HAEMATOLOGY
Questions&Answers

Q-1

A 35 year old first time donor suddenly passes out as she is donating blood. She is not known to have any medical problems in the past. Which of the following steps would be the least useful in managing this adverse event?

A. **Ensure donor is adequately hydrated and has not skipped a meal**
B. **Elevating the donor's legs as this is usually due to a vasovagal syncope**
C. **Ensure haemoglobin of the donor meets the minimum requirements for donation**
D. **The donation is continued along with simultaneous normal saline infusion**
E. **The donor should be encouraged to mobilise after they have recovered**

ANSWER:
The donation is continued along with simultaneous normal saline infusion

EXPLANATION:
This question may seem tricky, but it is actually really simple. You need to read the question well; it states, 'which would be the LEAST useful in managing the adverse event'

A is correct. Blood donors should ensure they are well hydrated and have eaten well before donating blood.

B is correct. Elevation of the legs would cause more blood to return to the heart and hence more blood to be pumped to the brain.

C is correct. People should not donate blood if their haemoglobin level is below the lower limit of normal.

E is correct. The donor should be encouraged to eat, rest and continue their normal activities as soon as possible after the donation.

This leaves us with D. If a donor faints whilst giving blood, YOU IMMEDIATELY STOP THE DONATION. You should never continue bleeding the donor if an adverse event

has occurred or is about to occur.

In general, you should not take more than 30 seconds to answer these types of questions.

Q-2

A 13 year old girl has mucosal bleeding and petechial rashes. She has been feeling tired lately. She looks pale. A blood count shows:

Haemoglobin 74 g/L
White cell count 1.9 x 10^9/L
Neutrophils 0.1 x 10^9/L
Platelets 24 x 10^9/L

Blood film morphology was unremarkable. Reticulocytes are absent. A bone marrow aspirate shows a gross reduction in all haematopoietic tissue that is replaced by fat spaces. What is the SINGLE most likely underlying diagnosis?

A. **Pernicious anaemia**
B. **Chronic myeloid leukaemia**
C. **Aplastic anaemia**
D. **Acute myeloid leukaemia**
E. **Acute lymphoblastic leukaemia**

ANSWER:
Aplastic anaemia

EXPLANATION:
She has signs and symptoms of anaemia. The blood picture showspancytopenia which rules out pernicious anaemia as an underlying cause.

Normal morphology rules out the possibility of acute myeloid leukaemia,and acute lymphoblastic leukaemia.

From the age alone we can exclude chronic myeloid leukaemia as it usuallypresents at age 40 to 50 years old (middle-age)

A bone marrow aspirate that shows a gross reduction in all haemopoietictissue that is replaced by fat spaces is seen classically in aplastic anaemia.Absent reticulocytes support the diagnosis.

Aplastic anaemia
Aplastic anaemia is a rare, potentially life-threatening failure ofhaemopoiesis characterised by pancytopenia and hypoplastic marrow (themarrow stops making cells).

Causes

Most cases are autoimmune, triggered by drugs (viruses, eg parvovirus,hepatitis) or irradiation.

Presentation
Aplastic anaemia can present abruptly over, or insidiously over, weeks tomonths. Clinical manifestations are proportional to the peripheral-blood cytopeniasand include:
• *Symptoms of anaemia* (pallor, headache, palpitations, dyspnoea,fatigue, or ankle oedema) Note: Anaemic symptoms are usually lesssevere due to the chronic onset
• *Symptoms of thrombocytopenia* (skin or mucosal haemorrhage,visual disturbance due to retinal haemorrhage, petechial rashes)
• *Infection* (a less common presentation) particularly upper and lowerrespiratory tracts, skin, mouth, and peri-anal
• There is no lymphadenopathy or hepatosplenomegaly (in theabsence of infection).

Diagnostic tests:
Marrow examination is needed for the diagnosis

Note: To define aplastic anaemia based on FBC and bone marrow findings, at least two of the following must be present:
• Haemoglobin <10 g/dL
• Platelet count < 50 x 109/L
• Neutrophil count <1.5 x 109/L

It is also important to note that the blood film morphology is unremarkable which differentiates it from some other types of leukaemias.

Q-3

A 5 year old child presents with fever and pallor. His parents say he always feels tired and is not as active as the other children around his age. On examination, splenomegaly was noted. Blood results show:

Hb 7 g/dL
WCC 2 x 10^9/L
Platelets 42 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Acute myeloid leukaemia**
B. **Acute lymphoblastic leukaemia**
C. **Chronic myeloid leukaemia**
D. **Chronic lymphocytic leukaemia**
E. **Hodgkin's lymphoma**

ANSWER:
Acute lymphoblastic leukaemia

EXPLANATION:

Acute lymphoblastic leukaemia (ALL)

Aetiology

Most cases of acute leukaemia arise with no apparent cause. There areseveral well known associations with the development of acute leukaemiathat are sometimes present. These include radiation exposure,chemotherapeutic agents, as well as some retroviruses.

Clinical Presentation

The most common presentation results from the effects of the leukaemicblast cells crowding out the normal marrow cells, resulting in symptoms ofpancytopenia even if the total white blood cell count is normal.

• Fatigue from anaemia is the most common presenting complaint.
• Bleeding, petechiae, purpura or ecchymoses (due tothrombocytopenia)
• Recurrent and severe infections (oral, throat, skin, perianalinfections commonly). This is because of the underproduction orabnormal function of white blood cells.
• Left upper quadrant fullness and early satiety due to splenomegaly(10-20%)

Acute lymphocytic leukaemia (ALL) is more common in children, and acutemyelogenous leukaemia (AML) is more common in adults, but they areindistinguishable clinically. This means you cannot determine the diagnosisonly from the clinical presentation.

ALL is more often associated with infiltration of other organs, but AML cando it as well. Enlargement of the liver, spleen, and lymph nodes and bonepain are common at presentation.

Diagnosis

The FBC is the first clue to the diagnosis. Depression of all three cell lines is common at presentation.

FBC

• Anaemia is usual and Hb may be below 5 g/L
• The white cell count can be low, normal, or elevated
• Thrombocytopenia

Many other disorders can present as pancytopenia similar to leukaemiasuch as aplastic anaemia, infections involving the marrow, metastaticcancer involving the marrow, vitamin B12 deficiency, SLE, hypersplenism,and myelofibrosis. However, none of these will have leukaemic blastscirculating in the peripheral blood. Although pancytopenia can cause all ofthe above, in PLAB, when pancytopenia is in the options, it is usuallyleukaemia, or aplastic anaemia.

A bone marrow biopsy showing numerous blasts confirms the diagnosis ofacute leukaemia.

It is very unlikely that the PLAB questions would ask you to differentiate theAML from ALL using specific test. However, if a child (young age) is givenwith signs and symptoms of pancytopenia, ALL would be the most likely asit is the commonest childhood leukaemia.

Note:
• ALL is the commonest childhood leukaemia. Peak age is 2–4 yearsold.
• The Philadelphia chromosome occurs in 15–30% (mostly adults) andis associated with a poor prognosis.

LEUKAEMIA COMPARISONS

ACUTE LEUKEMIAS	
Acute Lymphoblastic Leukaemia (ALL)	**Acute Myeloid Leukaemia (AML)**
• Fatigue from anaemia • Bleeding caused by thrombocytopenia • Recurrent and severe infections • Splenomegaly Acute lymphocytic leukaemia (ALL) is more common in children, and acute myelogenous leukaemia (AML) is more common in adults, but they are indistinguishable clinically In the exam, when pancytopenia is in the options, it is usually leukaemia, or aplastic anaemia. A bone marrow biopsy showing numerous blasts confirms the diagnosis of acute leukaemia	• Symptoms of anaemia • Bleeding caused by thrombocytopenia • Infection • Gingivitis is common, with swollen, bleeding gums FBC: Auer rods Total WBC count is often high. Neutrophils are usually depleted and blast cells are seen in their place Bone marrow aspiration is the diagnostic procedure
CHRONIC LEUKAEMIAS	
Chronic Lymphocytic Leukaemia (CLL)	**Chronic Myeloid Leukaemia (CML)**
CLL can often present as an asymptomatic elevation of white cells found on routine evaluation of patients during investigations for other health problems. These patients are exclusively older (majority over 50 years old) When patients do have signs and symptoms they are usually non-specific When should you suspect CLL? When an older patient has marked elevation in white cell count with marked	Mnemonic: CML – Crazy Massive Large Spleen Usually presents at age 40 to 50 years old (middle-age) • Fatigue (due to anaemia) • Weight loss • Night sweats • Massive splenomegaly • Gout due to rapid cell turnover • Leukocytosis is common (often > 100 x 10^9/L

lymphocytic predominance. “Smudge cells” are seen on smear	The characteristic feature in CML is the Ph chromosome, found in about 90% of cases. In the exam, look for massive enlargement of spleen

Q-4

A 33 year old woman complains of tiredness for the last 3 months. On routine blood test, she is found to have a haemoglobin of 85 g/L, low mean cell volume, and low ferritin. What is the SINGLE most likely diagnosis?

A. Iron deficiency
B. Folate deficiency
C. Thalassaemia
D. Anaemia of chronic disease
E. Sideroblastic anaemia

ANSWER:
Iron deficiency

EXPLANATION:
The table below is a short summary of common findings given in the exam to help you differentiate between the cause of the anaemia.

