Paracetamol should be continued as it has been shown to give benefits even to patients on large doses of morphine

Please see Q-28 for Palliative Care Prescribing: Pain

Q-114

A full blood count for a 38-year-old man is reported as follows:

Hb	**12.9 g/dl**
Platelets	**225 * 109/l**
WBC	**6.2 * 109/l**
Film	**Numerous Howell-Jolly bodies and pencil cells seen**

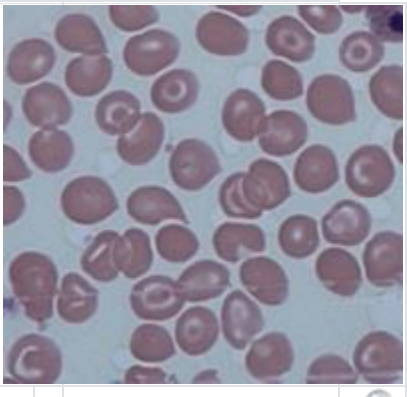
Which one of the following conditions is most likely to produce these results?

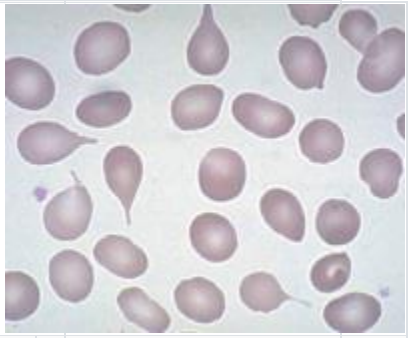
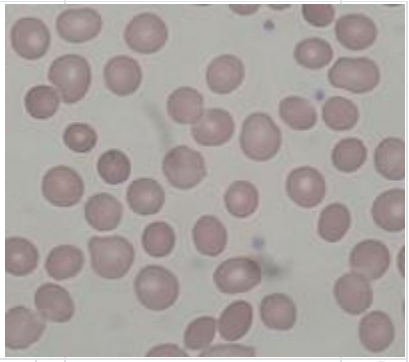
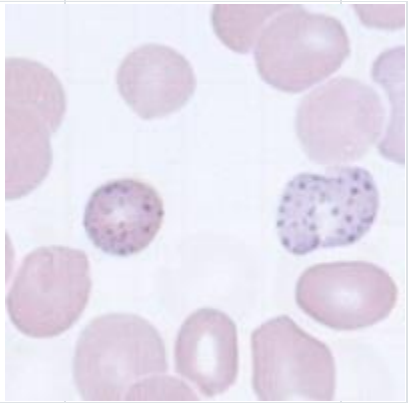
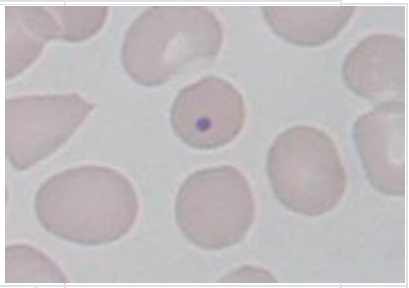
A. **Coeliac disease**
B. **HIV infection**
C. **Sickle-cell trait**
D. **Autoimmune hemolytic anaemia**
E. **Liver disease**

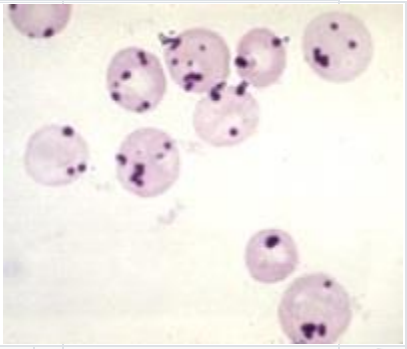
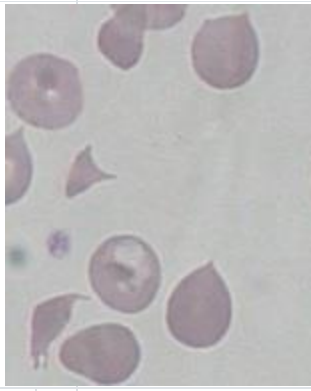
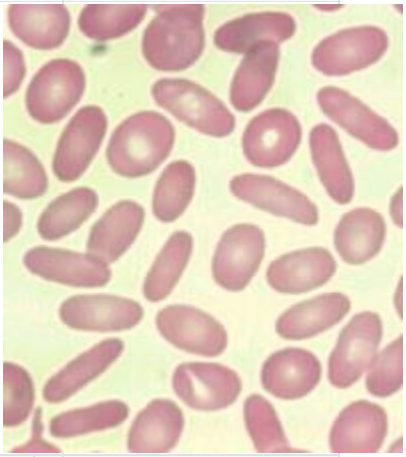
ANSWER:
Coeliac disease

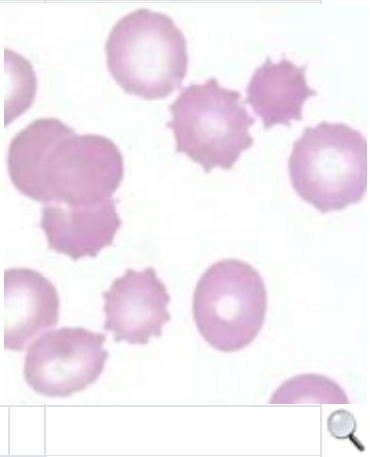
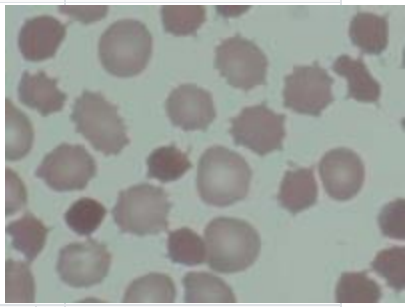
EXPLANATION:
Howell-Jolly bodies are seen in hyposplenism and pencil cells are a feature of iron-deficiency. Both of these are seen in coeliac disease.

BLOOD FILMS: PATHOLOGICAL CELL FORMS
Pathological red cell forms

Abnormality	Associated condition(s)	Appearance
Target cells	Sickle-cell/thala mia Iron-defi anaemia Hypospl Liver dis	

Abnormality	Associated condition(s)	Appearance
'Tear-drop' poikilocytes	Myelofib	
Spherocytes	Heredita spherocy Autoimn hemolyt anaemia	
Basophilic stippling	Lead poisonin Thalassa Siderobl anaemia Myelody	
Howell-Jolly bodies	Hypospl	

Abnormality	Associated condition(s)	Appearance
Heinz bodies	G6PD deficienc Alpha-thalassa	
Schistocytes ('helmet cells')	Intravascular haemolysis Mechanical heart valve Disseminated intravascular coagulation	
'Pencil' poikilocytes	Iron defi anaemia	

Abnormality	Associated condition(s)	Appearance
Burr cells (echinocytes)	Uraemia Pyruvate kinase deficiency	
Acanthocytes	Abetalipinemia	

Other blood film abnormalities:

- hypersegmented neutrophils: megaloblastic anaemia

Q-115

A 30-year-old female presents to the Emergency Department with epistaxis, which has now terminated. Her boyfriend reports she has a recent history of mucosal bleeding and has at times been very disorientated. On examination, she has a low-grade fever and appears confused and jaundiced. There is bruising over her legs and arms. A urine pregnancy test is negative. You receive the following blood results from the laboratory:

Hb	**85 g/l**
Platelets	**8 * 109/l**
WBC	**4.5 * 109/l**
MCV	**92 fl**
Na+	**138 mmol/l**
K+	**4.9 mmol/l**
Urea	**10.2 mmol/l**
Creatinine	**182 µmol/l**

Clotting studies are normal. Given the most likely diagnosis, what is the most appropriate management of this patient?

A. Platelet transfusion
B. Intravenous immunoglobulin
C. Plasma exchange
D. Intravenous methylprednisolone
E. Intravenous argatroban

ANSWER:
Plasma exchange

EXPLANATION:
This question requires you to identify correctly the haematological emergency and be aware of the correct management.

Thrombotic thrombocytopenic purpura (TTP) is classically characterised as a pentad of: thrombocytopenia, microvascular haemolysis, fluctuating neurological signs, renal impairment and fever.

Also in the differential diagnosis for severe thrombocytopenia is immune thrombocytopenic purpura (ITP). ITP is more common than TTP however would not present with the range of symptoms seen in this scenario.

TTP has an untreated mortality of up to 90% and therefore rapid plasma exchange (PEX) may be a life saving intervention. Platelet transfusion in TTP is only indicated if there is an on-going life-threatening bleed. Intravenous methylprednisolone is indicated after treatment with PEX has been completed.

There is no current role for intravenous immunoglobulin in the routine management of TTP, however there have been reports of its successful use in PEX- and steroid-refractory cases.

Intravenous argatroban is indicated in heparin-induced thrombocytopenia (HIT), however there is no history of recent heparin administration or hospitalisation in this patient, nor are the clinical signs consistent with HIT.

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 protease 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

Q-116

A 64-year-old female is brought to the Emergency Department by her family, who are concerned about her increasing confusion over the past 2 days. On examination she is found to be pyrexial at 38ºC. Blood tests reveal:

Hb	**9.6 g/dl**
Platelets	**65 * 109/l**
WCC	**11.1 * 109/l**
Urea	**23.1 mmol/l**
Creatinine	**366 µmol/l**

What is the most likely diagnosis?

A. Wegener's granulomatosis
B. Thrombotic thrombocytopenic purpura
C. Haemolytic uraemic syndrome
D. Idiopathic thrombocytopenic purpura
E. Rapidly progressive glomerulonephritis

ANSWER:
Thrombotic thrombocytopenic purpura

EXPLANATION:
HUS or TTP? Neuro signs point towards TTP
The combination of neurological features, renal failure, pyrexia and thrombocytopaenia point towards a diagnosis of thrombotic thrombocytopenic purpura

Please see Q-41 for Thrombotic Thrombocytopenic Purpura

Q-117

A 32-year-old demolitions worker comes to the haematology clinic for review. He has suffered from abdominal pain and lethargy for the past few months, and his GP has noted a microcytic anaemia. Over the past few weeks he has begun tripping over because of weakness of both lower legs. His blood pressure is 123/82 mmHg, pulse is 82 beats per minute and regular. The abdomen is soft and non-tender, the body mass index is 23 kg/m² and there is bilateral weakness of ankle dorsiflexion.

Investigations show the following:

Hb	**98 g/l**
MCV	**77 fL**
Blood film	**Basophilic stippling**
Platelets	**203 * 109/l**
WBC	**7.1 * 109/l**

What is the most likely diagnosis?

A. Iron deficiency anaemia
B. Lead poisoning
C. Porphyria cutanea tarda
D. Thalassaemia trait
E. Wilson's disease

ANSWER:
Lead poisoning

EXPLANATION:
The picture here with microcytic anaemia, basophilic stippling on the blood film, and peripheral motor neuropathy is consistent with lead poisoning. It's likely this patient was exposed during their work as a demolitions operative. Chelation therapy is the intervention of choice, with EDTA, DMSA and penicillamine all potential options.

The other conditions aren't associated with basophilic stippling. In addition, porphyria is associated with a photosensitive skin rash, and thalassaemia trait isn't associated with clinical symptoms. Wilson's tends to present earlier with either movement disorder or psychiatric symptoms.

Please see Q-61 for Lead Poisoning

Q-118

Which one of the following is not a recognised feature of methaemoglobinaemia?

A. Dyspnoea
B. 'Chocolate' cyanosis
C. Anxiety
D. Reduced pO2 but normal oxygen saturation on pulse oximetry
E. Acidosis

ANSWER:
Reduced pO2 but normal oxygen saturation on pulse oximetry

EXPLANATION:
Normal pO2 but decreased oxygen saturation is characteristic of methaemoglobinaemia

METHAEMOGLOBINAEMIA
Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe2+ to Fe3+. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe3+ cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

Congenital causes
- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

Acquired causes
- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

Features
- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO2 but decreased oxygen saturation

Management

- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

Q-119

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

ANSWER:
Tumour lysis syndrome

EXPLANATION:
Burkitt's lymphoma is a common cause of tumour lysis syndrome
Tumour lysis syndrome occurs as a result of cell breakdown following chemotherapy. This releases a large quantity of intracellular components such as potassium, phosphate and uric acid.

Please see Q-49 for Burkitt's Lymphoma

Q-120

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

ANSWER:
von Willebrand's disease

EXPLANATION:
Please see Q-18 for Von Willebrand's Disease

Q-121

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 * 109/l**
WBC	**21.2 * 109/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

ANSWER:
No treatment + go ahead with operation

EXPLANATION:
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

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients

Q-122

A 73-year-old woman is reviewed in the pre-op clinic prior to an elective hip replacement. 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 * 109/l**
WBC	**19.0 * 109/l**
Neuts	**4.2 * 109/l**
Lymphs	**14.1 * 109/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

ANSWER:
Chronic lymphocytic leukaemia

EXPLANATION:
Such a lymphocytosis in 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.