Microcytic	**Macrocytic**
Iron deficiency • Fe ↓ • Ferritin ↓ • TIBC ↑ *Thalassamia* • Normal iron studies • Electrophoresis to see type *Anaemia of chronic disease* • Fe ↓ • Ferritin ↑ • TIBC ↓ *Sideroblastic anaemia* • Fe ↑ • Ferritin ↑ • In sideroblastic anaemia, the body has iron available but cannot incorporate it into haemoglobin	**Megaloblastic** • Hypersegmented neutrophils *B12 deficiency* • Neurological problems • Subacute combined degeneration of the cord • Serum B12 ↓ *Folate deficiency* • Serum folate ↓ **Normoblastic (Non-megaloblastic** • Alcohol • Liver disease • Hypothyroidism • Pregnancy • Reticulocytosis • Myelodysplasia • Drugs: cytotoxics

Normocytic (normal MCV)

- Haemolytic anaemias: Bloods in general show ↑ LDH, ↑ unconjugated bilirubin, ↓haptoglobin, ↑ reticulocytes

Sickle cell

- Blood smear → Sickle cells
- Sickle solubility test → This test detects the presence of haemoglobin S but does not distinguish between sickle cell disease and trait
- Hb electrophoresis → For asymptomatic patients to see if patient has trait
- Treatment: Acute → IV fluids, morphine, O2, antibiotics
- Prophylaxis → Hydroxyurea. Also needs pneumococcal vaccines

Autoimmune haemolysis

- COOMBS test
- Treat with steroids

Hereditary spherocytosis

- Blood film → spherocytes
- Osmotic fragility test
- Treatment: Splenectomy

G6PD deficiency

- Blood film → Heinz bodies
- Check G6PD levels
- Treatment: stop offending drugs

Q-5

A 41 year old man has fatigue and palpitations. Physical examination reveals a red sore tongue, angular stomatitis and koilonychia. His blood tests show:

Haemoglobin 85 g/L
Mean cell volume 75 fL

What is the SINGLE most likely diagnosis?

A. **Folate deficiency**
B. **Vitamin B12 deficiency**
C. **Iron deficiency**
D. **Vitamin E deficiency**
E. **Haemolytic anaemia**

ANSWER:
Iron deficiency

EXPLANATION:
Angular stomatitis, sore red tongue can ben seen in both B12 deficiency andiron deficiency although angular stomatitis is more of a sign of irondeficiency. Koilonychia is usually seen in iron deficiency.

But the key to the question is the mean cell volume. As this is decreased, itcannot be B12 deficiency or folate deficiency. Iron deficiency leads tomicrocytic anaemia so we would expect the MCV to be low.

Iron-deficiency anaemia
Aetiology

- Blood loss from the gastrointestinal (GI) tract is the most commoncause of iron-deficiency anaemia in adult men and postmenopausalwomen
- Blood loss due to menorrhagia is the most common cause of irondeficiency in premenopausal women
- In tropical countries, infestation of the gut may cause irondeficiencyanaemia , especially with hookworm and schistosomiasis
- *Common causes of blood loss include:*
- Non-steroidal anti-inflammatory drug (NSAID) use
- Colonic carcinoma
- Gastric carcinoma
- Gastric or duodenal ulceration
- Dietary inadequacy
- Failure of iron absorption: Malabsorption conditions such as coeliacdisease
- Excessive requirements for iron: Pregnancy

Laboratory tests

• Low Haemoglobin
• Low Mean cell volume (MCV)
• Low Mean cell haemoglobin concentration (MCHC)
• High Red cell distribution width (RDW)
• Low serum ferritin
• High Total iron-binding capacity

The above laboratory test are important to remember for PLAB as they maybe asked

Q-6

A 69 year old male presented to Accident & Emergency following a fall. He had slippd and falledn in his home and his daughter had rushed him immediately to A&E. His past medical history is significant for atrial fibrillation, which he takes warfarin and atenolol for. He complains of a severe headache which he says is getting worse. There is a small, tender bump on the right side of his head. His Glasgow coma scale score is 15/15. A CT scan was done which shows a 1 cm by 2 cm right sided cerebral haematoma. Blood tests were also done and the results are as follows:

Haemoglobin 158 g/L (130-180 g/L)
Platelets 253 x 10^9/L (150-400 x 10^9/L)
Prothrombin time (PT) 19 secs (10-14 secs)
Activated partial thromboplastin time (APTT) 39 secs (35-45 secs)

International normalized ratio (INR) 3.3 (0.8-1.2)

Following the results of the CT scan and the results of the blood tests, he was admitted and 5 mg of vitamin K1 was given intravenously. What is the SINGLE next best treatment for this patient?

A. **Intravenous mannitol**
B. **Intravenous prothrombin complex concentrate**
C. **Intravenous blood transfusion**
D. **Intravenous fresh frozen plasma**
E. **Intravenous prothrombin complex concentrate and fresh frozen plasma**

ANSWER:
Intravenous prothrombin complex concentrate

EXPLANATION:
This patint has an INR (international normalised ratio) that is not within the therapeutic range and he has a major bleed. For the purposes of the exam, a major bleed is an intracranial or a gastrointestinal haemorrhage and a minor bleed is haematuria or epistaxis.

If INR is higher than the target with a major bleed:

- Stop warfarin
- Give intravenous vitamin K 5 mg
- Prothrombin complex concentrate – if not available then give fresh frozen plasma

WARFARIN AND HIGH INR MANAGEMENT
NICE CKS has given clear guidance on actions required if the INR is above the target range.

For major bleeding – stop warfarin, administer intravenous vitamin K1 (phytomenadione), administer prothrombin complex concentrate – if not available then give fresh frozen plasma

For INR more than 8 with minor or no bleeding – stop warfarin, administer intravenous or oral vitamin K1 (phytomenadione)

For INR between 6 and 8 with minor or no bleeding – stop warfarin, restart when INR less than 5.

For INR between 5 and 6 but more than 0.5 units above the target range – reduce the dose, or stop warfarin, restart when INR less than 5

For INR above target range but less than 5 – reduce or omit one or two doses and measure INR in 2 to 3 days.

Q-7

A 29 year old woman at 28 weeks gestation comes in for an antenatal visit. Her blood tests reveal:

Hb: 11.0 g/dL
MCHC: normal range
MHC: normal

What is the SINGLE best explanation for these blood results?

A. **Iron deficiency anaemia**
B. **Folate deficiency anaemia**
C. **Anaemia of chronic disease**
D. **Normal physiological phenomenon**
E. **Autoimmune anaemia**

ANSWER:
Normal physiological phenomenon

EXPLANATION:
The British Committee for Standards in Haematology has defined anaemia inpregnancy as the following values
Hb levels of:
<11.0g/dl in the first trimester
<10.5 g/dl in the second and third trimesters
<10.0 g/dl in the postpartum period.

Normal physiological changes in pregnancy

Haematological changes

- Plasma volume increases over the course of pregnancy by about50%. Dilutional anaemia is caused by the rise in plasma volume.Elevated erythropoietin levels increase the total red cell mass bythe end of the second trimester but haemoglobin concentrationsnever reach pre-pregnancy levels.
- Usually mean corpuscular volume (MCV) and mean corpuscularhaemoglobin concentration (MCHC) are unaffected.
- Serum iron falls during pregnancy whilst transferrin and total ironbinding capacity rise.

Knowing the new British criteria for diagnosing anaemia in pregnancy isextremely important for the PLAB 1 exam as is knowing the normalphysiological changes in pregnancy. Many people get caught out with someof these physiological changes and class them as pathological whereas infact, they are completely normal in pregnancy.

Q-8

A 67 year old man with history of weight loss complains of hoarseness of voice.

Chest x-ray reveals opacity in the right upper mediastinum. He denies any history of difficulty breathing. What is the SINGLE most appropriate investigation?

- **A. Laryngoscopy**
- **B. Bronchoscopy**
- **C. Lymph node biopsy**
- **D. Bronchoalveolar lavage**
- **E. Barium swallow**

ANSWER:
Lymph node biopsy

EXPLANATION:
Mediastinal masses are frequent and are sometimes discovered on a routine CXR in lymphoma.

Tissue diagnosis is the best way to diagnose lymphoma. Lymph node excision biopsy is what is usually done.

Q-9

A 21 year old man presents with mild jaundice.

Haemoglobin 75 g/L
Reticulocytes 7%

There are spherocytes seen on the blood film. He has no past medical history of any significance. What is the SINGLE most appropriate investigation?

- **A. G6PD enzyme assay**
- **B. Direct Coombs test**
- **C. Indirect Coombs test**
- **D. Bone marrow biopsy**
- **E. Sickle solubility test**

ANSWER:
Direct Coombs test

EXPLANATION:
The likely diagnosis here is the warm antibody induced haemolysis type of autoimmune haemolytic anaemia. Most cases are idiopathic with no underlying pathology. The low haemoglobin and high reticulocytes fit the picture. Mild jaundice and spherocytes can also be seen.

Direct Coombs test is the investigation of choice.

Autoimmune haemolytic anaemia
This occurs when RBCs react with autoantibody with or without a complement which leads to premature destruction of RBCs by reticuloendothelial system.

Types of autoimmune haemolytic anaemia
- Warm antibody type:
  - Idiopathic
  - Secondary to other autoimmune diseases e.g. Systemic lupus erythematosus (SLE)
  - Secondary to lymphoproliferative diseases e.g. Lymphoma, Chronic lymphatic leukaemia (CLL)
- Cold antibody type:
  - Idiopathic
  - Mycoplasma pneumoniae
  - Infectious mononucleosis

Warm antibody induced haemolysis
- Most cases are idiopathic with no underlying pathology
- Affects predominantly individuals >50 years of age
- Clinical features
  - Highly variable symptoms, asymptomatic or severely anaemic
  - Mild jaundice
  - Splenomegaly
- Diagnosis
  - Anaemia
  - Spherocytes on peripheral blood film
  - Increased reticulocytes
  - Detect on direct Coombs test

Cold haemagglutinin disease (CHAD)
- Describes syndrome associated with acrocyanosis in cold weather due to RBC agglutinates in blood vessels of skin. Caused by RBC antibody that reacts most strongly at temperatures below 32°C.
- May be idiopathic or secondary to infection with Mycoplasma or EBV (infectious mononucleosis)
- Clinical features
  - Acrocyanosis (blue discoloration of extremities e.g. fingers, toes) in cold conditions
  - Splenomegaly
- Diagnosis
  - Anaemia
  - Increased reticulocytes
  - Positive direct Coombs test

Q-10

A 47 year old man who is on warfarin therapy is due for a hemicolectomy. He is

on warfarin for recurrent pulmonary embolism. What advice would you give him prior to his surgery?

A. **Continue with warfarin**
B. **Continue with warfarin and add heparin**
C. **Stop warfarin and start aspirin**
D. **Stop warfarin and start heparin**
E. **Stop warfarin**

ANSWER:
Stop warfarin and start heparin

EXPLANATION:
Warfarin should always be stopped 5 days before planned surgery. Heparin is used instead of warfarin prior to surgery in patients with intermediate to high risk of thromboembolism, recent TIA or patients with mechanical cardiac valves.

Surgery and Warfarin
If the person needs to have surgery or any other invasive procedure, they may need to temporarily stop taking warfarin.

Surgery — in general, warfarin is usually stopped 5 days before planned surgery, and once the person's international normalized ratio (INR) is less than 1.5 surgery can go ahead.

Warfarin is usually resumed at the normal dose on the evening of surgery or the next day if haemostasis is adequate.

(In practice, you would need to adhere to local guidelines in Perioperative Bridging of Warfarin in Adult Patients Undergoing Elective Surgery). See example of local guidelines of guys and st thomas.)

Q-11

A 62 year old man presents with bone pain at his ribs and back pain which have been present for the last couple of months. He has been feeling tired lately and finds himself always thirsty. Blood tests were requested on his last visit which show:

Haemoglobin 90 g/L
Calcium 4.0 mmol/L
Alkaline phosphatase (ALP) 118 U/L
Erythrocyte sedimentation rate (ESR) 88 mm/h
eGFR 45

What cell type is most likely to be found in abundance in the bone marrow?

A. **Plasma cell**
B. **Myeloid cell**
C. **Bence-Jones protein**
D. **Megakaryocytyes**
E. **Reticulocytes**

ANSWER:
Plasma cell

EXPLANATION:
The clinical picture here is one of multiple myeloma. Multiple myeloma is a clonal abnormality of plasma cells. Bone pain that is at the back and ribs are common presentations. Hypercalcaemia and an elevated ESR are features of multiple myeloma. Around 50% of patients with multiple myeloma would have renal impairment as seen in this stem by having an eGFR of 45.

Bence-Jones is a protein not a cell.

MULTIPLE MYELOMA
A clonal abnormality of plasma cells resulting in their overproduction replacing the bone marrow as well as the production of large quantities of functionless immunoglobulins.

Clinical Presentation
- Bone disease
  - Bone pain is the most common clinical manifestation.
  - This is most commonly in the back and the ribs, secondary to pathologic fractures.
- Recurrent bacterial infection
  - Due to abnormal immunoglobulin production which are functionally impaired *Remember, although there are large quantities of immunoglobulins, they do not function well)*
- Renal failure
- Anaemia → may present with weakness, fatigue, and pallor
- Hypercalcaemia → may present with polyuria, polydipsia, and altered mental status

Rarely, symptoms of a hyperviscosity syndrome such as blurry vision, and confusion, may occur.

Diagnosis
- Although a normochromic, normocytic anaemia is the most common laboratory finding, this is not specific for myeloma.
- A serum protein electrophoresis with a markedly elevated monoclonal immunoglobulin spike is present in almost all cases
- Urine protein electrophoresis: looks for the presence of Bence Jones' protein.
- Plain x-ray of the skeletal system and skull will reveal the punched out lytic lesion

caused by the overproduction of osteoclast activating factor from the plasma cells.
- Hypercalcaemia from the destruction of bone. Note that the hypercalcaemia is associated with normal alkaline phosphatase.
- Elevation in the BUN and creatinine from the damage to the kidney from the immunoglobulins
- A bone marrow biopsy with abundance of plasma cells confirms a diagnosis of multiple myeloma
- Rouleaux formation can be seen on blood film (rouleaux means a cylindrical packet of coins)

Management
This is beyond what will be asked in PLAB part 1

Q-12

A 39 year old woman presents with yellowing of her sclera and the complaint of feeling tired all the time. She has no other complaints however, she mentions that she had an upper respiratory tract infection a week ago. Her blood tests are as follows:

Haemoglobin: 95 g/L
Bilirubin 28 micromol/L
Mean cell volume (MCV): 98 fL
Alanine transferase (ALT): 25 U/L
Aspartate transaminase (AST): 23 U/L
Alkaline phosphatase (ALP): 72 U/L
Gamma glutamyl transferase (GGT): 33 U/L

A peripheral blood smear is significant for polychromasia and scattered spherocytes but no fragmented red blood cells or target cells were seen. What is the SINGLE best diagnostic investigation?

A. Direct antiglobulin test
B. Indirect antiglobulin test
C. Osmotic fragility test
D. Bone marrow aspiration
E. Ultrasound of spleen

ANSWER:
Direct antiglobulin test

EXPLANATION:
This patient has a haemolytic anaemia. A direct antiglobulin test is a synonym for a direct Coombs test.

The direct Coombs test is used to test for autoimmune haemolytic anaemia or in other words any condition of an anaemia caused by immune system lysis or destruction of red

blood cells.

Some examples of diseases that test positive for a direct Coombs test include alloimmune haemolysis (such as Rhesus disease), autoimmune haemoloysis (such as systemic lupus erythematosus) or drug-induced immune-mediated haemolysis.

The term “polychramasia” used in this stem refers to a disorder where there is an abnormally high amount of immature red blood cells. A haemolytic anaemia such as this case (or any other form of anaemia) would trigger erythropoeitin release and increase the rate of which red blood cells are produced and released from the bone marrow. When levels of erythropoeitin are high, immature red cells would be released into the bloodstream.

COOMBS TEST
There are two Coombs tests:
1. The direct Coombs test (DCT, also known as direct antiglobulin test or DAT)
2. The indirect Coombs test (also known as indirect antiglobulin test or IAT)

Direct Coombs test
- Used to test for **autoimmune haemolytic anaemia**
  - It is used to detect these antibodies or complement proteins that are bound to the surface of red blood cells. *Basically, it is used to test patients RED BLOOD CELLS.*
  - A positive Coombs test indicates that an immune mechanism is attacking the patient's own RBCs. Examples:
    - ***Common examples of alloimmune haemolysis***
      - Haemolytic disease of the newborn (also known as HDN or erythroblastosis fetalis)
      - Rh D haemolytic disease of the newborn (also known as Rh disease)
      - ABO haemolytic disease of the newborn
      - Alloimmune haemolytic transfusion reactions
    - ***Common examples of autoimmune haemolysis***
      - Cold agglutinin disease : Infectious mononucleosis
    - ***Drug-induced immune-mediated hemolysis***
      - Penicillins, Cephalosporins

Indirect Coombs test
- Used in **prenatal testing of pregnant women** and in **testing blood prior to a blood transfusion**.
  - It detects antibodies against RBCs that are present unbound in the patient's serum. In this case, serum is extracted from the blood sample taken from the patient and tested. *Basically, it is used to test patients SERUM (not red blood cells)*
  - If agglutination occurs, the indirect Coombs test is positive.
    - ***Examples of use:***

o Blood transfusion preparation : Antibody screening, cross matching
o Antenatal antibody screening: to screen pregnant women for IgG antibodies that are likely to pass through the placenta into the fetal blood and cause haemolytic disease of the newborn

Direct Coombs test	**Indirect Coombs test**
Tests a patient's RED BLOOD CELLS How the test works: 1. Blood sample is taken 2. The RBCs are washed (patient's plasma is removed) 3. RBCs are incubated with anti-human globulin (Coombs reagent) 4. If this produces agglutination of RBCs, the direct Coombs test is positive. 5. A positive Coombs test indicates that an immune mechanism is attacking the patient's own RBCs	Tests a patient's SERUM How the test works 1. Blood sample is taken 2. Serum is extracted from the blood sample 3. Serum incubated with RBCs of known antigenicity, that is, RBCs with known reference values from another patient's blood sample. 4. Anti-human globulin is then added 5. If agglutination occurs, the indirect Coombs test is positive.

Q-13

A 6 year old boy is brought to the hospital by his mother with bleeding from his gums and nose. His mother complains that he has been having recurrent sore throats that come and go in last couple of months. Pale conjunctivae is noticed on examination. What is the SINGLE most likely single cell type associated with his diagnosis?

A. Clumped platelets
B. Microcytes
C. Granulocyte without blast cells
D. Blast cells
E. Mature lymphocytes

ANSWER:
Blast cells

EXPLANATION:
Before looking at the cell types, think of the diagnosis. The most likely diagnosis here is Acute lymphoblastic leukaemia (ALL) as he is young, suffering recurrent infections (due to abnormal WBCs), and having pale conjunctiva (anaemia). The bleeding gums and nosebleeds tell you that he has thrombocytopaenia.

Acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML) both have numerous blast cells.

Acute lymphoblastic leukaemia (ALL)

Aetiology

Most cases of acute leukaemia arise with no apparent cause. There are several well known associations with the development of acute leukaemia that are sometimes present. These include radiation exposure, chemotherapeutic agents, as well as some retroviruses.