Please see Q-83 for Chronic Lymphocytic Leukaemia

Q-123

A 45-year-old woman who is being treated for Hodgkin's lymphoma with ABVD chemotherapy is reviewed on the haematology ward.

Six days ago she was admitted with a fever of 38.9ºC. After admission she was immediately started on piperacillin with tazobactam (Tazocin). Her blood count on arrival was as follows:

Hb	**10.1 g/dl**
Platelets	**311 * 109/l**
WBC	**0.8 * 109/l**
Neutrophils	**0.35 * 109/l**
Lymphocytes	**0.35 * 109/l**

After 48 hours she remained febrile and tachycardic, Tazocin was stopped and meropenem + vancomycin prescribed.

Today, six days after being admitted she remains unwell with a temperature of 38.4ºC. Blood pressure is 102/66 mmHg and the heart rate is 96/min. Respiratory examination remains unremarkable and blood/urine cultures have failed to show any cause for the fever. What is the most appropriate next step?

A. Add amphotericin B
B. Add G-CSF
C. Add gentamicin
D. Add aciclovir
E. Refer for a stem cell transplant

ANSWER:
Add Amphotericin B

EXPLANATION:
This patient meets the diagnostic criteria for neutropenic sepsis. After failing to respond to standard empirical treatment the questions is what to do next.

There are no guidelines that can fit every patient & scenario. The decision to use antifungals is now often taken after risk stratifying patients and ordering investigations such as HRCT, Aspergillus PCR etc to determine the likelihood of systemic fungal infection. For the purposes of the exam however the answer is often to give antifungals empirically.

G-CSF is not used routinely in neutropenic sepsis.

Please see Q-3 for Neutropenic Sepsis

Q-124

A patient develops methaemoglobinaemia after being prescribed isosorbide mononitrate. Which substance is most likely to be depleted?

A. Pyruvate kinase
B. Hyponitrite reductase
C. Pyridoxine 5-dehydrogenase
D. Glucose-6-phosphate dehydrogenase
E. NADH

ANSWER:
NADH

EXPLANATION:
Please see Q-118 for Methaemoglobulinaemia

Q-125

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

ANSWER:
Methotrexate

EXPLANATION:
Methotrexate - inhibits dihydrofolate reductase and thymidylate synthesis

Please see Q-1 for Cytotoxic Agents

Q-126

A 72-year-old man with longstanding Waldenström's macroglobulinemia presents to rheumatology clinic with joint pains and generalised weakness.

Which of the following would be most indicative of Type I cryoglobulinaemia?

A. **Livedo reticularis**
B. **Raynaud's phenomenon**
C. **Arthralgia**
D. **Membranoproliferative glomerulonephritis**
E. **Low C4 levels**

ANSWER:
Raynaud's phenomenon

EXPLANATION:
Raynaud's - Type I cryoglobulinaemia
Cryoglobulinaemia can be caused by paraprotein bands such as those in Waldenström's macroglobulinemia and multiple myeloma. Meltzer's triad of arthralgia, weakness and palpable purpura are common to all types of cryoglobulinaemia - as are membranoproliferative glomerulonephritis and low C4 levels.

Raynaud's occurs most commonly in type 1 cryoglobulinaemia and its presence can be helpful in ascertaining the underlying cause.

Please see Q-98 for Cryoglobulinaemia

Q-127

A 54-year-old gentleman is diagnosed with diffuse large B-cell lymphoma and is started on chemotherapy. Two days following his first treatment, he presents to the emergency department with nausea, vomiting, and myalgia. On examination, he appears clinically dehydrated. A diagnosis of tumour lysis syndrome (TLS) is suspected. Which of the following would be in keeping with this diagnosis?

A. **Low phosphate**
B. **Low uric acid**
C. **Low lactate dehydrogenase (LDH)**
D. **Low creatinine**
E. **Low corrected calcium**

ANSWER:
Low corrected calcium

EXPLANATION:
Of the choices, low corrected calcium is the only biochemistry result which would be in keeping with TLS. All of the other biochemistry markers are elevated in TLS. TLS can occur when a large amount of cancer cells are destroyed, causing a release of their intra-cellular content into the bloodstream. This occur due to chemotherapy, but can also occur without chemotherapy. Potassium and phosphate are releasfed from the cells, causing both to be high. As phosphate precipitates calcium, the serum concentration of calcium becomes low.

TUMOUR LYSIS SYNDROME
Tumour lysis syndrome (TLS) is a potentially deadly condition related to the treatment of high grade lymphomas and leukaemias. It can occur in the absence of chemotherapy but is usually triggered by the introduction of combination chemotherapy. On occasion it can occur with steroid treatment alone. Awareness of the condition is critical as prophylactic medication can be given to prevent the potentially deadly effects of tumour cell lysis.

Patients at high risk of TLS should be given IV allopurinol or IV rasburicase immediately prior to and during the first days of chemotherapy. Rasburicase is a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin. Allantoin is much more water soluble than uric acid and is therefore more easily excreted by the kidneys. Patients in lower risk groups should be given oral allopurinol during chemotherapy cycles in an attempt to avoid the condition.

TLS occurs from the breakdown of the tumour cells and the subsequent release of chemicals from the cell. It leads to a high potassium and high phosphate level in the presence of a low calcium. It should be suspected in any patient presenting with an acute kidney injury in the presence of a high phosphate and high uric acid level.

From 2004 TLS has been graded using the Cairo-Bishop scoring system -
Laboratory tumor lysis syndrome: abnormality in two or more of the following, occurring within three days before or seven days after chemotherapy.

- uric acid > 475umol/l or 25% increase
- potassium > 6 mmol/l or 25% increase
- phosphate > 1.125mmol/l or 25% increase
- calcium < 1.75mmol/l or 25% decrease

Clinical tumor lysis syndrome: laboratory tumor lysis syndrome plus one or more of the following:

- increased serum creatinine (1.5 times upper limit of normal)
- cardiac arrhythmia or sudden death
- seizure

Q-128

You are the haematology registrar. A 42-year-old lady has been referred by her GP with a persistently elevated platelet count. It was incidentally found on a blood test originally six months ago at 632 x10^9/L. The latest reading was 848 x10^9/L which was the highest it has been yet. She is otherwise well but does suffer with regular headaches which she takes simple analgesia for. You suspect a diagnosis of essential thrombocytosis and arrange a JAK-2 test which is negative (including an exon 12 test). Which is the most likely other gene mutation responsible for this condition?

A. **BCR-ABL**
B. **MPL**
C. **CMYC**
D. **Platelet factor 4**
E. **CALR**

ANSWER:
CALR

EXPLANATION:
CALR (calreticulin) is a more commonly found gene mutation in ET in around 20% of JAK-2 negative patients.

MPL (myeloproliferative leukaemia protein) is less common at less then 10%.

BCR-ABL is associated with the myeloproliferative disorder chronic myeloid leukaemia.

CMYC is a proto-oncogene associated with many malignancies including Burkitt's lymphoma.

Platelet factor 4 (PF4 complex) is the antigen found in heparin-induced thrombocytopenia.

Please see Q-5 for Thrombocytosis

Q-129

Which of the following cytotoxic agents is most associated with ototoxicity?

A. Vincristine
B. Bleomycin
C. Cisplatin
D. Doxorubicin
E. Cyclophosphamide

ANSWER:
Cisplatin

EXPLANATION:
Cisplatin may cause ototoxicity

Please see Q-1 for Cytotoxic Agents

Q-130

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

ANSWER:
Flow cytometry for CD59 and CD55

EXPLANATION:
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

Q-131

A 62-year-old woman who is known to have metastatic breast cancer presents with increasing shortness of breath. She is currently receiving a chemotherapy regime. On examination she has a third heart sound and the apex beat is displaced to the 6th intercostal space, anterior axillary line. Which one of the following chemotherapeutic agents is most likely to be responsible?

A. Paclitaxel
B. Docetaxel
C. Bleomycin
D. Dactinomycin
E. Doxorubicin

ANSWER:
Doxorubicin

EXPLANATION:
Doxorubicin may cause cardiomyopathy

<u>Please see Q-1 for Cytotoxic Agents</u>

Q-132

A 48-year-old female presents to her family physician complaining of post-coital pain. She initially thought that this was related to her age but recently she has been feeling a constant dull pain in her pelvis. She also reports having a foul-smelling discharge from her vagina. Her past medical and surgical history reveal nothing significant along but she says that she has had several sexual partners in her early teenage years and twenties. She currently smokes about 10 cigarettes a day for the past 10 years and does not consume alcohol. On examination, the doctor finds an irregular mass on her cervix. Which of the following best describes the mechanism for the strongest risk factor for this patient's condition?

A. Human papilloma virus 16 and 18 produces oncoproteins which causes inhibition of the tumor suppressor genes causing cervical carcinoma
B. Cigarette smoking produces dysplasia of the squamocolumnar junction leading to cervical cancer
C. Having multiple sexual partners increase the risk of getting HIV which then expresses viral proteins leading to cervical dysplasia and carcinoma
D. Human papilloma virus 16 and 18 produces oncoproteins which then activate oncogenes causing cervical carcinoma
E. The patients age is the strongest risk factor as the cervical cells lose their repair capacity and then progress on to dysplasia and carcinoma

ANSWER:
Human papilloma virus 16 and 18 produces oncoproteins which causes inhibition of the tumor suppressor genes causing cervical carcinoma

EXPLANATION:
This patient has presented with the signs and symptoms typical of a cervical carcinoma. The onset of a constant dull pelvic pain indicates a possible invasion of pelvic structures and nerves. The strongest risk factor in this patient is having several sexual partners at a very young age, which then puts her at risk of being infected with the human papilloma virus.

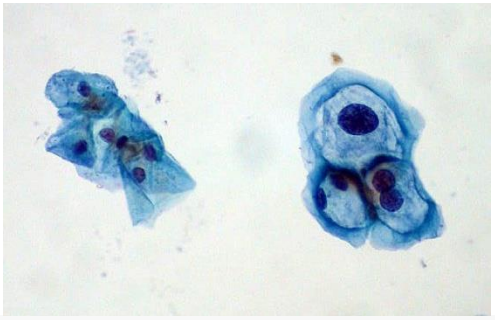
1: Having multiple sexual partners is the strongest risk factor for the development of cervical carcinoma. This is because having multiple sexual partners greatly increases the chance of being infected with the human papilloma virus. The 16 and 18 viral strain then triggers the carcinogenesis by inhibiting the tumor suppressor gene p53 and RB.
2: Although cigarette smoking will have an oncogenic effect, it is not the strongest risk factor here.
3: HIV is a risk factor for cervical carcinoma. However, it is a lesser risk factor than the human papilloma virus which is much more common.
4: Although the human papilloma virus does represent the strong risk factor, it does not cause the activation of oncogenes. Instead, it causes the inhibition of tumor suppressor genes.
5: Age in itself has not been reported to be a risk factor for the development of cervical carcinoma. An older person is more likely to develop cervical carcinoma if that person has for instance been exposed to the human papilloma virus, which then has more time to induce the process of carcinogenesis via the inhibition of tumor suppressor genes.

CERVICAL CANCER: HUMAN PAPILLOMA VIRUS INFECTION

Human papilloma virus (HPV) infection is the most important risk factor for developing cervical cancer. Subtypes 16,18 & 33 are particularly carcinogenic.