Clinical Presentation
The most common presentation results from the effects of the leukaemic blast cells crowding out the normal marrow cells, resulting in symptoms of pancytopenia even if the total white blood cell count is normal.
• Fatigue from anaemia is the most common presenting complaint.
• Bleeding, petechiae, purpura or ecchymoses (due to thrombocytopenia)
• Recurrent and severe infections (oral, throat, skin, perianal infections commonly). This is because of the underproduction or abnormal function of white blood cells.
• Left upper quadrant fullness and early satiety due to splenomegaly (10-20%)

Acute lymphocytic leukaemia (ALL) is more common in children, and acute myelogenous leukaemia (AML) is more common in adults, but they are indistinguishable clinically. This means you cannot determine the diagnosis only from the clinical presentation.

ALL is more often associated with infiltration of other organs, but AML can do it as well. Enlargement of the liver, spleen, and lymph nodes and bone pain are common at presentation.

Diagnosis
The FBC is the first clue to the diagnosis. Depression of all three cell lines is common at presentation.

FBC
• Anaemia is usual and Hb may be below 5 g/L
• The white cell count can be low, normal, or elevated
• Thrombocytopenia

Many other disorders can present as pancytopenia similar to leukaemia such as aplastic anaemia, infections involving the marrow, metastatic cancer involving the marrow, vitamin B12 deficiency, SLE, hypersplenism, and myelofibrosis. However, none of these will have leukaemic blasts circulating in the peripheral blood. Although pancytopenia can cause all of the above, in PLAB, when pancytopenia is in the options, it is usually leukaemia, or aplastic anaemia.

A bone marrow biopsy showing numerous blasts confirms the diagnosis of acute leukaemia.

It is very unlikely that the PLAB questions would ask you to differentiate the AML from ALL using specific test. However, if a child (young age) is given with signs and

symptoms of pancytopenia, ALL would be the most likely as it is the commonest childhood leukaemia.

Note:
• ALL is the commonest childhood leukaemia. Peak age is 2–4 years old.
• The Philadelphia chromosome occurs in 15–30% (mostly adults) and is associated with a poor prognosis.

Q-14

A 55 year old man presents with "rubbery" painless lump on his neck. He also has significant weight loss over the past 6 months, fever and night sweats. The diagnosis of Hodgkin's lymphoma was later confirmed with a lymph node excision biopsy. What type of cell is associated with Hodgkin's lymphoma?

A. T-cells
B. Reed-Sternberg cells
C. B-cells
D. Macrophages
E. Auer rods

ANSWER:
Reed-Sternberg cells

EXPLANATION:
A very easy and direct question. The diagnostic cells in Hodgkin's lymphoma are Reed-Sternberg cells.

HODGKIN'S LYMPHOMA
Hodgkin's lymphoma is a malignant tumour of the lymphatic system that is characterised histologically by the presence of multinucleated giant cells (Reed-Sternberg cells)

There are subtypes of Hodgkin's lymphoma but these are not commonly asked.

Presentation
• Enlarged but otherwise asymptomatic lymph node, typically in the lower neck or supraclavicular region.
  • The lymph nodes are described as painless, non-tender, and 'rubbery'
• Mediastinal masses are sometimes discovered on a routine CXR.
• Systemic symptoms of drenching night sweats, unexplained fever >38°C, and weight loss of >10% over six months are termed B symptoms and are identified in approximately 25% of patients.
• Pruritus
• Lethargy
• Other findingsinclude splenomegaly (30%) and hepatomegaly (10%)
• Superior vena cava syndrome (SVC syndrome may occur due to ta compresion from

mediastinal lymph node

Diagnosis
• Tissue diagnosis: Lymph node excision biopsy if possible

Q-15

A 90 year old woman is brought to the hospital complaining of back pain and has been referred to the orthopaedic surgeon. She has been saying that her mother is due to visit her today and that somebody must have broken her lower back as she is in agony. Her blood tests show:

Haemoglobin 109 g/L
Serum urea 7.5 mmol/L
Serum creatinine 293 micromol/L
Serum calcium 3.02 mmol/L

What SINGLE investigations is most likely to lead to a diagnosis?

A. **Ultrasound KUB**
B. **X-ray Spine**
C. **Intravenous urogram**
D. **Urine protein electrophoresis to look for Bence-Jones protein**
E. **Mental state exam**

ANSWER:
Urine protein electrophoresis to look for Bence-Jones protein

EXPLANATION:
Multiple myeloma is the suspected diagnosis here and needs to be dealt with by the haematologist.

Elevation in the BUN and creatinine is seen due to the damage to the kidney from the immunoglobulins. Anaemia is the most common laboratory finding in multiple myeloma.

She is 90 years old. It is unlikely that her mother is still alive. The statement that she thinks her mother is going to visit her today points to some sort of confusion. This confusion can be seen in multiple myeloma due to hyperviscosity and also hypercalcaemia.

Q-16

A 63 year old man presents with back pain, polydipsia and polyuria which have been present for the last couple of weeks. He complains of being tired lately. He has recurrent nose bleeds which started 6 months ago. His previous full blood count shows a normocytic, normochromic anaemia. His eGFR was found to be 40. Monoclonal proteins were seen during further investigations of which he was referred to secondary care. What is the SINGLE most appropriate investigation to perform next that would lead to a diagnosis?

A. **Bone marrow biopsy**
B. **Vitamin D levels**
C. **Electrophoresis**
D. **Computed tomography scan of whole body**
E. **Renal biopsy**

ANSWER:
Bone marrow biopsy

EXPLANATION:
The signs and symptoms together with the normochromic, normocytic anaemia are indicative of multiple myeloma. Nosebleeds occur because the abnormal plasma cells found in multiple myeloma inhibit the production of platelets.

Electrophoresis is already performed in this quesiton as monoclonal proteins can only be seen during electrophoresis.

Once monoclonal proteins are found on electrophoresis, patients are usually referred to haematology under the 2 week wait pathway. 2 week wait pathway means that you are considering malignancy and the patient would be seen in secondary caere within 2 weeks. Secondary care would arrange a bone marrow biopsy, skeletal survey and 24 hour urine collection before constructing a plan. Amongst the options of investigations, bone marrow biopsy would show an increased amount of plasma cells.

Q-17

A 32 year old woman has just had a laparoscopic cholecystectomy a few hours ago. The nurse notices that she has a sore left leg with swollen varicose vein extending from the mid-thigh to the ankle. She informs the nurse that she has had that before surgery. She has no calf tenderness or calf swelling. What is the SINGLE most appropriate action?

A. **Prescribe nonsteroidal anti-inflammatory drugs (NSAIDs)**
B. **Prescribe antibiotics**
C. **Request for D-dimers**
D. **Request thrombophilia screen**
E. **Reassure**

ANSWER:
Prescribe nonsteroidal anti-inflammatory drugs (NSAIDs)

EXPLANATION:
The condition that is described here is superficial thrombophlebitis. NSAIDs have been shown to be effective in managing the pain for superficial thrombophlebitis.

Thrombophilia is not required for investigation of patients with superficial thrombophlebitis.

D-dimers would not be beneficial as it would usually be high after surgery. Furthermore, it would be raised in both superficial thrombophlebitis and deep vein thrombosis.

SUPERFICIAL THROMBOPHLEBITIS

Superficial thrombophlebitis also known as superficial venous thrombosis occurs when there is both thrombosis and inflammation of superficial veins most commonly affecting the great saphenous vein of the legs.

The vast majority of superficial thrombophlebitis do not require antibiotics as they are not infective. However, if there are signs of infection, flucloxacillin can be used.

Treatment for superficial thrombophlebitis evolves around

- Symptom reduction
- Prevention of deep venous thrombosis and pulmonary embolism

Symptom reduction

- Treatment of pain
  - Oral or topical NSAIDs
  - Paracetamol
- Management of swelling
  - Compression stockings
  - Leg elevation

Prevention of deep venous thrombosis and pulmonary embolism

- If has other risk factors for a DVT present, subcutaneous low molecular weight heparin or fondaparinux can be used to prevent DVT
- If no other risk factors for DVT, low molecular weight heparin or fondaparinux not required.
- If thrombosis is within 3 cm of the saphenofemoral junction, the British Haematology Society guidelines recommend considering patients for treatment with low molecular weight heparin or fondaparinux.

Are ultrasounds needed?

The short answer is yes!

- SIGN guidelines state that if there are clinical signs of superficial thrombophlebitis affecting the proximal long saphenous vein, ultrasound scan is required to exclude concurrent deep vein thrombosis.
- British Haematology Society guidelines state that patients with lower limb superficial venous thrombosis should have ultrasound assessment to exclude deep venous thrombosis, particularly if affecting the proximal long saphenous vein.

Are D-dimers required?

D-dimer is of little value as it cannot differentiate superficial from deep venous thrombosis. It is seen elevated in both.

A 66 year old woman is confused, and lethargic. Her son reports gradual confusion over the last 4 months. On examination, she looks pale. Blood tests have been done which shows a megaloblastic anaemia. Both B12 deficiency and folate deficiency was diagnosed on further investigation. What is the SINGLE most likely treatment for her anaemia?

A. **Oral folic acid and start intramuscular vitamin B12 when folic acid levels are normal**
B. **Intramuscular vitamin B12 and start oral folic acid when vitamin B12 levels are normal**
C. **Oral folic acid only**
D. **Intramuscular vitamin B12 only**
E. **Iron tablets**

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

EXPLANATION:
It is important in a patient who is deficient in both vitamin B12 and folic acid to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord. Once the vitamin B12 levels are normal, then start oral folic acid

FOLATE DEFICIENCY
Folate deficiency represents the other main deficiency cause of megaloblastic anaemia. (The other main deficiency is B12 deficiency).

What are megaloblastic anaemias?
- A heterogeneous group of disorders sharing common morphological characteristics. Erythrocytes are larger and have higher nuclear-to-cytoplasmic ratios compared to normoblastic cells.
  - Neutrophils can be hypersegmented
  - Megakaryocytes are abnormal.

Causes:
Dietary deficiency
• Malabsorption (eg, coeliac disease, jejunal resection, inflammatory bowel disease).
• Poor intake
• Alcohol excess (also causes impaired utilisation)

Antifolate drugs
Example: Sulfasalazine, methotrexate

Diagnosis:
Haematological features for folate deficiency are indistinguishable from those of B12 deficiency (macrocytic, megaloblastic anaemia). Distinction is on basis of demonstration

of reduced red cell and serum folate. Vitamin B12 levels should be assessed at the same time due to the close relationship in metabolism.

In PLAB, one distinction that may help you choose between B12 and folate deficiency is the diet. Good food sources of folate include broccoli, brussels sprouts, asparagus, peas (basically vegetables). Thus if the given scenario is a vegetarian, it is unlikely that he is suffering from folate deficiency. In that case, pick B12 deficiency.

Management:
Folic acid 5 mg/d PO for 4 months.

Note: 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. Once the vitamin B12 levels are normal, then start oral folic acid.

Q-19

A 10 year old girl presents with pallor and features of renal failure. She has haematuria as well as proteinuria. The serum urea and creatinine are elevated. These symptoms started after an episode of bloody diarrhoea 4 days ago. What is the SINGLE most likely diagnosis?

A. Thrombotic thrombocytopaenic purpura
B. Haemolytic uraemic syndrome
C. Idiopathic thrombocytopaenic purpura
D. Henoch-Schonlein purpura
E. Acute renal failure

ANSWER:
Haemolytic uraemic syndrome

EXPLANATION:
Most cases of haemolytic uremic syndrome develop in children after 2 to 14 days of diarrhoea often bloody, due to infection with a certain strain of E. coli. Common features include abdominal pain, fever, features of renal failure like nausea/vomiting can also occur.

Renal function and electrolytes would show a rise in urea and creatinine. This is due to dehydration but, if associated with haemolysis and thrombocytopenia, then it would indicate the onset of HUS.

A brief description:

Henoch-Schönlein purpura (HSP) Vs Haemolytic uraemic syndrome (HUS) Vs Thrombotic thrombocytopenic purpura (TTP)

Henoch-Scholein Purpura	Haemolytic Uraemic Syndrome	Thrombotic Thrombocytopenic

		Purpura
- Purpura - Abdomnial pain - Arthritis - Glomerulonephritis - Periarticular disease - Periarticular oedema Features of IgA nephropathy may occur e.g. haematuria, renal failure	Triad 1. Acute renal failure 2. Microangiopathic haemolytic anaemia (MAHA) 3. Thrombocytopenia	Pentad (Triad of HUS) + 4. Neurological manifestation 5. Fever
Seen in Children	Seen in Children	
Usually follows an upper respiratory tract infection	Associated with E. coli	Inhibition of ADAMTS 13 • ADAMTS 13 is responsible for breakdown of VWF – Without ADAMTS 13, coagulation occurs

Haemolytic uraemic syndrome (HUS)
HUS consists of a triad of haemolytic anaemia, uraemia, and thrombocytopenia.

The anaemia will be intravascular in nature and will have an abnormal blood smear showing schistocytes, helmet cells, and fragmented red cells.

LDH and reticulocyte count will be elevated and the haptoglobin decreased.

90% are caused by E. coli strain O157. This produces a verotoxin that attacks endothelial cells. Occurs after eating undercooked contaminated meat.

Signs and Symptoms:
The classical presenting feature is profuse diarrhoea that turns bloody 1 to 3 days later. It is rare for the diarrhoea to have been bloody from the outset. About 80-90% of children from whom the organism is isolated will develop blood in the stool. It is usually at this stage that they are admitted to hospital.

Most adults infected with E. coli O157 remain asymptomatic.

There is often fever, abdominal pain and vomiting

Management
• Treatment is supportive e.g. Fluids, blood transfusion and dialysis if required
• Do not give antibiotics to those with possible HUS. The organism may release more toxins as it dies if antibiotics are given and may worsen the disease.
• The indications for plasma exchange in HUS are complicated. As a general rule plasma exchange is reserved for severe cases of HUS not associated with diarrhoea

Q-20

A 65 year old man is brought by ambulance to the hospital for a suspected stroke. The patient is on warfarin as part of his management for atrial fibrillation. INR was ordered as part of a series of investigations and results have returned to show an INR of 7.9. A computed tomography scan was performed and reveals an intracranial haemorrhage. He currently has a blood pressure of 90/50 mmHg and a heart rate of 120 beats per minute. As part of the management for the high INR and bleeding, vitamin K was administered intravenously. What other products can be given as part of the management for warfarin overdose?

A. **Cryoprecipitate**
B. **Fresh frozen plasma**
C. **Red cell concentrate**
D. **Prothrombin complex concentrate**
E. **Tranexamic acid**

ANSWER:
Prothrombin complex concentrate

EXPLANATION:
For major bleedings, these are the necessary steps:

- Stop warfarin
- Give intravenous vitamin K 5 mg
- Prothrombin complex concentrate – if not available then give fresh frozen plasma

Q-21

A 15 year old boy has marked pallor and jaundice. He has to receive regular blood transfusions to maintain his haemoglobin above a certain level. His medical history includes diabetes. He has obvious skull bossing and hepatosplenomegaly. What is the SINGLE most likely diagnosis?

A. **Hereditary spherocytosis**
B. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
C. **Alpha thalassemia trait**
D. **Beta thalassemia major**
E. **Hereditary sideroblastic anaemia**

ANSWER:
Beta thalassemia major

EXPLANATION:
The signs and symptoms point towards a beta thalassaemia major.

Alpha thalassemia trait have mild anaemia and are usually clinically asymptomatic

Thalassaemias

Thalassaemia is not a very commonly asked topic. You should only go through this if you have time to spare. We have only included the important points of thalassaemia.

Important points to know:

- *α thalassaemia major* → is usually lethal in utero. It should be considered when hydrops fetalis is diagnosed
- *β thalassaemia major* → Presents in infancy often includes failure to thrive, vomiting feeds, sleepiness, stunted growth and irritability. In severe, untreated cases there may be:
- Hepatosplenomegaly
- Bony deformities (frontal bossing). The extra medullary haemopoiesis occurs in response to anaemia.
- Marked pallor and slight to moderate jaundice
- Iron overload can cause endocrinopathy with diabetes, thyroid, adrenal and pituitary disorders
- β-thalassaemia carrier status is often confused with iron deficiency due to reduced MCV and MCH. But note that in iron deficiency, serum ferritin and iron is low while in thalassaemia they are usually high.

Management for thalassaemia major:

- Lifelong blood transfusions are needed to maintain a haemoglobin level higher than 9.5 g/dL (or some authors say 9.0 g/dL)
- Iron chelation to prevent overload syndrome (Oral deferiprone + desferrioxamine SC twice weekly)
- A histocompatible marrow transplant can offer the chance of a cure

Q-22

A 50 year old man presents fatigue, weight loss and complaints of abdominal fullness. An abdominal examination reveals splenomegaly extending towards the right iliac fossa.

Blood report shows the following:

Haemoglobin 82 g/L
White cell count 102 x 10^9/L
Platelets 160 x 10^9/L

Philadelphia chromosome was positive on cytogenetic analysis. What is the SINGLE most likely diagnosis?

A. **Acute lymphoblastic leukaemia (ALL)**
B. **Acute myeloid leukaemia (AML)**
C. **Chronic myeloid leukaemia (CML)**
D. **Chronic lymphocytic leukaemia (CLL)**
E. **Lymphoma**

ANSWER:
Chronic myeloid leukaemia (CML)

EXPLANATION:
Anaemia, raised WBC count are known features of chronic myeloid leukaemia (CML). Splenomegaly (particularly if massive) is very suggestive of chronic myeloid leukaemia (CML) and Philadelphia chromosome is diagnostic of chronic myeloid leukaemia (CML).

Note that platelets can be normal in CML.

Chronic myeloid leukaemia (CML)
CML is a clonal bone marrow stem cell disorder in which a proliferation of **mature granulocytes** (neutrophils, eosinophils and basophils) and their precursors is found.

CML typically progresses through three stages:
1. Chronic phase
The immune system is competent and patients are asymptomatic for prolonged periods - (typically 4-5 years) More than 90% of patients are diagnosed in the initial chronic phase.

2. Accelerated phase
In about two thirds of patients, the chronic phase transforms into an accelerated phase characterised by a moderate increase in blast cells, increasing anaemia or thrombocytopenia.

3. Blast crisis or blastic phase
After a variable amount of time (usually months) the accelerated phase progresses to acute blastic transformation. Features of blastic phase include bone marrow or peripheral blasts ≥30%, severe constitutional symptoms due to tumour burden (weight loss, fever, night sweats, bone pain), infection and bleeding

Clinical Presentation
Usually presents at age 40 to 50 years old (middle-age)
85-90% of patients are diagnosed in the chronic phase and in recent years about 40% of patients have been diagnosed before any symptoms developed, with incidental abnormalities spotted on a blood test.