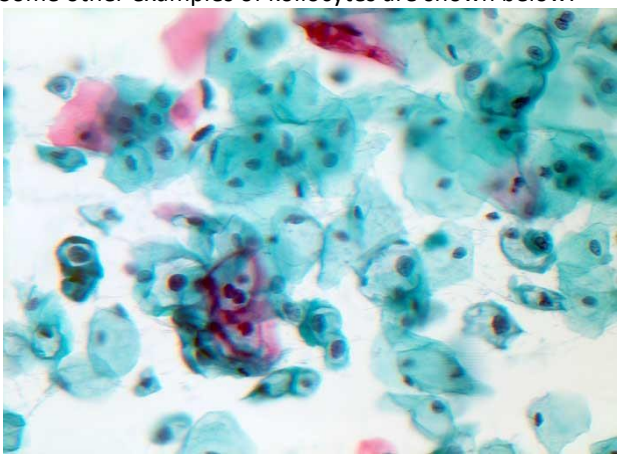
Infected endocervical cells may undergo changes resulting in the development of koilocytes. These have the following characteristics:

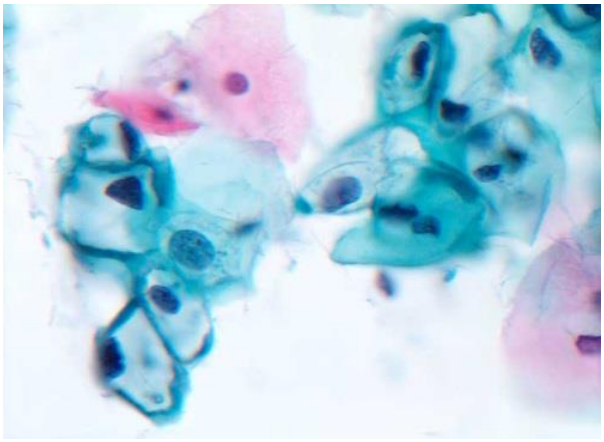
- enlarged nucleus
- irregular nuclear membrane contour
- the nucleus stains darker than normal (hyperchromasia)
- a perinuclear halo may be seen

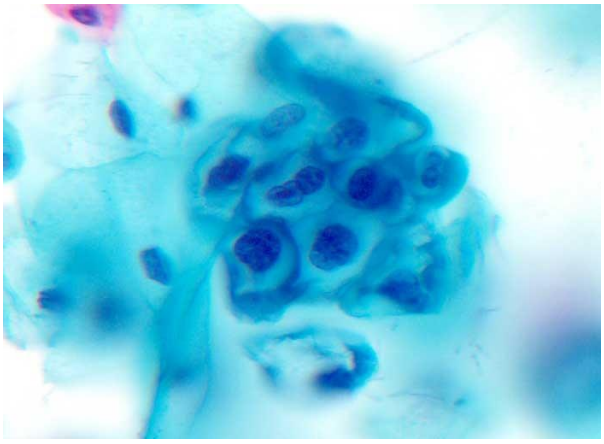


Pap smear with a group of normal cervical cells on the left and HPV-infected cells showing features typical of koilocytes on the right

Some other examples of koilocytes are shown below:







Q-133

A 21-year-old man attends the emergency department after noticing blood in his urine. He has been feeling fatigued and generally unwell for the last two days and has been finding himself getting out of breath easily. His housemates had commented yesterday that he was 'turning yellow', but he had assumed they were teasing him for being unwell and had ignored them.

He is normally fit and well and is not on any regular medications. He has however recently started taking primaquine in preparation for a volunteering trip to Tanzania next week.

On examination, he is clearly jaundiced and tachypnoeic. His urine sample is a dark brown and is positive for blood and bilirubin. He is afebrile and normotensive, though is requiring some supplemental oxygen.

You are awaiting the rest of his test results but have received the following from the lab so far:

Hb	**115 g/l**
MCV	**90 fL**
Haematocrit	**0.3 L/L**
Platelets	**250 * 109/l**
WBC	**10.2 * 109/l**
Reticulocyte count	**2.1%**
Peripheral blood film	**Presence of schistocytes, spherocytes and bite cells noted**

What is the most likely reason for this presentation?

A. Sickle cell crisis
B. Post-infectious haemolytic anaemia
C. G6PD deficiency
D. Hereditary spherocytosis
E. Pyruvate kinase deficiency

ANSWER:
G6PD deficiency

EXPLANATION:
Malaria prophylaxis can trigger haemolytic anaemia in those with G6PD deficiency
This man is presenting with signs and symptoms of a haemolytic anaemia, the most likely cause of which is G6PD deficiency. A number of foods and medications can trigger haemolysis in individuals with G6PD deficiency, an important class of which are quinine-based anti-malarial medications. The temporal link between starting malaria prophylaxis and developing signs of haemolysis makes this the most likely cause.

While a sickle cell crisis can trigger haemolysis, there is nothing to suggest this patient has sickle cell disease, and no sickle cells are present on the blood film.

Post-infectious haemolysis can occur with atypical pneumonias such as Mycoplasma (cold-agglutinin disease) and infections that induce hypersplenism such as mononucleosis. There is nothing to suggest an infectious cause in this scenario, however.

Congenital haemoglobin defects such as spherocytosis can also cause haemolysis. While there are spherocytes on this man's blood film, these are present to different degrees in haemolytic anaemias of any cause and as such are not specific.

Pyruvate kinase deficiency is the next most common inherited metabolic disorder after G6PD deficiency. Haemolysis in these patients tends to be triggered in times of significant physiological stress.

Please see Q-60 for G6PD Deficiency

Q-134

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

A. **Serum IgE levels**
B. **Serum C3 levels**
C. **Serum tryptase levels**
D. **Serum C4 levels**
E. **Serum C1-INH levels**

ANSWER:
Serum C4 levels

EXPLANATION:
Hereditary angioedema - C4 is the best screening test inbetween attacks

Please see Q-2 for Hereditary Angioedema

Q-135

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**

ANSWER:
Tyrosine kinase

EXPLANATION:
Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor

Please see Q-105 for Chronic Myeloid Leukaemia

Q-136

A 75-year-old male patient presents to the urology clinic with a 1-month history of passing frank haematuria. A flexible cystoscopy reveals a mass of the bladder wall and the biopsy reveals transitional cell carcinoma.

Which industry was he likely to have worked in?

A. **Feed production**
B. **Military personnel**
C. **Rubber industry**
D. **Dyestuffs and pigment manufacture**
E. **Refrigerant production before 1974**

ANSWER:
Dyestuffs and pigment manufacture

EXPLANATION:
Exposure to aniline dyes is a risk factor for transitional cell carcinoma

Aniline dyes are used in dyestuffs and pigment manufacture. Exposure to aniline dyes is a risk factor for transitional cell carcinoma.

Feed production may expose to aflatoxin.

The military may expose to mustard gas.

Rubber industry may expose to nitrosamines.

Refrigerant production before 1974 may expose to vinyl chloride.

CARCINOGENS

Carcinogen	Cancer
Aflatoxin (produced by *Aspergillus*)	Liver - (hepatocellular carcinoma)
Aniline dyes	Bladder (transitional cell carcinoma)
Asbestos	Mesothelioma and bronchial carcinoma
Nitrosamines	Oesophageal and gastric cancer
Vinyl chloride	Hepatic angiosarcoma

Q-137

A 30-year-old man is investigated for enlarged, painless cervical lymph nodes. A biopsy is taken and a diagnosis of Hodgkin's lymphoma is made. Which one of the following types of Hodgkin's lymphoma carries the best prognosis?

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

ANSWER:
Lymphocyte predominant

EXPLANATION:
Hodgkin's lymphoma - best prognosis = lymphocyte predominant

Please see Q-29 for Hodgkin's Lymphoma: Histological Classification and Prognosis

Q-138

A 65-year-old female with metastatic breast cancer is reviewed in clinic. Her husband reports that she is increasingly confused and occasionally appears to talk to relatives that are not in the room. She undergoes investigations for reversible causes, of which none are found. If conservative measures fail and she continues to be confused/agitated, what is the most appropriate management?

A. **Subcutaneous midazolam**
B. **Oral lithium**
C. **Oral haloperidol**
D. **Oral diazepam**
E. **Oral quetiapine**

ANSWER:
Oral haloperidol

EXPLANATION:
Oral haloperidol is the most appropriate treatment here. If the patient was in the terminal phase and agitated then subcutaneous midazolam would be indicated

Please see Q-46 for Palliative Care Prescribing: Agitation and Confusion

Q-139

A 54-year-old man who has developed disseminated intravascular coagulation secondary to sepsis is reviewed. Twenty minutes ago he started to bleed per rectum. Blood products including packed red cells and fresh frozen plasma have been ordered. What is the single most important factor in determining whether cryoprecipitate should be given?

A. A low fibrinogen level
B. A high prothrombin time
C. A high activated partial thromboplastin time
D. A low platelet count
E. A low haemoglobin

ANSWER:
A low fibrinogen level

EXPLANATION:
A low fibrinogen level is the major criteria determining the use of cryoprecipitate in bleeding

BLOOD PRODUCTS: FFP, CRYOPRECIPITATE AND PROTHROMBIN COMPLEX
NICE published guidelines on the use of blood products in 2015.

Fresh frozen plasma (FFP)
- most suited for 'clinically significant' but without 'major haemorrhage' in patients with a prothrombin time (PT) ratio or activated partial thromboplastin time (APTT) ratio > 1.5
- typically 150-220 mL
- can be used prophylactically in patients undergoing invasive surgery where there is a risk of significant bleeding
- In contrast to red cells, the universal donor of FFP is AB blood because it lacks any anti-A or anti-B antibodies

Cryoprecipitate
- contains concentrated Factor VIII:C, von Willebrand factor, fibrinogen, Factor XIII and fibronectin, produced by further processing of Fresh Frozen Plasma (FFP). Clinically it is most commonly used to replace fibrinogen
- much smaller volume than FFP, typically 15-20mL
- most suited for patients for 'clinically significant' but without 'major haemorrhage' who have a fibrinogen concentration < 1.5 g/L
- example use cases include disseminated intravascular coagulation, liver failure and hypofibrinogenaemia secondary to massive transfusion. It may also be used in an emergency situation for haemophiliacs (when specific factors not available) and in von Willebrand disease
- can be used prophylactically in patients undergoing invasive surgery where there is a risk of significant bleeding where the fibrinogen concentration < 1.0 g/L

Prothrombin complex concentrate
- used for the emergency reversal of anticoagulation in patients with either severe bleeding or a head injury with suspected intracerebral haemorrhage
- can be used prophylactically in patients undergoing emergency surgery depending on the particular circumstance

Q-140

A 29-year-old woman who has a history of recurrent pulmonary emboli is identified as having factor V Leiden. How does this particular inherited thrombophilia increase her risk of venous thromboembolic events?

A. Decreased levels of factor V
B. Increased levels of factor V
C. Activated factor V is inactivated much more slowly by activated protein C
D. Activated factor V is inactivated much more quickly by activated protein C
E. Decreased antithrombin III levels

ANSWER:
Activated factor V is inactivated much more slowly by activated protein C

EXPLANATION:
In patients with factor V Leiden, activated factor V is inactivated 10 times more slowly by activated protein C than normal

Please see Q-21 for Factor V Leiden

Q-141

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

ANSWER:
Activated protein C resistance

EXPLANATION:

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

Gain of function polymorphisms

- factor V Leiden (activated protein C resistance): most common cause of thrombophilia
- prothrombin gene mutation: second most common cause

Deficiencies of naturally occurring anticoagulants

- antithrombin III deficiency
- protein C deficiency
- protein S deficiency

The table below shows the prevalence and relative risk of venous thromboembolism (VTE) of the different inherited thrombophilias:

Condition	Prevalence	Relative risk of VTE
Factor V Leiden (heterozygous)	5%	4
Factor V Leiden (homozygous)	0.05%	10
Prothrombin gene mutation (heterozygous)	1.5%	3
Protein C deficiency	0.3%	10
Protein S deficiency	0.1%	5-10
Antithrombin III deficiency	0.02%	10-20

Acquired

Antiphospholipid syndrome

Drugs

- the combined oral contraceptive pill

Q-142

A 56-year-old man is investigated for lethargy. A full blood count shows the following:

Hb 8.6 g/dl
Platelets 42 * 109/l
WBC 36.4 * 109/l

*****Blood film shows 30% myeloid blasts with Auer rods - please liase with haematologist*****

Given the likely diagnosis, which one of the following is associated with a good prognosis?

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**

ANSWER:

Translocation between chromosome 15 and 17

EXPLANATION:

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.

Please see Q-24 for Acute Myeloid Leukaemia

Q-143

A 65-year-old man comes for review. He has a history of small cell lung cancer and ischaemic heart disease. His cancer was diagnosed five months ago and he has recently completed a course of chemotherapy. From a cardiac point of view he had a myocardial infarction two years ago following which he had primary angioplasty with stent placement. He has had no angina since.

For the past week he has become increasingly short-of-breath. This is worse at night and is associated with an occasional non-productive cough. He has also noticed that his wedding ring feels tight. Clinical examination is of his chest is unremarkable. He does however have distended neck veins and periorbital oedema. What is the most likely diagnosis?

A. **Heart failure secondary to chemotherapy**
B. **Tumour lysis syndrome**
C. **Nephrotic syndrome secondary to chemotherapy**
D. **Superior vena cava obstruction**
E. **Hypercalcaemia**

ANSWER:

Superior vena cava obstruction

EXPLANATION:

Please see Q-13 for Superior Vena Cava Obstruction

Q-144

Which one of the following statements regarding the aetiology of venous thromboembolism (VTE) is correct?

A. **Third generation combined oral contraceptive pills are safer than second generation ones**
B. **VTE develops in around 5% of patients with Goodpasture's syndrome**
C. **Female gender is a risk factor recurrent VTE**
D. **The second trimester of pregnancy is associated with a greater risk than the puerperium**
E. **Tamoxifen therapy increases the risk of VTE**

ANSWER:
Tamoxifen therapy increases the risk of VTE

EXPLANATION:
Please see Q-96 for Venous Thromboembolism: Risk Factors

Q-145

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 * 109/l**
WBC	**15.1 * 109/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

ANSWER:
Plasma exchange

EXPLANATION:
TTP - plasma exchange is first-line
This patient has thrombotic thrombocytopenic purpura, a condition associated with pregnancy

Please see Q-115 for Thrombotic Thrombocytopenic Purpura: Management

Q-146

A 34-year-old man who is known to have glucose-6-phosphate dehydrogenase deficiency presents with symptoms of a urinary tract infection. He is prescribed an antibiotic. A few days later he becomes unwell and is noticed by his partner to be pale and jaundiced. What drug is mostly likely to have been prescribed?

A. Co-amoxiclav
B. Trimethoprim
C. Ciprofloxacin
D. Cefalexin
E. Erythromycin

ANSWER:
Ciprofloxacin

EXPLANATION:
The sulfamethoxazole in co-trimoxazole causes haemolysis in G6PD, not the trimethoprim

Please see Q-60 for G6PD Deficiency

Q-147

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

ANSWER:
Gastric cancer

EXPLANATION:
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. Pancreas
6. Oesophagus
7. Stomach
8. Bladder
9. Non-Hodgkin's lymphoma
10. Ovarian

*excludes non-melanoma skin cancer

Q-148

A 4-year-old child with a deforming mandibular neck swelling. Biopsy of the lesion reveals a 'starry sky' appearance under microscopy.

Infection with which virus is an essential step in the pathogenesis of this disease?

A. HTLV-1
B. EBV
C. HPV
D. HIV
E. HSV-2

ANSWER:
EBV

EXPLANATION:
EBV infection is implicated in the pathogenesis of Burkitt's lymphoma
EBV is identifiable in nearly all cases of Burkitt's lymphoma.

HTLV-1 is associated with adult T cell lymphoma

HPV is associated with cervical and anal cancers

HIV infection is important in the pathogenesis of immunodeficiency-associated Burkitt's lymphoma. However, in the endemic variant clearly described here the disease may occur in HIV negative children.

HSV-2 causes genital herpes

Please see Q-49 for Burkitt's Lymphoma

Q-149

A 60-year-old woman is investigated for painful fingers and toes in cold weather. She has previously been diagnosed with Raynaud's phenomenon but she is now experiencing significant purplish discolouration of her peripheries and nose as well as generally feeling tired and lethargic. Blood tests shows the following:

Hb	**99 g/l**
Platelets	**156 * 109/l**
WBC	**5.9 * 109/l**
Blood film	**Spherocytes seen**

What is the next best investigation?

A. Complement levels
B. Osmotic fragility test
C. Anti-nuclear antibody
D. Flow cytometry of blood
E. Direct antiglobulin test

ANSWER:
Direct antiglobulin test

EXPLANATION:
This lady is likely to have cold agglutinin disease, a form of autoimmune hemolytic anemia.

Please see Q-4 for Autoimmune Haemolytic Anaemia

Q-150

A 67-year-old woman is reviewed 6 months after she had a mastectomy following a diagnosis of breast cancer. Which one of the following tumour markers is most useful in monitoring her disease?

A. CA 125
B. CD 34
C. CA 15-3
D. CA 19-9
E. CD 117

ANSWER:
CA 15-3

EXPLANATION:
Please see Q-6 for Tumour Markers

Q-151

A 27-year-old woman presents to the Emergency Department with a sudden onset of swelling of the hands and face. She describes multiple similar episodes over the past few years, but this episode is the most severe. She cannot recall any obvious precipitant. On previous occasions, the symptoms have subsided within thirty minutes but on this occasion they have worsened over the course of an hour. On examination, there is significant swelling of the lips which are dry and shiny. The tongue is not enlarged. There is no stridor and the chest is clear. Respiratory rate is 22 and oxygen saturations are 96% on air. The hands are swollen and slightly erythematous but there is no pain or itching and no lymphadenopathy. Heart rate is 106bpm and blood pressure is 118/79mmHg. Tympanic temperature is 36.7°C. A diagnosis of hereditary angioedema is suspected.

Which one of the following is not implicated in the pathogenesis of hereditary angioedema?

A. C1-esterase inhibitor
B. Bradykinin
C. Histamine
D. Kallikrein
E. High molecular weight kininogen

ANSWER:
Histamine

EXPLANATION:

Hereditary angioedema (HAE) is pathophysiologically separate from anaphylaxis and is treated differently. Therapeutic options are: intravenous infusion of human C1-esterase inhibitor or subcutaneous injection of the bradykinin receptor inhibitor icatibant

Hereditary angioedema (HAE) is an autosomal dominantly inherited immune condition characterised by episodic swelling of the extremities, intra-abdominal viscera and mucous membranes. Often attacks are unprecipitated although sometimes exogenous oestrogens in the form of contraception can be traced, as well as exposure to angiotensin-converting enzyme inhibitors. The primary pathophysiological defect is in the complement cascade and deficiencies in factors C4 and C1-esterase inhibitor are seen in type I. In type II HAE C1-esterase inhibitor levels are normal but the enzyme is dysfunctional and activity is low. An acquired form of HAE is described in which all complement levels are low. In type III HAE the clinical features of angioedema are present but immunological testing reveals normal levels and activity of complement factors. Ultimately, failure of C1-esterase inhibitor leads to upregulation of the rest of the complement system and membrane attack complex, but also it leads to activation of the signalling protein kallikrein which acts directly on the vascular wall to increase permeability, and it cleaves high molecular weight kininogen to release bradykinin, again a potent peripheral vasodilator giving rise to the symptoms of HAE.

HAE should be recognised as a separate entity from anaphylaxis since the clinical signs are different, as is the pathophysiology of the condition and its treatment. Anaphylaxis is an IgE mediated immune phenomenon related to a specific allergen causing massive mast cell degranulation and histamine release. HAE is driven by complement dysregulation and consequent release of the inflammatory cytokines bradykinin and kallikrein. Anaphylaxis is characterised by rapidly progressive, itchy, erythematous, oedematous rash, swelling of the lips, tongue and airways with accompanying hypovolaemic hypotension and cardiovascular collapse due to increased tissue permeability. Anaphylaxis is a medical emergency and death can ensue in minutes unless treated properly. HAE in comparison may present recurrently and often with no obvious precipitant. Usually, its course is more insidious with the evolution of symptoms over minutes to hours. Swelling will often only affect an isolated limb and it is not itchy or painful and minimally erythematous. Hypotension is rarely seen and cardiovascular instability is extremely unlikely. HAE can be fatal however if swelling of the upper airways causes obstruction, and in some cases, prophylactic intubation and mechanical ventilation may be appropriate. Since the driving mechanism is not histamine in HAE, steroids and antihistamines are of no value. Where there is no haemodynamic compromise, adrenaline is not warranted and may even worsen the situation due to increased plasma glucose load and risk of capillary rupture.

Knowledge of the cytokine cascade in HAE allows for knowledge of its management. Since the initiating pathophysiological hallmark is a deficiency or reduced effectiveness of C1-esterase inhibitor, exogenous administration of synthetic or reconstituted inhibitor should be effective.

National guidelines released in 2013 recommend treatment of episodes of HAE with the administration of reconstituted human C1-esterase inhibitor. In the UK two brands are available; either Cinryze which is dosed at 1000 unit administration or Berinert at 20 units/kg. Both are administered as slow intravenous infusions. Interestingly, a good clinical response is often seen to these drugs even in HAE type III where C1-esterase levels are normal.

An alternative to exogenous C1-esterase inhibitor is icatibant which is a specific antagonist at B2 bradykinin receptors in vascular smooth muscle. The 30mg dose may be repeated up to three times in 24 hours but a rapid resolution of symptoms is often seen. Many patients with HAE are supplied with their own icatibant autoinjectors for use in the pre-hospital setting at the onset of symptoms.

Ecallantide is a selective inactivator of the cytokine kallikrein. It is highly effective in the treatment of HAE in the United States but has no European licence at this current time.

Please see Q-2 for Hereditary Angioedema

Q-152

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

ANSWER:

Dohle bodies in the white cells

EXPLANATION:

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

Q-153

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

ANSWER:
Waldenstrom's macroglobulinaemia

EXPLANATION:
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.

Please see Q-74 for Waldenstrom's Macroglobulinaemia

Q-154

A 15-year-old girl presents with abdominal pain. She is normally fit and well and currently takes a combined oral contraceptive pill. The patient is accompanied by her mother, who is known to have hereditary spherocytosis. The pain is located in the upper abdomen and is episodic in nature, but has become severe today. There has been no change to her bowel habit and no nausea or vomiting. What is the most likely diagnosis?

A. Inferior vena cava thrombosis
B. Acute pancreatitis
C. Renal vein thrombosis
D. Gastritis
E. Biliary colic

ANSWER:
Biliary colic

EXPLANATION:
This patient has hereditary spherocytosis resulting in chronic haemolysis and gallstone formation. An important differential in a poorly patient with hereditary spherocytosis would be splenic rupture

Please see Q-20 for Hereditary Spherocytosis

Q-155

A 54-year-old man is investigated for a chronic cough. A chest x-ray arranged by his GP shows a suspicious lesion in the right lung. He has no past history of note and is a life-long non-smoker. An urgent bronchoscopy is arranged which is normal. What is the most likely diagnosis?

A. Lung sarcoma
B. Squamous cell lung cancer
C. Lung adenocarcinoma
D. Small cell lung cancer
E. Lung carcinoid

ANSWER:
Lung adenocarcinoma

EXPLANATION:
Lung adenocarcinoma
- ***most common type in non-smokers***
- ***peripheral lesion***

The clues are the absence of a smoking history and normal bronchoscopy, which suggests a peripherally located lesion.

LUNG CANCER: NON-SMALL CELL
There are three main subtypes of non-small cell lung cancer:

Squamous cell cancer
- typically central
- associated with parathyroid hormone-related protein (PTHrP) secretion → hypercalcaemia
- strongly associated with finger clubbing
- hypertrophic pulmonary osteoarthropathy (HPOA)

Adenocarcinoma
- typically peripheral
- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers

Large cell lung carcinoma

- typically peripheral
- anaplastic, poorly differentiated tumours with a poor prognosis
- may secrete β-hCG

Q-156

A 68-year-old man who takes warfarin for atrial fibrillation is taken to the emergency department after being involved in a road traffic accident. His GCS is reduced and a CT head shows an intracranial haemorrhage. Bloods on admission show the following:

Hb	**13.2 g/l**
Platelets	**222 * 109/l**
WBC	**11.2 * 109/l**
INR	**3.1**

In addition to vitamin K, which one of the following blood products should be given?

A. Cryoprecipitate
B. Platelet transfusion
C. Prothrombin complex concentrate
D. Packed red cells
E. Fresh frozen plasma (FFP)

ANSWER:
Prothrombin complex concentrate

EXPLANATION:
Prothrombin complex concentrate is used for the emergency reversal of anticoagulation in patients with severe bleeding or a head injury

Please see Q-139 for Blood Products: FFP, Cryoprecipitate and Prothrombin Complex

Q-157

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 * 109/l**
WBC	**70.3 * 109/l**
Blood film:	**Lymphocytosis. Smudge cells seen**

Four months previously her white cell count was 30.5 * 109/l. What is the most appropriate management?

A. Imatinib
B. Chlorambucil
C. No treatment, monitor full blood count
D. Fludarabine, cyclophosphamide and rituximab
E. Allogeneic stem cell transplantation

ANSWER:
Fludarabine, cyclophosphamide and rituximab

EXPLANATION:
CLL - treatment: Fludarabine, Cyclophosphamide and Rituximab (FCR)
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 a combination of fludarabine, cyclophosphamide and rituximab (FCR) is the most appropriate treatment. Chlorambucil used to be the first-line treatment of choice but studies have shown it not to be as effective as FCR.