- Fatigue (due to anaemia)
- Weight loss
- Night sweats
- Abdominal discomfort → from massive enlargement of spleen (this is common)
- Splenomegaly → this is the most common physical finding, which may extend towards the right iliac fossa (Seen in >75%)
- Hepatomegaly
- Enlarged lymph nodes (rare)
- Low grade fever

• Gout due to rapid cell turnover

Note: Enlarged lymph nodes are rare and infection are uncommon because these white cells retain the majority of their function

Investigations at presentation

- FBC:
  - Leukocytosis is common (often >100 x 109/L)
  - Differential shows granulocytes at all stages of development (increased numbers of neutrophils, myelocytes, basophils, eosinophils)
  - Platelets may be elevated, decreased or normal levels
  - A mild-to-moderate, usually normochromic and normocytic, anaemia is common
- Peripheral blood smear - all stages of maturation seen
- Biochemistry - U&Es are usually normal at presentation, lactate dehydrogenase is usually raised, serum urate may be raised.
- Bone marrow aspiration and biopsy are essential to quantify the percentage of blasts and basophils, to assess the degree of fibrosis and to obtain material for cytogenetic-molecular analyses.
- Cytogenetics - the characteristic feature in CML is the Ph chromosome, found in about 90% of cases. (oxford says > 80%). This can be found on cytogenetic analysis of blood or bone marrow.

Take home notes:

- *The main feature of the disease is an elevated white blood cell count consisting predominantly of neutrophils. Blasts are either absent or present in very small amounts.*
- *The Philadelphia chromosome is present in more than 90% of patients with chronic myeloid leukaemia (CML).*
- *In PLAB, look for the massive enlargement of spleen*

Q-23

A 4 year old boy presents with haemrthrosis following a minor fall. His grandfather and uncle have similar bleeding problems throughout their lives. What is the SINGLE most likely mode of inheritance.

A. Autosomal co-dominant
B. Autosomal dominant
C. Autosomal recessive
D. X-linked
E. Mitochondrial gene defect

ANSWER:
X-linked

EXPLANATION:
Haemophilia A and B

- Are congenital bleeding disorders with low levels of factor VIII (haemophilia A, classical haemophilia) or IX (haemophilia B, Christmas disease).
- Sex-linked inheritance.
- Males are typically affected
- Female carriers are rarely symptomatic

Clinical presentation
- Haemophilia A and B are clinically indistinguishable
- Symptoms depend on the factor level.
- History of spontaneous bleeding into joints, especially the knees, ankles and elbows, without a history of significant trauma. Spontaneous haemarthrosis are virtually pathognomonic
- Intramuscular haemorrhage may also occur. Spontaneous bleeding into arms, legs, or any site. The bleeding may lead to nerve compression, or compartment syndrome

Investigations
- Prothrombin time, bleeding time, fibrinogen levels and von Willebrand factor are normal
- Activated partial thromboplastin time (APTT) is usually prolonged but can be normal in mild disease
- Factor VIII/XI assay to diagnose

Remember these test to distinguish haemophilia from Von Willebrand disease
- *Haemophilia*
- *Only aPTT is prolonged*
- *Has factor type bleeding (deep bleeding into muscles and joints)*
- *Von willebrand disease*
- *aPTT and bleeding time are prolonged*
- *Has platelet type bleeding (mucosal bleeding)*

Haemophilia A-specific treatment
- Desmopressin raises factor VIII levels, and may be sufficient to treat Haemophilia type A
- Major bleeds (eg haemarthrosis): May need treatment with recombinant factor VIII
- Do not give IM injections when factor is low

Haemophilia B-specific treatment
- Recombinant factor IX is the treatment of choice
- Note: Desmopressin has no value in treatment of haemophilia B

Avoid NSAIDS and IM injections!
Questions may arise with this topic. In PLAB, in whichever scenario, avoid NSAIDS and IM injection as the answer in Haemophilia. NSAIDs must not be employed for the fear of gastrointestinal haemorrhage. If needed, give opiates for pain relief and if given

parenterally, pick intravenously (IV) or possibly subcutaneously (SC) but not intramuscularly (IM). IM injection will produce a large and painful haematoma.

Q-24

A 42 year old woman with septicaemia suddenly develops purpura all over his legs and arms. Her blood tests show:

Haemoglobin 118 g/L
White cell count 15.8 x 10^9/L
Platelets 28 x 10^9/L

Prothrombin time, and activated partial thromboplastin time are prolonged. D-dimers were elevated. What is the SINGLE most likely diagnosis?

A. Pulmonary embolism
B. Disseminated intravascular coagulation
C. Deep vein thrombosis
D. Factor V Leiden mutation
E. Warfarin interaction

ANSWER:
Disseminated intravascular coagulation

EXPLANATION:
Disseminated intravascular coagulation (DIC)
Presentation
• Ecchymoses or spontaneous bleeding at venepuncture sites, and the site of trauma
• Bleeding from ears, nose and throat, gastrointestinal tract
• Petechiae, purpura

Diagnosis
No single laboratory test that can establish or rule out the diagnosis of DIC, therefore assess the whole clinical picture, taking into account the clinical condition of the patient, and all available laboratory results.

• Thrombocytopenia (in up to 98% of cases) → around 50% of them would have a platelets count less than 50 x 109/L
• Fibrin degradation products (inc. D-dimer) is elevated
• Prothrombin time (PT) is elevated
• Activated partial thromboplastin time (aPTT) is elevated
• Fibrinogen level low

Remember, everything is elevated except platelets and fibrinogen.

Treatment

• Treat the underlying condition
• Transfusion of platelets or plasma (components) for patients with severe bleeds
• In bleeding patients with DIC and prolonged PT and aPTT, administer fresh frozen plasma (FFP)

Q-25

A 51 year old vegan presents with complaints of peripheral paresthesia, mild shortness of breath and fatigue. Examination reveals that she has angular stomatitis and a sore red tongue. What is the SINGLE most likely cell type to be seen on a blood film?

A. Numerous blast cells
B. Oval macrocytic red cells
C. Spherocytes
D. Microcytic hypochromic red cells
E. Heinz bodies

ANSWER:
Oval macrocytic red cells

EXPLANATION:
Angular stomatitis is a known sign for iron deficiency anaemia however vitamin B12 deficiency is sometimes responsible for angular stomatitis, and commonly occurs together with folate deficiency

The appearance of the tongue in vitamin B12 deficiency is described as "beefy" or "fiery red and sore".

Peripheral paresthesia is also a known symptom of vitamin B12.

Vitamin B12 deficiency has RBC changes which include oval macrocytosis

Q-26

A 53 year old man presents complaining of weight loss, lethargy, increasing abdominal discomfort and gout for the past year. On examination, spleen is palpated 5 cm below the left costal margin. His blood tests show:

Haemoglobin 105 g/L
White cell count 202 x ^{109}/L
Platelets 103 x 10^9/L
85% neutrophils
Serum urea 7.0 mmol/L
Serum creatinine 151 micromol/L
Sodium 140 mmol/L
Potassium 4 mmol/L
Philadelphia chromosome positive

What is the SINGLE most likely diagnosis?

A. **Chronic myeloid leukaemia**
B. **Chronic lymphocytic leukaemia**
C. **Acute myeloid leukaemia**
D. **Malaria**
E. **Lymphoma**

ANSWER:
Chronic myeloid leukaemia

EXPLANATION:
The clincher here is the massive spleen. Although there are many causes of massive spleen, for the purpose of PLAB, massive spleen can only be caused by chronic myeloid leukaemia (CML) or Malaria

Weight loss, lethargy, increasing abdominal discomfort support the diagnosis of CML.

If you see a middle aged man/woman with a huge spleen → likely to be Chronic myeloid leukaemia (CML). Malaria would likely have a travel history of some sort.

Mnemonic: CML → Crazy Massive Large Spleen

Q-27

A 75 year old man with chronic back pain and lethargy for several months was referred to secondary care where further investigations were carried out. Amongst the investigations was a bone marrow biopsy which was reported as having abundance of plasma cells. What is the SINGLE most likely diganosis?

A. **Multiple myeloma**
B. **Ankylosing spondylitis**
C. **Amyloidosis**
D. **Leukaemia**
E. **Myelofibrosis**

ANSWER:
Multiple myeloma

EXPLANATION:
A bone marrow biopsy with abundance of plasma cells is diagnostic for multiple myeloma.

Q-28

A 38 year old female presents with the complaint of worsening tiredness. She says that she first began to notice her increasing fatigability two weeks ago. On

examination, she appeaers to be mildly jaundiced. No other significant signs appear on physical examination. Her heart rate is 79 beats/minute and her blood pressure is 120/70 mmHg. Baseline bloods were taken and the results are as follows:

Haemoglobin 92 g/L
Mean cell volume (MCV) 98 fL
White cell count (WCC) 8 x 10^9/L
Bilirubin 29 micromol/L
Alanine transferase (ALT) 21 U/L
Aspartate transaminase (AST) 27 U/L
Alkaline phosphatase (ALP) 140 U/L
Gamma glutamyl transferase (GGT) 39 U/L

What is the SINGLE most appropriate diagnostic investigation for this patient?

A. **Bone marrow aspiration**
B. **Direct antiglobin test**
C. **Faecal occult blood test**
D. **Serum antinuclear antibodies**
E. **Vitamin B12 levels**

ANSWER:
Direct antiglobin test

EXPLANATION:
All the indications point toward this patient having a haemolytic anaemia.

A direct antiglobin test is a synonym for a direct Coombs test which would be appropriate to test for autoimmune haemolytic anaemia.

Haemolysis causes an increase in the serum bilirubin levels, which is present in this patient's blood results.

The only blood values that are not within the normal range for this patient are her haemoglobin levels, her MCV value and her bilirubin levels. Everything else is within the normal range.

What about the increased MCV?
While it is true that most cases of an increased mean cell volume can be seen in the macrocytic anaemias notably B12 deficiency and folate deficiency which are, by definition, not haemolytic anaemias, some immunologically-mediated haemolytic anaemias may be seen to have spherocytes on microscopy and have an increased MCV. These immunologically-mediated haemolytic anaemias would have a positive direct Coombs test.