As with many haematological cancers such patients are often entered into randomised trials

Please see Q-121 for Chronic Lymphocytic Leukaemia: Management

Q-158

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

ANSWER:
MYC gene

EXPLANATION:
Please see Q-56 for Haematological Malignancies: Genetics

Q-159

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

ANSWER:
Liver cirrhosis

EXPLANATION:
HYPOSPLENISM
Causes

- splenectomy
- sickle-cell
- coeliac disease, dermatitis herpetiformis
- Graves' disease

- systemic lupus erythematosus
- amyloid

Features
- Howell-Jolly bodies
- siderocytes

Q-160

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

ANSWER:
Protein C deficiency

EXPLANATION:
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

Q-161

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

ANSWER:
Vincristine

EXPLANATION:
Vincristine - peripheral neuropathy
Vincristine is associated with peripheral neuropathy. Urinary hesitancy may develop secondary to bladder atony.

Please see Q-1 for Cytotoxic Agents

Q-162

A 35-year-old woman presents with menorrhagia and a persistent sore throat. A full blood count shows the following:

Hb 6.8 g/dl
Platelets 45 * 109/l
WBC 1.4 * 109/l
Neutrophils 0.8 * 109/l

Which one of the following medications is most likely to account for this finding?

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

ANSWER:
Trimethoprim

EXPLANATION:
Trimethoprim may cause pantcytopaenia

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

Q-163

A 22-year-old female presents to the emergency department with angioedema on 5 occasions in a six month period. No obvious trigger was identified and she does not improve significantly when given IM adrenaline.

Her symptoms are caused by a deficiency of which substance?

A. Bradykinin
B. C1 esterase inhibitor
C. Eosinophil peroxidase
D. Kallikrien
E. Neutrophil elastase

ANSWER:
C1 esterase inhibitor

EXPLANATION:
Hereditary angioedema is caused by deficiency of C1 esterase inhibitor
Hereditary angioedema is caused by a deficiency of C1 esterase inhibitor.

Please see Q-2 for Hereditary Angioedema

Q-164

A 77-year-old lady is admitted by the emergency department complaining of difficulty coping at home. She is unable to mobilise independently and has a poor appetite due to difficulty swallowing. She has a diagnosis of oesophageal cancer but is not thought to be a candidate for chemotherapy. Her GP recently started her on nitrofurantoin for a urinary tract infection.

On examination she is a thin, frail lady who is alert and oriented. There is no neurological deficit in the upper limbs. She has weakness of hip flexion and knee extension in both legs, but markedly more so on the right. You are able to elicit some loss of pinprick sensation on the anterior thigh. Her reflexes are brisk with an upgoing plantar on the right.

Her blood results are as follows:

Hb 101 g/l
Platelets 440 * 109/l
WBC 8.4 * 109/l
MCV 99 fL
Na+ 136 mmol/l
K+ 4.8 mmol/l
Urea 3.7 mmol/l
Creatinine 52 µmol/l

What is the next most appropriate step in this patient's management?

A. Transfer to hospice
B. Refer for physiotherapy
C. MRI imaging of the spinal cord
D. Check B12 and folate levels
E. Stop nitrofurantoin

ANSWER:
MRI imaging of the spinal cord

EXPLANATION:
A patient with new lower limb neurology and a history of cancer should raise the suspicion of metastatic spinal cord compression, which is best demonstrated on MRI.

Although nitrofurantoin and B12 deficiency could cause a peripheral neuropathy, both are less urgent problems than cord compression.

Please see Q-36 for Spinal Cord Compression

Q-165

A 69-year-old male patient presents to the oncology clinic with a 3-months history of right upper quadrant discomfort, weight loss and anorexia. Ultrasound liver raises the suspicion of a hepatocellular carcinoma.

Which carcinogen had he likely been exposed to?

A. Nitrosamine
B. Aflatoxin
C. Aniline dye
D. Arsenic
E. Benzene

ANSWER:
Aflatoxin

EXPLANATION:
Exposure to aflatoxin is a risk factor for hepatocellular carcinoma
Exposure to aflatoxin is a risk factor for hepatocellular carcinoma.

Exposure to nitrosamine is a risk factor for gastric and oesophageal carcinoma.

Exposure to aniline dye is a risk factor for transitional cell carcinoma.

Exposure to arsenic is a risk factor for lung malignancy and liver angiosarcoma.

Exposure to benzene is a risk factor for leukaemia.

Please see Q-136 for Carcinogens

Q-166

Which of the following is a cause of extravascular haemolysis?

A. Hereditary spherocytosis
B. Paroxysmal nocturnal haemoglobinuria
C. Disseminated intravascular coagulation
D. Mismatched blood transfusion
E. Haemolytic uraemic syndrome

ANSWER:
Hereditary spherocytosis

EXPLANATION:
Please see Q-22 for Haemolytic Anaemias: By Site

Q-167

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

ANSWER:
Female sex

EXPLANATION:

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

Chromosomal changes

- deletion of the long arm of chromosome 13 (del 13q) is the most common abnormality, being seen in around 50% of patients. It is associated with a good prognosis
- deletions of part of the short arm of chromosome 17 (del 17p) are seen in around 5-10% of patients and are associated with a poor prognosis

Q-168

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

ANSWER:

Deletions of chromosome 5

EXPLANATION:

Acute myeloid leukaemia - poor prognosis: deletion of chromosome 5 or 7

Please see Q-24 for Acute Myeloid Leukaemia

Q-169

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 detect disease recurrence?

A. CRP + beta-HCG
B. Testosterone + beta-HCG
C. ESR + alpha-fetoprotein
D. Alpha-fetoprotein + beta-HCG
E. LDH + ESR

ANSWER:

Alpha-fetoprotein + beta-HCG

EXPLANATION:

Please see Q-6 for Tumour Markers

Q-170

A 15-year-old girl is referred to haematology. She started having periods three years ago which have always been heavy and prolonged. Unfortunately the menorrhagia has responded poorly to trials of tranexamic acid and the combined oral contraceptive pill. Blood tests show the following:

Hb	**10.3 g/dl**
Plt	**239 * 109/l**
WBC	**6.5 * 109/l**
PT	**12.9 secs**
APTT	**37 secs**

What is the most likely diagnosis?

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

ANSWER:

Von Willebrand's disease

EXPLANATION:

Von Willebrand's disease is the most likely diagnosis as it is the most common inheritied bleeding disorder. The mildy elevated APTT is consistent with this diagnosis.

The mild anaemia is consistent with the long history of menorrhagia.

Please see Q-18 for Von Willebrand's Disease

Q-171

A 40-year-old lady presents with fatigue, shortness of breath and palpitations. She has a history of hypothyroidism and migraine. On examination, she is comfortable at rest with normal cardiovascular, respiratory and abdominal examination although her conjunctiva appears pale.

Her full blood count results are shown below:

Hb	**98 g/l**
Platelets	**146 * 109/l**
WBC	**3.5 * 109/l**

On further testing, her B12 level is 95 fL and her blood film displays hypersegmented polymorphs.

What would be the most appropriate next set of investigations?

A. Folate levels and anti-gastric parietal cell antibodies
B. Schilling test
C. Iron studies
D. Folate levels and LDH
E. Colonoscopy

ANSWER:
Folate levels and anti-gastric parietal cell antibodies

EXPLANATION:
This patient has a macrocytic anaemia due to B12 deficiency demonstrated by the low B12 levels and hypersegmented polymorphs on blood film. The next step is to identify the cause of the B12 deficiency by investigating for pernicious anaemia and checking folate levels (combined B12 and folate deficiency are common). Anti-gastric parietal cell antibodies are present in 90% patients with PA (but also 5-10% patients without PA). Other tests for PA are anti-intrinsic factor antibodies which are more specific but less sensitive than anti-parietal cell antibodies (present in 50%). In the past, Schilling tests using radioisotope labelled B12 were used.

Explanation for other options:
2. Schilling test no longer used in clinical practice due to shortage of B12 radioisotope and less invasive means of testing available
3. Folate levels are useful and LDH would be raised in pernicious anaemia but this is a non-specific finding and does not aid diagnosis
4. Colonoscopy not indicated at this stage and would be more useful in a microcytic anaemia when GI blood loss would be a possible cause
5. This patient has a macrocytic rather than microcytic anaemia (which would fit with iron deficiency)

Please see Q-15 for Vitamin B12 Deficiency

Q-172

An 85-year-old patient has been diagnosed with monoclonal gammopathy of uncertain significance. He is keen to know what this means for his future health. Which of the following statements below is correct?

A. This diagnosis is likely to cause a reduction in his life expectancy of more than 10 years
B. 10% of patients with MGUS go on to develop myeloma over 10 years
C. He should start chemotherapy as soon as possible
D. 40% of patients with MGUS go on to develop myeloma over 10 years
E. 60% of patients with MGUS will develop Waldenstrom's macroglobulinaemia during their lifetime

ANSWER:
10% of patients with MGUS go on to develop myeloma over 10 years

EXPLANATION:
10% of patients with MGUS go on to develop myeloma over 10 years
The correct answer is: 10% of patients with MGUS will go on to develop myeloma over 10 years. MGUS is a pre-malignant condition but many patients never develop malignant disease or die from other causes before malignant transformation.

This patient is elderly and the diagnosis is very unlikely to cause such a large reduction in his life expectancy. A monoclonal gammopathy can also be found in Waldenstrom's macroglobulinaemia but MGUS does not transform into Waldenstrom's.

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)

Q-173

A 52-year-old female patient presents to the oncology clinic with an 8-months history of poor appetite and weight loss. She also complains of a right upper quadrant discomfort which has been present for the last 3 months. An ultrasound scan reveals multiple lesions in the liver suggestive of liver metastasis. A tumour marker profile reveals a raised level of CA 15-3.

What is the most likely primary tumour?

A. Colorectal carcinoma
B. Small cell lung carcinoma
C. Breast carcinoma
D. Ovarian carcinoma
E. endometrial carcinoma

ANSWER:
Breast carcinoma

EXPLANATION:
CA 15-3 is a tumour marker in breast cancers
CA 15-3 is a tumour marker in breast cancers.

Bombesin is a tumour marker in small cell lung cancers.

Carcinoembryonic antigen (CEA) is a tumour marker in colorectal cancers.

CA 125 is a tumour marker in ovarian cancers and also endometrial cancers.

Please see Q-6 for Tumour Markers

Q-174

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

ANSWER:
Lethargy

EXPLANATION:
Myelofibrosis - most common presenting symptom - lethargy
Whilst all the above may be seen in myelofibrosis lethargy is the most common

MYELOFIBROSIS
Overview

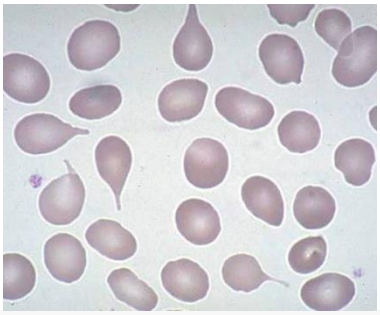
- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

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)



Blood film showing the typical 'tear-drop' poikilocytes of myelofibrosis

Q-175

A patient is due to start chemotherapy for metastatic colorectal cancer. What is the main advantage of using capecitabine instead of fluorouracil?

A. Current data shows increased survival
B. Less cardiotoxic
C. Oral administration
D. Less nausea
E. Not renally excreted therefore can be used in patients with chronic kidney disease

ANSWER:
Oral administration

EXPLANATION:
Capecitabine is an orally administered prodrug which is enzymatically converted to 5-fluorouracil in the tumour.

Please see Q-1 for Cytotoxic Agents

Q-176

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

ANSWER:
Common variable immunodeficiency

EXPLANATION:
Please see Q-86 for Primary Immunodeficiency

Q-177

A 40-year-old female has been diagnosed with haemolytic uraemic syndrome after an episode of severe diarrhoea. She has a haemoglobin of 84 mg/dL. Which of the following blood results is most likely to be found?

A. Low haptoglobin
B. Low bilirubin
C. Elevated magnesium
D. Low urea
E. Increased HbF

ANSWER:
Low haptoglobin

EXPLANATION:
Low haptoglobin levels are found in haemolytic anaemias
The patient has an intravascular haemolytic anaemia secondary to haemolytic uraemic syndrome. Haptoglobin levels are reduced in intravascular haemolysis because they

bind to free haemoglobin released from lysed erythrocytes. The complexes are then removed from the plasma by the hepatic reticulo-endothelial cells. Haptoglobin levels decrease if the rate of haemolysis is greater than the rate of haptoglobin production.

Bilirubin levels are likely to be elevated because of increased metabolism of haem. Magnesium may be low because of diarrhoea or unaffected. Urea would be increased due to acute kidney injury. HbF is found in patients with inherited haemoglobinopathies and not in acquired haemolytic anaemias.

Please see Q-22 for Haemolytic Anaemias: By Site

Q-178

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

ANSWER:
Bone pain

EXPLANATION:
Please see Q-74 for Waldenstrom's Macroglobulinaemia

Q-179

A 22-year-old man with sickle cell anaemia presents with pallor, lethargy and a headache. 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

ANSWER:
Aplastic crisis

EXPLANATION:
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

Please see Q-69 for Sickle-Cell Crises

Q-180

A 25-year-old female patient presents with massive haemorrhage. You are working in the hospital blood bank and are asked to prepare 2 units each of Red cells and Fresh Frozen Plasma (FFP) when the result of the group and save is available.

The patient's sample is grouped as B RhD negative. You manage to procure some Group B red cells from the fridge but there is no Group B FFP available.

FFP from a donor of which blood group would be best to give?

A. A RhD negative
B. A RhD positive
C. AB RhD negative
D. AB RhD positive
E. RhD positive

ANSWER:
AB RhD negative

EXPLANATION:
The universal donor of fresh frozen plasma is AB RhD negative blood
This patient is blood group B RhD negative, meaning her red cells possess B antigens only from the ABO grouping, and she naturally produces anti-A antigens in her plasma. Therefore, she needs to receive red cells with only B antigen or no antigens at all (i.e. Groups B or O) but needs to receive FFP that does not have anti-B in it. Group O donors naturally produce anti-A and anti-B, Group A donors naturally produce only anti-B, so she can only receive FFP from groups B or AB.

Group AB is the universal donor for FFP because they produce neither anti-A or anti-B and is therefore compatible with all ABO groups.

In many cases the RhD status would not matter for blood transfusion, however as this is a woman of childbearing age who is RhD negative, she should receive RhD negative blood in order to avoid problems with future pregnancies in which the foetus is RhD positive.

Please see Q-139 for Blood Products: FFP, Cryoprecipitate and Prothrombin Complex

Q-181

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

ANSWER:
Prevents microtubule disassembly

EXPLANATION:
Taxanes such as docetaxel - prevents microtubule depolymerisation & disassembly, decreasing free tubulin Like other taxanes the principal mechanism of action is the prevention of microtubule disassembly.

Please see Q-1 for Cytotoxic Agents

Q-182

A blood film is reported as follows:

Howell-Jolly bodies, target cells and occasional Pappenheimer bodies are seen

What is the most likely underlying cause?

A. Iron-deficiency anaemia
B. Lead poisoning
C. Myelofibrosis
D. Sideroblastic anaemia
E. Post-splenectomy

ANSWER:
Myelofibrosis

EXPLANATION:
BLOOD FILMS: TYPICAL PICTURES
Hyposplenism e.g. post-splenectomy
- target cells
- Howell-Jolly bodies
- Pappenheimer bodies
- siderotic granules
- acanthocytes

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

Q-183

A 30 year-old man presents with recurrent abdominal pain. This is not associated with food, heartburn, indigestion or dysphagia. He has had no weight loss. His blood tests have been normal and he has been given a diagnosis of irritable bowel syndrome. Despite lifestyle modifications and laxatives, he has still had recurrent pain. He then presents with swelling of his lips and tongue. This is not itchy and he is systemically well, but does have a stridor.

What would be the most successful management out of the following options?

A. Supportive care
B. Adrenaline
C. Prednisolone
D. Fresh frozen plasma
E. Chlorphenamine

ANSWER:
Fresh frozen plasma

EXPLANATION:
This patient has a history and acute presentation in keeping with hereditary angioedema. This is caused by a deficiency of C1-esterase inhibitor. It is normally treated with C1-INH concentrate, however when this is unavailable, fresh frozen plasma is the next best treatment. The lack of itching in this case and the fact that he is systemically well point away from anaphylaxis as a cause. Hereditary angioedema rarely responds to treatment with adrenaline or antihistamines. In a real life situation this patient would probably be treated as anaphylaxis, but the question asks what the most successful treatment would be, and in this case it would be FFP.

Please see Q-2 for Hereditary Angioedema

Q-184

A 29-year-old man presented to the hospital after he had two episodes of bright red urine in the morning. He is very worried and tells the attending doctor that he has never had such an episode before. He has just started working at an engineering firm and is planning to get married in a few months. He reports feeling tired for the past few months but thought this was due to his job which required him to travel to construction sites every day. He has no significant family history. He had an appendectomy when he was a child but other than that he has never been admitted to the hospital. A blood test reveals a hemoglobin concentration of 11.5 g/dL and a reticulocyte of 14% of red blood cells. Which of the findings is the most likely to be reported upon flow cytometry of a blood sample from this patient?

A. C3 negative cells
B. CD55 negative cells
C. CD59 negative cells
D. C5 to C9 negative cells
E. CD55 and CD59 negative cells

ANSWER:
CD55 and CD59 negative cells

EXPLANATION:
This patient presented with the signs and symptoms consistent with a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH). This condition is an acquired and chronic form of intrinsic hemolytic anemia. Patients can

present with hematuria, or even simply symptoms of anemia. Venous thrombosis is also a common occurrence. The classic triad is hemolytic anemia, pancytopenia, and venous thrombosis. Flow cytometry is the gold standard laboratory investigations and shows CD55 and CD59 negative red and blood cells.

1: A deficiency of C3 is a complement deficiency disorder. Since C3 plays an important role in the activation of both the classical and alternative complement pathways, a C3 deficiency confers a higher risk of acquiring recurrent bacterial infections.
2: It is true that this will be present in this patient's cells. However, PNH patients will also have a deficiency of CD59.
3: It is true that this will be present in this patients' cells. However, PNH patients will also have a deficiency of CD55.
4: This would indicate terminal complement deficiency. This condition involves a deficiency of the complements forming the membrane attack membrane. C5 to C9 deficiency confers a high risk of infection with Neisseria organisms.
5: The gold standard in the diagnosis of PNH is flow cytometry, and patients usually have a deficiency of both CD55 and CD59 on their red as well as their white blood cells. Eculizumab is a humanized monoclonal antibody which has been approved for the treatment of PNH. It works mainly via the inhibition of the terminal complement cascade.

Please see Q-130 for Paroxysmal Nocturnal Haemoglobinuria

Q-185

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

ANSWER:
Hydration + mesna

EXPLANATION:
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

Mesna
- 2-mercaptoethane sulfonate Na
- a metabolite of cyclophosphamide called acrolein is toxic to urothelium
- mesna binds to and inactivates acrolein helping to prevent haemorrhagic cystitis

Q-186

A patient is diagnosed with acute lymphoblastic leukaemia after presenting with lethargy and easy bruising. 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

ANSWER:
Philadelphia chromosome positive

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

Please see Q-88 for Acute Lymphoblastic Leukaemia: Prognostic Features

Q-187

John, a 35-year-old gentleman on the gastrointestinal ward has been suffering from melaena for a week. His haemoglobin level today is 60g/L and the consultant has requested that you transfuse John a unit of packed red blood cells. Within minutes of starting the transfusion, John complains of itching and stinging sensations on his trunk. On examination, you observe red raised welts over his abdomen and chest. His blood pressure is unaltered from prior to the transfusion at 130/70mmHg, his temperature is 37ºC and there are no signs of dyspnoea, wheezing, stridor or angioedema. Which one of the following management options is the most appropriate?

A. Temporary transfusion termination and an antihistamine
B. Permanent transfusion termination, generous fluid resuscitation with saline solution and inform the lab
C. Permanent transfusion termination, intramuscular adrenaline, antihistamines, corticosteroids, bronchodilators and supportive care
D. Temporary transfusion termination and an antipyretic
E. Permanent transfusion termination and high dose immune globulin therapy

ANSWER:
Temporary transfusion termination and an antihistamine

EXPLANATION:
For urticarial blood transfusion reactions without anaphylaxis, an antihistamine should be given and the transfusion temporarily stopped
This patient is suffering from an urticarial rash following blood transfusion, hence the transfusion should be stopped and an antihistamine given. Once the symptoms resolve, the transfusion may be continued with no need for further workup.

Additional IM adrenaline, corticosteroids, bronchodilators and supportive care would only be required for symptoms of anaphylaxis or severe allergic reaction. This patient does not have angioedema or signs of breathing difficulties.

Permanent termination with generous fluid resuscitation and informing the lab is not appropriate and is the management of acute haemolytic transfusion reaction. There is no fever, abdominal/chest pain or hypotension to indicate this complication.

Temporary transfusion termination with an antipyretic is used to treat non-haemolytic febrile reaction, however, there is no fever here to indicate this complication.

High dose immunoglobulin is used to treat post-transfusion purpura, which is a rare, delayed transfusion reaction

(BMJ Best Practice)

Please see Q-23 for Blood Product Transfusion Complications

Q-188

A 64-year-old woman with metastatic breast cancer is brought in by her husband. Over the past two days she has developed increasingly severe back pain. Her husband reports that her legs are weak and she is having difficulty walking. On examination she has reduced power in both legs and increased tone associated with brisk knee and ankle reflexes. There is some sensory loss in the lower limbs and feet but perianal sensation is normal. What is the most likely diagnosis?

A. Spinal cord compression at T10
B. Cauda equina syndrome
C. Guillain Barre syndrome
D. Hypercalcaemia
E. Paraneoplastic peripheral neuropathy

ANSWER:
Spinal cord compression at T10

EXPLANATION:
The upper motor neuron signs point towards a diagnosis of spinal cord compression above L1, rather than cauda equina syndrome.

Please see Q-36 for Spinal Cord Compression

Q-189

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

A. Passive absorption in the terminal ileum
B. Active absorption in the middle to terminal part of jejunum
C. Active absorption by the parietal cells of the stomach
D. Active absorption in the terminal ileum
E. Passive absorption in the proximal ileum

ANSWER:
Active absorption in the terminal ileum

EXPLANATION:
Vitamin B12 is actively absorbed in the terminal ileum
A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Please see Q-15 for Vitamin B12 Deficiency

Q-190

A 54-year-old man who is about to start chemotherapy for a high-grade lymphoma is given intravenous rasburicase to help lower the risk of tumour lysis syndrome. What is the mechanism of action of this drug?

A. Inhibits urate oxidase
B. Converts uric acid to allantoin
C. Inhibits xanthine oxidase
D. Converts uric acid to hypoxanthine
E. Guanylic oxidase inhibitor

ANSWER:
Converts uric acid to allantoin

EXPLANATION:
Rasburicase - a recombinant version of urate oxidase, an enzyme that metabolizes uric acid to allantoin

Please see Q-127 for Tumour Lysis Syndrome

Q-191

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

ANSWER:
IgG paraprotein band = 18g/l

EXPLANATION:
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

Please see Q-172 for MGUS

Q-192

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 * 109/l**
WBC	**5.3 * 109/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. **EMA binding test**
E. **Direct Coombs' test**

ANSWER:
EMA binding test

EXPLANATION:
This patient likely has hereditary spherocytosis (HS) as evidenced by the normocytic anaemia, gallstones and family history. The British Journal of Haematology guidelines state that a clinical diagnosis of HS can sometimes be made for classical histories. However, if the case is more equivocal then a diagnostic test is recommended, such as the EMA binding test.

The EMA binding test uses flow cytometry to determine the amount of fluorescence (reflecting EMA bound to specific transmembrane proteins) derived from individual red cells.

Please see Q-20 for Hereditary Spherocytosis

Q-193

A 65-year-old man who is undergoing bone marrow transplant requires a blood transfusion. Irradiated packed red cells are requested. What is the purpose of requesting irradiated blood products in this situation?

A. **Depletes the packed cells of platelets reducing the risk of thrombotic complications**
B. **Ensures the blood products are free of viruses and organisms**
C. **Destroys HLA markers reducing the risk of blood transfusion reaction**
D. **Reduces the HbA2/Hb ratio**
E. **Depleted T-lymphocyte numbers reduce the risk of transfusion graft versus host disease**

ANSWER:
Depleted T-lymphocyte numbers reduce the risk of transfusion graft versus host disease

EXPLANATION:
Irradiated blood products are used as they are depleted in T-lymphocytes
The most common indications for irradiated blood products are conditions where the immune system is compromised.

BLOOD PRODUCTS: CMV NEGATIVE AND IRRADIATED BLOOD
Cytomegalovirus (CMV) is transmitted in leucocytes. As most blood products (except granulocyte transfusions) are now leucocyte depleted CMV negative products are rarely required.

Irradiated blood products are used to avoid transfusion graft versus host disease (TA-GVHD) caused by engraftment of viable donor T lymphocytes.

The table below shows the indications for CMV and irradiated blood:

Situation	CMV negative	Irradiated
Granulocyte transfusions	✓	✓
Intra-uterine transfusions	✓	✓
Neonates up to 28 days post expected date of delivery	✓	✓
Pregnancy: Elective transfusions during pregnancy (not during labour or delivery)	✓	
Bone marrow / stem cell transplants		✓
Immunocompromised (e.g. chemotherapy or congenital)		✓
Patients with/previous Hodgkins Disease		✓
HIV		

Q-194

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 * 109/l**
WBC	**15.2 * 109/l**

Film seen **Leucoerythroblastic picture. Tear-drop poikilocytes**

What is the most likely diagnosis?