Q-29

A 21 year old man has episodic right upper quadrant pain. An abdominal ultrasound reveals gallstones. His father had a splenectomy when he was young. His blood tests show:

Haemoglobin 91 g/L
Mean cell haemoglobin concentration 369 g/L
Platelets 250 x 10^9/L
White cell count 6.3 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Hereditary spherocytosis**
B. **Glucose-6-dehydrogenase (G6PD) deficiency**
C. **Alpha thalassemia**
D. **Beta thalassemia**
E. **Hereditary sideroblastic anaemia**

ANSWER:
Hereditary spherocytosis

EXPLANATION:
The evidence of increased MCHC, gallstones and family history points towards hereditary spherocytosis.

Hereditary Spherocytosis
Hereditary Spherocytosis is the most common inherited RBC membrane defect characterized by variable degrees of haemolysis, spherocytic RBCs with increased osmotic fragility.

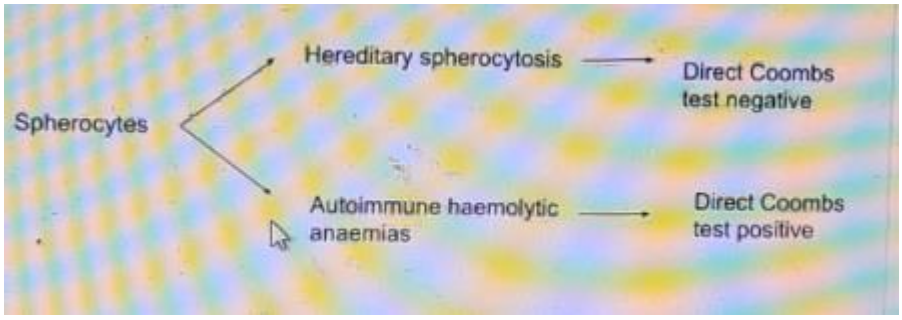
Approximately 75% of cases display an autosomal dominant pattern of inheritance; the rest are recessive forms and de novo mutations.

Clinical features
- Patients may present at any age with haemolytic anaemia, jaundice (either from haemolysis or gallstones) and splenomegaly
- 20-30% of patients have mild disease with an increased red cell turnover compensated with adequate replacement. They are neither symptomatic nor anaemic, but may have mild splenomegaly, slight reticulocytosis and minimal spherocytes visible.
- 60-70% of patients have moderate disease and half of these present in childhood with anaemia.
- Neonates with severe hereditary disease do not always present at birth with anaemia, but haemoglobin may fall dramatically over the first few weeks of life and may be severe enough to require exchange transfusion.
- Occasional aplastic crises occur, e.g. with parvovirus B19 infection.

Diagnosis
(These are the 3 most important test that you need to know in the exam for Hereditary Spherocytosis)
- Blood film shows spherocytes and increased reticulocytes
- MCHC would be elevated
- Osmotic fragility test → confirms presence of spherocytes but does not permit hereditary spherocytosis to be distinguished from other spherocytic haemolytic disorders such as autoimmune haemolytic anaemia. This is not reliable until six months of age.

Some authors mention that osmotic fragility test is unreliable and is no longer recommended. However, it is still considered the gold standard despite missing up to 20% of cases. In the PLAB exam, osmotic fragility test may be given as a choice for a diagnostic test for Hereditary Spherocytosis. Pick it if it is.

Note:
Spherocytosis almost always refers to hereditary spherocytosis but note that spherocytes are found in hereditary spherocytosis and also autoimmune haemolytic anaemias. The test to distinguish the two would be a direct Coombs test. Hereditary spherocytosis has a negative direct Coombs test but autoimmune haemolytic anaemias have a positive direct Coombs test



Management
Steroid therapy
- effective in augmenting haemoglobin levels during haemolytic crises in patients with moderate disease

Folate supplementation

Splenectomy
- eliminates anaemia and hyperbilirubinaemia and lowers the high reticulocyte number to nearly normal levels
- Splenectomy is curative in most patients but increased recognition of the long-term risks of splenectomy has led to re-evaluation of the role of splenectomy.

Mild cases do not usually require folate supplements or splenectomy

Complications

- Rapid haemolysis can be triggered by viral infections and produce jaundice, anaemia and occasionally abdominal pain and tender splenomegaly. Supportive treatment is usually all that is needed.
- Aplastic crises (aplastic anaemia). They are most commonly caused by infection with parvovirus B19 and usually last 10-14 days. This can be life-threatening.

When you see parvovirus B19 in the exam, immediately think of sickle cell anaemia or hereditary spherocytosis

Parvovirus and anaemia

Although most patients have a decrease of erythropoiesis (production of red blood cells) during parvovirus infection, it is most dangerous in patients with sickle cell anaemia or hereditary spherocytosis, as they are heavily dependent on erythropoiesis due to the reduced lifespan of the red cells.

Q-30

A 45 year old man presents fatigue. He is otherwise asymptomatic. Blood report shows the following:

Haemoglobin 82 g/L
White cell count 132 x 10^9/L
Platelets 550 x 10^9/L

There was an increased number of neutrophils, basophils, eosinophils. Peripheral blood smear shows all stages of maturation. What is the SINGLE most likely diagnosis?

A. **Acute lymphoblastic leukaemia (ALL)**
B. **Acute myeloid leukaemia (AML)**
C. **Chronic myeloid leukaemia (CML)**
D. **Chronic lymphocytic leukaemia (CLL)**
E. **Lymphoma**

ANSWER:
Chronic myeloid leukaemia

EXPLANATION:
Anaemia, raised WBC count are known features of chronic myeloid leukaemia (CML).

Myeloid cells include neutrophils, basophils, eosinophils, erythrocytes, and platelets. An increased number of neutrophils, basophils, eosinophils are consistent with CML.

Note that platelets can be low, normal or raised in CML.

Q-31

A 10 year old boy is brought to the hospital with a rash over his buttocks associated with abdominal pain and vomiting. He is accompanied by his mother and stepfather. His mother had left him for the weekend with the stepfather and she was called to come back from holiday as he started to have blood in his urine with the rash. Social services have been notified. What is the most likely diagnosis?

A. **Non accidental injury**
B. **Idiopathic thrombocytopenic purpura**
C. **Henoch Schonlein purpura**
D. **Acute lymphoblastic leukaemia (ALL)**
E. **Haemolytic uraemic syndrome**

ANSWER:
Henoch-Schonlein purpura

EXPLANATION:
Rash over buttock, abdominal pain and vomiting, blood in urine or stool suggest Henoch-Schönlein purpura.

A mixed picture question like this can be sometimes confusing as in this question there are some features of a non accidental injury (stepfather). Be sure to evaluate all the signs and symptoms before jumping to the conclusion that this is a non accidental injury.

Henoch-Schönlein purpura (HSP)
Presentation:
• Purpura (non-blanching) over buttocks and extensor surfaces
• Arthralgia (especially in the knees and ankles)
• Abdominal pain

Diagnosis:
• Mainly a clinical diagnosis
• Look for elevated ESR, IgA
• Raised creatinine ; labs consistent with nephropathy

Treatment:
• Self-limiting; conservative management
• NSAIDs for arthralgic pain → beware of choosing this option if case stem has impaired renal involvement!
• Corticosteroids can improve associated arthralgia and the symptoms associated with gastrointestinal dysfunction

Q-32

A 7 year old boy has recurrent episodes of spontaneous bleeding into his knee joints and muscles. Factor IX was found deficient. What is the SINGLE most

likely diagnosis?

A. **Haemophilia A**
B. **Christmas disease**
C. **Von Willebrand's disease**
D. **Sickle cell anaemia**
E. **Thalassaemia**

ANSWER:
Christmas disease

EXPLANATION:
Factor Ix deficiency is evidence of haemophilia B (Christmas disease)

Q-33

A 22 year old Greek man presents with rapid symptoms of anaemia and jaundice following treatment of malaria. He is noted to have Heinz bodies on a blood film. What is the SINGLE most likely diagnosis?

A. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
B. **Anaemia of chronic disease**
C. **Pernicious anaemia**
D. **Thalassaemia trait**
E. **Hereditary sideroblastic anaemia**

ANSWER:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency

EXPLANATION:
Heinz bodies are pathognomic for G6PD deficiency. In PLAB, if you see a question that has Heinz bodies on a blood film, you can almost be certain that this is G6PD deficiency.

Haemolysis in this case was elicited by treatment of malaria. Usually primaquine is the culprit.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency
Glucose-6-phosphate dehydrogenase (G6PD) deficiency is X-linked and clinically important cause of oxidant haemolysis. It affects all races but is most common in those of African, Asian or Mediterranean descent.

Deficiency of the G6PD enzyme results in reduced glutathione making the red cells vulnerable to oxidative damage and thus liable to haemolysis.