A. **Myelodysplasia**
B. **Chronic lymphocytic leukaemia**
C. **Myelofibrosis**
D. **Chronic myeloid leukaemia**
E. **Post-splenectomy**

ANSWER:
Myelofibrosis

EXPLANATION:
Myelofibrosis is associated with 'tear drop' poikilocytes on blood film
Thrombocytopenia and leucopenia are seen in progressive disease.

Please see Q-174 for Myelofibrosis

Q-195

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

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

ANSWER:
Wiskott-Aldrich syndrome

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

Please see Q-86 for Primary Immunodeficiency

Q-196

A 48-year-old man presents with a swollen, red and painful left calf. After being referred to the deep vein thrombosis (DVT) clinic he is diagnosed with having a proximal DVT and commenced on low-molecular weight heparin whilst awaiting review by the warfarin clinic.

There is no obvious precipitating factor for this such as recent surgery or a long haul flight. He is generally fit and well and takes no regular medication other than propranolol as migraine prophylaxis. There is no history of venous thromoboembolism in his family.

Other than commencing warfarin, what further action, if any, is required?

A. **No further action is required**
B. **Investigate for underlying malignancy + check anti-phospholipid antibodies**
C. **Check anti-phospholipid antibodies + hereditary thrombophilia screen**
D. **Check anti-Xa levels**
E. **Perform an echocardiogram**

ANSWER:
Investigate for underlying malignancy + check anti-phospholipid antibodies

EXPLANATION:
NICE would recommend doing a chest x-ray, blood and urine tests initially to exclude an underlying malignancy. If these are normal, a CT abdomen and pelvis should be arranged as the patient is > 40 years. They also recommend checking anti-phospholipid antibodies for the first unprovoked DVT/PE. There is no history to support an inherited thrombophilia.

Please see Q-33 for Deep Venous Thrombosis: Diagnosis and Management

Q-197

A 75-year-old male patient has metastatic colorectal cancer. He spends most of his day resting in bed or in his chair and requires assistance with his activities of daily living. What is his Eastern Cooperative Oncology Group (ECOG) score?

A. **0**
B. **1**
C. **2**
D. **3**
E. **4**

ANSWER:
3

EXPLANATION:
ECOG SCORE
The ECOG score is a 'performance status' scale, or a score that measures the functional status a patient. It is used to decide if a patient is a good or poor candidate for future oncological therapies.
Those with a poor functional status is a poor candidate for further chemotherapy.

0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Q-198

What is the underlying problem in methaemoglobinaemia?

A. The oxidation of Fe2+ in haemoglobin to Fe3+
B. The reduction of Fe2+ in haemoglobin to Fe+
C. The oxidation of Fe3+ in haemoglobin to Fe2+
D. The reduction of Fe2+ in haemoglobin to Fe3+
E. The reduction of Fe3+ in haemoglobin to Fe2+

ANSWER:
The oxidation of Fe2+ in haemoglobin to Fe3+

EXPLANATION:
Methaemoglobinaemia = oxidation of Fe2+ in haemoglobin to Fe3+

Please see Q-118 for Methaemoglobulinaemia

Q-199

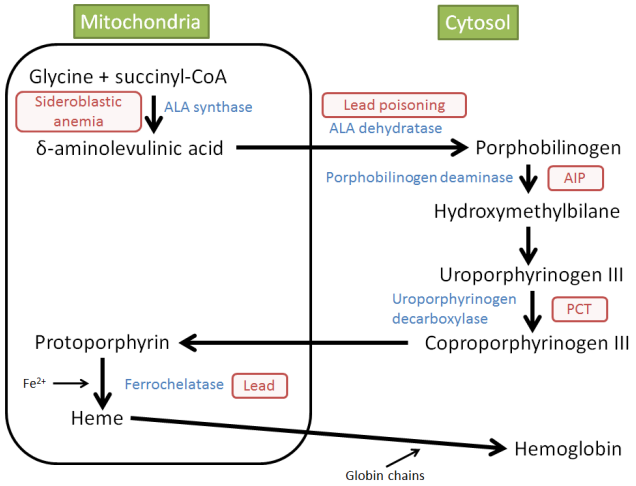
Acute intermittent porphyria is due to a defect in:

A. ALA synthetase
B. PPG oxidase
C. Uroporphyrinogen decarboxylase
D. Ferrochelatase
E. Porphobilinogen deaminase

ANSWER:
Porphobilinogen deaminase

EXPLANATION:
AIP - porphobilinogen deAminase; PCT - uroporphyrinogen deCarboxylase

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



Acute intermittent porphyria (AIP)
- autosomal dominant
- defect in porphobilinogen deaminase
- female and 20-40 year olds more likely to be affected
- typically present with abdominal symptoms, neuropsychiatric symptoms
- hypertension and tachycardia common
- urine turns deep red on standing

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

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

Q-200

An 80-year-old man has spent his whole working life as a loft insulator and is concerned that he may have been exposed to asbestos. He has been informed of the risk of mesothelioma but wants to know if there are any other conditions for which he is at higher risk than the general population. Which of the following is also proven to have a causal link with asbestos exposure?

A. Bronchiectasis
B. Type II diabetes
C. Bronchial carcinoma
D. Basal cell carcinoma of the skin
E. Ischaemic heart disease

ANSWER:
Bronchial carcinoma

EXPLANATION:
Exposure to asbestos is a risk factor for bronchial carcinoma as well as mesothelioma
Answer 3 is correct. Asbestos is well known to increase the risk of mesothelioma, but also increases the risk of bronchial carcinoma, laryngeal cancer and ovarian cancer. There is also some limited evidence that asbestos may increase the risk of cancer of the stomach, pharynx and bowel.

Exposure to asbestos also increases the risk of some benign diseases, including pleural plaques, diffuse pleural thickening, asbestos related benign pleural effusions and asbestosis.
Please see Q-136 for Carcinogens

Q-201

A patient is started on cyclophosphamide for vasculitis associated with Wegener's granulomatosis. Which of the following is most characteristically associated with cyclophosphamide?

A. Haemorrhagic cystitis
B. Cardiomyopathy
C. Ototoxicity
D. Alopecia
E. Weight gain

ANSWER:
Haemorrhagic cystitis

EXPLANATION:
Cyclophosphamide may cause haemorrhagic cystitis

Please see Q-1 for Cytotoxic Agents

Q-202

You are asked to review a 60-year-old Greek man with known glucose-6-phosphate dehydrogenase (G6PD) deficiency who was admitted with malaria and a chest infection. He has developed jaundice and haemolytic anaemia after starting some medications this morning.

Which of these medications are most likely to have precipitated his crisis?

A. Clarithromycin
B. Amoxicillin
C. Artesunate
D. Primaquine
E. Salbutamol

ANSWER:
Primaquine

EXPLANATION:
Primaquine is a well known cause of haemolysis in G6PD deficiency and is used in the treatment of malaria. Artesunate is generally considered safe to use in G6PD deficiency. Penicillins and macrolides are safe antibiotics to use in G6PD deficiency.

Source: BNF

Please see Q-60 for G6PD Deficiency

Q-203

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

ANSWER:
Interferon-alpha

EXPLANATION:
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%

Q-204

A 28-year-old gentleman was diagnosed with Hodgkin's lymphoma after presenting to his GP with painless lymphadenopathy. Following a staging positron emission tomography (PET) scan, nodes involving both sides of the diaphragm were found. Which stage of the Ann-Arbor classification does his presentation fall under?

A. Stage I
B. Stage II
C. Stage III
D. Stage IV
E. Stage V

ANSWER:
Stage III

EXPLANATION:
Stage III of the Ann-Arbor clinical staging of lymphomas involve lymph nodes on both sides of the diaphragm
The Ann-Arbor classification is used for Hodgkin's lymphoma and is split into 4 stages according to the spread of the disease.

Stage I - involves a single regional lymph node

Stage II - involves two or more lymph nodes on one side of the diaphragm

Stage IV - distant spread involving one or more extra lymphatic organs

Stage V - Not part of the Ann-Arbor classification

Please see Q-9 for Hodgkin's Lymphoma: Staging

Q-205

A 64-year-old man is referred to the oncology clinic with progressively worsening lower back pain over the last 3 months. He also reports an 8-month history of weight loss. MRI lumbar spine confirms the suspicion of bone metastasis.

What is the most likely primary tumour?

A. Leukaemia
B. Breast carcinoma
C. Colorectal carcinoma
D. Prostate carcinoma
E. Lung carcinoma

ANSWER:
Prostate carcinoma

EXPLANATION:
Prostate cancer is the most common primary tumour that metastasises to the bone
Prostate cancer is the most common primary tumour that metastasises to the bone

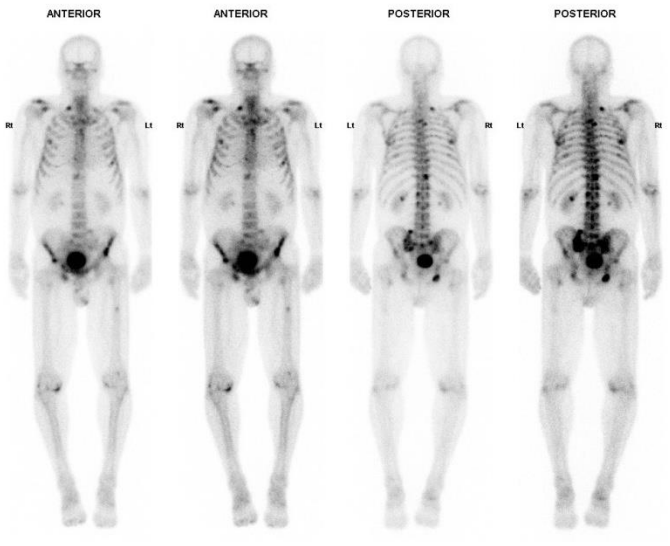
It is unusual to have bone metastasis in leukaemia.

Breast, colorectal and lung cancers can all lead to bone metastasis but the question is asking for the most likely tumour and statistically speaking, prostate cancer is the most common primary tumour that metastasises to the bone.

BONE METASTASES
Most common tumour causing bone metastases (in descending order)
- prostate
- breast
- lung

Most common site (in descending order)
- spine
- pelvis
- ribs
- skull
- long bones

Other than bone pain, features may include:
- pathological fractures
- hypercalcaemia
- raised ALP



Isotope bone scan (using technetium-99m labelled diphosphonates which accumulate in the bones) from a patient with metastatic prostate cancer. The scan demonstrates multiple, irregular, randomly distributed foci of high grade activity involving the spine, ribs, sternum, pelvic and femoral bones. The findings are in keeping with multiple osteoblastic metastasis.

Q-206

A 59-year-old female patient presents with headache, lethargy, and a purpuric rash on her shins.

Hb	**89 g/l**
Platelets	**68 * 109/l**
WBC	**2.6 * 109/l**
Protein Electrophoresis	**paraprotein 2g/L**
Immunoprotein Electrophoresis	**monoclonal IgM**
C4	**low limit of normal**
Rheumatoid Factor	**elevated**

What is the most likely diagnosis?

A. Hepatitis C infection
B. Rheumatoid arthritis
C. Sjogren syndrome
D. Waldenstrom's macroglobulinaemia
E. Monoclonal gammopathy of unclear significance

ANSWER:
Waldenstrom's macroglobulinaemia

EXPLANATION:
Waldenstrom macroglobulinaemia is a lymphoplasmacytic lymphoma (lymphoplasmacytic infiltration in the bone marrow or lymphatic tissue) associated with an IgM monoclonal protein in the serum. It is essentially a bone marrow-based disease. Patients may develop constitutional symptoms, pancytopenia (especially anaemia and thrombocytopenia), organomegaly, neuropathy, and symptoms associated with immunoglobulin deposition or hyperviscosity.

Please see Q-74 for Waldenstrom's Macroglobulinaemia

Q-207

A 74-year-old male is seen on the acute medical ward with a history of persistent frontal headaches associated with blurred vision for the past week. On further questioning, the patient reports a history of worsening fatigue and shortness of breath over the preceding 2 months.

The results of preliminary investigations are as follows:

Hb	**98 g/l**
Platelets	**100 * 109/l**
WBC	**6 * 109/l**
ESR	**50mm/hr**

On examination you note that the patient has enlarged cervical lymph nodes and palpable splenomegaly.

Which of the following conditions is most likely to be the cause of the patient's symptoms?

A. Hodgkin's lymphoma
B. Multiple myeloma
C. Acute myeloid leukaemia
D. Waldenstrom's macroglobulinaemia
E. Acute lymphoblastic leukaemia

ANSWER:
Waldenstrom's macroglobulinaemia

EXPLANATION:
Patients with Waldenstrom's macroglobulinaemia often present with issues secondary to hyperviscosity
Waldenstrom's macroglobulinaemia is a form of lymphoplasmacytoid lymphoma (LPL), characterised by a monoclonal IgM paraproteinaemia. This paraproteinaemia leads to systemic symptoms of hyperviscosity such as headaches, visual disturbances and in rarer cases, strokes and ischaemic organ damage.

Many patients often present with issues secondary to this hyperviscosity, as well as the more generalised systemic symptoms and signs common to many haematological diseases.

1) Hodgkin's lymphoma, although likely to cause cervical lymphadenopathy and splenomegaly, is not usually associated with thrombocytopaenia or issues secondary to hyperviscosity

2) Multiple myeloma often causes bony pain in areas of lesions and isn't often associated with lymphadenopathy or organomegaly

3) AML doesn't usually cause lymphadenopathy or splenomegaly.

5) ALL is less common in adults, and although capable of causing lymphadenopathy and splenomegaly, would not usually be associated with symptoms of hyperviscosity

Please see Q-74 for Waldenstrom's Macroglobulinaemia

Q-208

A 72-year-old woman 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

ANSWER:
Immunophenotyping

EXPLANATION:
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

Please see Q-83 for Chronic Lymphocytic Leukaemia

Q-209

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

ANSWER:
Causes cross-linking in DNA

EXPLANATION:
Cisplatin - causes cross-linking in DNA

Please see Q-1 for Cytotoxic Agents

Q-210

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

A. Wiskott-Aldrich syndrome
B. Common variable immunodeficiency
C. Bruton's congenital agammaglobulinaemia
D. Di George syndrome
E. Chronic granulomatous disease

ANSWER:
Chronic granulomatous disease

EXPLANATION:

Please see Q-86 for Primary Immunodeficiency

Q-211

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

ANSWER:
Haemarthrosis

EXPLANATION:

Please see Q-130 for Paroxysmal Nocturnal Haemoglobinuria

Q-212

A 56 year old man is treated with doxorubicin for transition cell carcinoma of the bladder. Which one of the following adverse effects is most characteristically associated with this drug?

A. Ototoxicity
B. Pulmonary fibrosis
C. Peripheral neuropathy
D. Cardiomyopathy
E. Haemorrhagic cystitis

ANSWER:
Cardiomyopathy

EXPLANATION:

Doxorubicin may cause cardiomyopathy

Please see Q-1 for Cytotoxic Agents

Q-213

A 67-year-old gentleman presents with the blurring of his vision. This was sudden in onset and associated with this was shortness of breath and headache which came on gradually following the blurry vision. His past medical history includes treatment of squamous cell carcinoma of the lung which has failed to shrink despite the chemotherapy. On examination, he is short of breath with bulging veins on his forehead. Fundoscopic examination reveals papilloedema. His face appears swollen. Pemberton sign is positive. You administer oxygen and called for help. What is the next immediate step in managing this?

A. Administer dexamethasone
B. IM adrenaline
C. Topical latanoprost
D. Full blood count
E. Mannitol

ANSWER:
Administer dexamethasone

EXPLANATION:

SVC obstruction can cause visual disturbances such as blurred vision
This is superior vena cava obstruction. Due to the malignancy present, the superior vena cava has been compressed by a tumour. This is confirmed by the bulging of the veins on the forehead (back pressure due to compression), the papilloedema which is a sign of raised intracranial pressure and Pemberton sign. This is when you ask a patient to raise their arms until they touch the side of their face. If they develop cyanosis or worsening of their shortness of breath or facial congestion, it is said to be positive. The next best step would be a steroid to dampen the inflammatory response to a tumour and swelling. Then either a stent or radiotherapy/ chemotherapy would be given.

IM adrenaline would be useful if this was anaphylaxis. It would not be appropriate here.

Latanoprost is a treatment for glaucoma. It is a prostaglandin analogue and serves to reduce ocular pressure. This would not be the next immediate treatment in this condition.

A full blood count will be taken, but it is not the main priority.

Mannitol would not be suitable here. It is given to reduce intracranial pressure. However, dexamethasone is more effective.

Please see Q-13 for Superior Vena Cava Obstruction

Q-214

A 54-year-old man presents to his GP with a one-month history of fever, malaise and weight loss. He also complains of abdominal fullness and early satiety. His past medical history and travel history is unremarkable and he is not on any regular medications. On examination, the GP detects splenomegaly.

The results of his full blood count and white cell differential are presented below:

Hb	**123 g/l**	**(130-180 g/l)**
MCV	**85.6 fL**	**(80-100 fL)**
Platelets	**420 * 109/l**	**(140-400 * 109/l)**
WBC	**102 * 109/l**	**(4-11 * 109/l)**
Neutrophils	**51.0 %**	**(50-70%)**
Bands	**23.0 %**	**(0-4%)**
Lymphocytes	**2.0 %**	**(20-40%)**
Monocytes	**2.0 %**	**(2-8%)**
Eosinophils	**1.0 %**	**(0-5%)**
Basophils	**3.0 %**	**(0-2%)**

What is the most likely diagnosis?

A. Acute myeloid leukaemia
B. Acute lymphocytic leukaemia
C. Chronic myeloid leukaemia
D. Chronic lymphocytic leukaemia
E. Essential thrombocytosis

ANSWER:
Chronic myeloid leukaemia

EXPLANATION:
In chronic myeloid leukaemia there is an increase in granulocytes at different stages of maturation +/- thrombocytosis
Acute myeloid leukaemia - blood tests will reveal immature blood cells (blasts).

Acute lymphocytic leukaemia - far more common in children and blood tests will reveal immature blasts.

Chronic lymphocytic leukaemia - a malignancy of the lymphoid lineage so there will be a raised lymphocyte count.

Essential thrombocytosis - although patients with essential thrombocytosis can have a raised white cell count, these patients tend to have much higher platelet counts (typically >450 * 109/l).

The white cell differential in this case demonstrates granulocytes at different stages of maturation (immature band forms and mature neutrophils) which is suggestive of chronic myeloid leukaemia. The platelet count may also be raised in these patients.

Please see Q-105 for Chronic Myeloid Leukaemia

Q-215

A 45-year-old man attends ambulatory care with a 2-month history of worsening fatigue. On further questioning he states that whilst he has lost some weight recently, he had attributed this to reduced appetite, stating that he has been feeling full after eating relatively little. On direct questioning he states that on a few occasions over the last 2 weeks he has woken feeling sweaty with damp sheets. On examination the patient has pale conjunctiva and there is a large, firm mass in the left upper quadrant of the abdomen. He is haemodynamically stable, afebrile and there are no signs of respiratory distress.

Initial bloods show:

Hb	**105 g/l**
Platelets	**150 * 109/l**
WBC	**50 * 109/l**

The F1 clerking the patient requested an abdominal CT which has been reported by the radiologist as showing massive splenomegaly.

A blood film has been sent and the patient has been discussed with the on-call haematologist who has arranged a bone marrow biopsy and cytogenetics. However, the results of these investigations are not yet available.

Which of the following findings would support a diagnosis of chronic myeloid leukaemia (CML) rather than myelofibrosis?

A. t(15;17) translocation
B. t(8;21) translocation
C. Low leucocyte alkaline phosphatase score
D. Raised leucocyte alkaline phosphatase score
E. Massive splenomegaly

ANSWER:
Low leucocyte alkaline phosphatase score

EXPLANATION:
Leucocyte alkaline phosphatase is low in CML but raised in myelofibrosis
The correct answer here is a low leucocyte alkaline phosphatase (LAP) score.

LAP is found within mature white blood cells (WBCs).

Low LAP levels are found in conditions associated with immature/undeveloped WBCs (e.g. CML), whereas pathologies associated with mature WBCs (such as myelofibrosis) cause high LAP levels.

t(15; 18) translocation is associated with acute promyelocytic leukaemia (APML)

t(8;21) translocation is associated with acute myeloid leukaemia (AML)

the Philadelphia chromosome t(9;22) creates a BCL-ABL1 fusion gene that codes for a constitutively active tyrosine kinase receptor. This is associated with 95% of CML cases and is the target for imatinib (a tyrosine kinase inhibitor).

Massive splenomegaly is seen in both CML and myelofibrosis

Please see Q-12 for Leucocyte Alkaline Phosphatase

Q-216

A 10-year-old boy is referred to you following his 7th course of antibiotics for lower respiratory tract infection in the last 6 years. He has difficult to control eczema for which he is currently on a topical steroid cream. His bloods are as follows

Hb	**139 g/l**

Platelets 65 * 109/l
WBC 12.3 * 109/l

In which of the following genes may you expect to see an abnormality?

A. WASP
B. PKD1
C. CFTR
D. HFE1
E. RET

ANSWER:
WASP

EXPLANATION:
The combination of frequent infections, eczema and thrombocytopenia are characteristic of the Wiskott-Aldrich syndrome, which is caused by an abnormality in the WASP gene.

The PKD1 gene is associated with polycystic kidney disease, CFTR with cystic fibrosis, HFE1 with haemochromatosis and RET an oncogene associated with multiple endocrine neoplasia and also Hirschsprung's disease.

Please see Q-14 for Wiskott-Aldrich Syndrome

Q-217

A 60-year-old man is known to have renal cell carcinoma and is currently undergoing treatment. He presents to the medical take with a one month history of worsening central lower back pain which he cannot manage with analgesia at home and which is worse at night. He has no other new symptoms. Which investigation should be performed next?

A. X-ray whole spine
B. CT lumbar spine
C. MRI whole spine
D. MRI lumbar spine
E. X-ray lumbar and sacral spine

ANSWER:
MRI whole spine

EXPLANATION:
An MRI whole spine should be performed in a patient suspected of spinal metastases
Spinal metastases should be high on your list of differentials for this patient. He is known to have a type of cancer which readily metastasises to the bone, and has progressive back pain. He, therefore, needs urgent imaging of his spine. MRI whole spine is preferable because patients with spinal metastases often have metastases at multiple levels within the spine. Plain radiographs and CT should not be performed as they have a lower sensitivity for revealing lesions and cannot exclude cord compression.

Imaging should be performed within 1 week if there are symptoms suspicious for spinal metastases but no neurological symptoms, and within 24 hours if there are symptoms suggestive of malignant spinal cord compression.

SPINAL METASTASES
Patients may present with spinal metastases before developing metastatic spinal cord compression. It is, therefore, important to detect these patients early before any neurological compromise develops.

Symptoms and findings
- Unrelenting lumbar back pain
- Any thoracic or cervical back pain
- Worse with sneezing, coughing or straining
- Nocturnal
- Associated with tenderness

If any neurological features are present then spinal cord compression must be suspected and acted on promptly. Without neurological features, a whole spine MRI should be completed within one week. The whole spine should be imaged as patients commonly present with multi-level disease.

Q-218

Transmission of which type of infection is most likely to occur following a platelet transfusion?

A. Syphilis
B. Malaria
C. Hepatitis B
D. Bacterial
E. HIV

ANSWER:
Bacterial

EXPLANATION:
As platelet concentrates are generally stored at room temperature they provide a more favourable environment for bacterial contamination than other blood products.

Please see Q-23 for Blood Product Transfusion Complications

Q-219

A 25-year-old female presents with recurrent sinopulmonary infections. What test is most likely to confirm a primary immunodeficiency?

A. IgG level
B. B cell level
C. T cell level
D. Complement (CH50) assay
E. IgM level

ANSWER:
IgG level

EXPLANATION:

The most common clinically significant primary immunodeficiency is common variable immunodeficiency or CVID. IgA deficiency is more common, but most are asymptomatic. CVID is characterized by reduced serum immunoglobulins and heterogeneous clinical features. A well-accepted definition of CVID includes three key features: the presence of hypogammaglobulinaemia of two or more immunoglobulin isotypes (low IgG, IgA, or IgM), recurrent sinopulmonary infections, and impaired functional antibody responses. However, IgG is more likely to be deficient than IgM.

The criteria for impaired functional antibody responses include absent isohaemagglutinins (eg. antibodies associated with blood transfusion reactions), poor responses to protein (diphtheria, tetanus) or polysaccharide vaccines (S pneumoniae), or both.

Mature B-cells are more likely to be absent in X-linked Bruton's agammaglobulinemia.

Please see Q-86 for Primary Immunodeficiency

Q-220

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)

ANSWER:

t(15;17)

EXPLANATION:

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