↓ *G6PD enzyme* → ↓ *glutathione* → ↑ *red cell susceptibility to oxidative stress*

- Being X-linked, the disease affects mainly men but in areas of high frequency it is not uncommon to find homozygous women. *(In the exam, it is usually always male patient)*
- Most individuals with the G6PD defect are asymptomatic and unaware of their status
- Haemolysis occurs after exposure to oxidants or infection.
- Acute episodes of haemolysis with fava beans (termed favism)

There are many drugs that can elicit haemolysis in patients with G6PD deficiency. One drug that you would definitely need to look out for in the exam is → antimalarials: primaquine

Presentation:
• Most are asymptomatic
• May be a history of neonatal jaundice, severe enough to require exchange transfusion
• May have history of drug-induced haemolysis
• Gallstones are common
• Pallor from anaemia
• During a crisis jaundice occurs
• Back or abdominal pain (usually occurs when >50% haemolysis occurs)
• Splenomegaly may occur

There are typically 4 ways the patient might present in PLAB. Below are the specifics:

Drug-induced haemolysis in G6PD deficiency
• Begins 1-3 days after ingestion of drug
• Anaemia most severe 7-10 days after ingestion
• Associated with low back and abdominal pain
• Urine becomes dark (black sometimes)
• Red cells develop Heinz body inclusions
• Haemolysis is typically self-limiting

Haemolysis due to infection and fever
• 1-2 days after onset of fever
• Mild anaemia develops
• Commonly seen in pneumonic illnesses

Favism
• Hours/days after ingestion of fava beans (broad beans)
• Urine becomes red or very dark
• Shock may develop and it may be fatal

Neonatal jaundice
• May develop kernicterus (possible permanent brain damage)

Laboratory investigation (Important for exam)
• In steady state (i.e. no haemolysis) the RBCs appear normal
• Heinz bodies is seen on blood film in drug-induced haemolysis. Bite cells are also seen. Bite cells are cells with Heinz bodies that pass through the spleen and have part of the membrane removed

Laboratory investigations (Less important for exam)
• Spherocytes and RBC fragments on blood film is seen if there is severe haemolysis
• Increased reticulocytes
• Increased unconjugated bilirubin
• decreased haptoglobins

Diagnosis
G6PD enzyme activity - is the definitive test

Diagnosis should not be done during the haemolytic episode but be done during the steady state which is around 6 weeks after the episode of haemolysis. The reason behind this is the diagnosis is difficult during haemolytic episode since reticulocytes have increased levels of enzyme and may get abnormal result.

Management
• Avoidance of precipitating drugs, and broad (fava) beans
• Transfuse in severe haemolysis or symptomatic anaemia
• IV fluids to maintain good urine output
• In infants, exchange transfusion may be required
• Splenectomy may be of value in severe recurrent haemolysis

Q-34

A 49 year old lady complains of headaches, dizziness and pruritus. She says that the pruritus is worsened after taking a hot bath. A recent FBC revealed that she has a haemoglobin of 192 g/L. What is the SINGLE most useful test to establish the diagnosis of polycythaemia rubra vera?

A. JAK mutation screen
B. Leukocyte alkaline phosphatase
C. Serum erythropoeitin
D. Oxygen saturation with arterial blood gas greater than 92%
E. Bone marrow aspiration

ANSWER:
JAK mutation screen

EXPLANATION:
It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV. JAK2 mutation is now a major criteria in the diagnosis of polycythaemia rubra vera.

Polycythaemia rubra vera (PRV)
Polycythaemia rubra vera (PRV) is the most common form of primary polycythaemia. It is a malignant proliferation of a clone derived from one pluripotent marrow stem cell.
- There is excess proliferation of RBCs, WBCs, and platelets, leading to hyperviscosity and thrombosis
- More commonly found in patients who are more than 60 years old
- A mutation in JAK2 is present in >90%

Presentation
- It may be discovered on routine blood count in a person with no related symptoms or there may be nonspecific complaints of lethargy and tiredness
- About a third present with symptoms due to thrombosis. Features include stroke, myocardial infarction, deep vein thrombosis and pulmonary embolism
- Headaches, dizziness, sweating, and tinnitus
- Bleeding from gums or easy bruising is usually mild but gastrointestinal haemorrhage can be more severe. This is secondary to abnormal platelet function
- Pruritus which is typically worse after a hot shower or bath
- Splenomegaly is present in about 75% of patients (oxford says 60%)
- Hypertension is common
- Erythema, warmth, pain, and even sometimes infarction of the distal extremities. Burning sensation in fingers and toes, are characteristic but not very common
- Facial plethora
- Gout from increased cell turnover

Note:
- There is usually an abnormally low serum erythropoietin

Management
- Venesection
- Chemotherapy options include:
  - Younger than 40 years of age: first-line is interferon
  - Older than 40 years of age: first-line is hydroxycarbamide (hydroxyurea)
- Low dose aspirin 75mg OD → To reduce thrombotic events

Q-35

A 32 year old man presents with fatigue, weakness, weight loss. On examination, cervical lymphadenopathy and splenomegaly is noted. What is the SINGLE most likely diagnosis?

A. Haemophilus influenzae infection
B. Streptococcal infection
C. Toxoplasmosis
D. Non-Hodgkin lymphoma
E. Pneumocystis infection

ANSWER:
Non-Hodgkin lymphoma

EXPLANATION:
There are two major points mentioned here: cervical lymphadenopathy and splenomegaly.

This combination makes Non-Hodgkin lymphoma as the most likely cause.

Toxoplasmosis although uncommon, may have cervical lymphadenopathy and splenomegaly as well. But weight loss is not seen in toxoplasmosis hence non-hodgkin's lymphoma remains the top choice.

Non-Hodgkin lymphoma
This includes all lymphomas without Reed-Sternberg cells

Most are derived from B-cell lines; diffuse large B-cell lymphoma (DLBCL) is commonest.

Common Signs and Symptoms
- Painless, slowly progressive peripheral lymphadenopathy is the most common clinical presentation
- Primary extranodal involvement and systemic symptoms (fatigue, weakness, fever, night sweats, weight loss) are not common at presentation but are common in patients with advanced or endstage disease.
  Note: fever, night sweats, weight loss are less common than in Hodgkin's lymphoma, and indicates disseminated disease
- Bone marrow is frequently involved and may be associated with pancytopenia - anaemia, infection, bleeding (platelets).
- Splenomegaly
- Hepatomegaly

Q-36

A 20 year old man presents with development of low back pain, shortness of breath and dizziness 3 days after taking primaquine to treat malaria. His past medical history is significant for neonatal jaundice. What is the SINGLE most likely diagnosis?

A. Haemolytic anaemia
B. Pulmonary embolism
C. Allergy to primaquine
D. Thalassaemia trait
E. Hereditary sideroblastic anaemia

ANSWER:
Haemolytic anaemia

EXPLANATION:
Haemolysis in this case was elicited by the treatment of malaria using primaquine. This patient has G6PD deficiency.

Q-37

A 51 year old man complains of headache and pruritus. He had a deep vein thrombosis recently. Recent blood reports show the following:

Haemoglobin 192 g/L
White cell count 15 x 10^9/L
Platelets 809 x 10^9/L

Erythropoietin was found to be low. What is the SINGLE most likely diagnosis?

A. **Myelofibrosis**
B. **Polycythaemia rubra vera (PRV)**
C. **Essential thrombocythemia**
D. **Chronic myeloid leukaemia (CML)**
E. **Chronic lymphocytic leukaemia (CLL)**

ANSWER:
Polycythaemia rubra vera (PRV)

EXPLANATION:
The signs and symptoms are consistent with polycythaemia rubra vera (PRV)

About a third of patients with PRV present with symptoms due to thrombosis. This includes DVT like in this question.

PCV is usually associated with a low serum level of the hormone erythropoietin (EPO).

Q-38

A 17 year old girl has prolonged bleeding after a routine dental extraction. Her father and paternal grandomother have experienced similar problems. What is the SINGLE most likely mode of inheritance?

A. **Autosomal co-dominant**
B. **Autosomal dominant**
C. **Autosomal recessive**
D. **X-linked**
E. **Mitochondrial gene defect**

ANSWER:
Autosomal dominant

EXPLANATION:

Although type 3 von Willebrand disease is actually autosomal recessive, majority of von Willebrand's disease is autosomal dominant.

Von Willebrand disease
The 3 important points you need to know in Von Willebrand disease in PLAB is:

1. It presents with mucosal bleeding → Epistaxis, menorrhagia (behaves like a platelet disorder)
2. AAutosomal dominant (type 3 is recessive)
3. Role of Von Willebrand's factor is:
   a. Promotes platelet aggregation
   b. Carrier molecule for factor VIII

Investigation
• Bleeding time → prolonged
• APTT → 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
• Factor VIII concentrate

Comparing the 3 important bleeding disorders in PLAB

Von Willebrand disease	**Haemophilia**	**Disseminated intravascular coagulation (DIC)**
Platelet type bleeding (mucosal bleeding)	Factor type bleeding (deep bleeding into muscles and joints)	Bleeding everywhere • Venepuncture sites • GI tract • Ear nose throat • Skin: Purpura
aPTT prolonged Bleeding time prolonged	aPTT is prolonged	aPTT prolonged Bleeding time prolonged PT prolonged

Q-39

A 5 year old boy has swelling at the knee after falling on the ground with rashes on his buttocks. His blood tests show:

Haemoglobin 119 g/L

White cell count 8 x 10^9/L
Platelets 259 x 10^9/L
Prothrombin time 12 seconds
Activated partial thromboplastin time 61 seconds

What is the SINGLE most likely diagnosis?

A. **Haemolytic uraemic syndrome**
B. **Haemophilia**
C. **Henoch-Schonlein purpura**
D. **Osler Weber Rendu syndrome**
E. **Von Willebrand disease**

ANSWER:
Haemophilia

EXPLANATION:
As a general rule, platelet deficiency causes petechial haemorrhages and ecchymoses (bruising) whilst clotting factor deficiency produces haematomas and haemarthroses. This question gives a mixed picture where there are descriptions of both platelet deficiency (petechial haemorrhages seen on his buttocks) and factor deficiency (bleeding/swelling at his knee). However, the prolonged aPTT supports the diagnosis of haemophilia thus that is the answer. We can only hope that in PLAB, these mixed picture questions are low in number for you exam.

Q-40

A 4 year old boy presents with fever, and decreased appetite. On examination, there are palpable non-tender nodules along the deep cervical chain in the neck. He has a history of recurrent throat infections. His mother describes him as always feeling tired. On examination, splenomegaly was noted. Blood results show:

Haemoglobin 9 g/dL
MCV 80 fl
White cell count 2 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Acute myeloid leukaemia**
B. **Acute lymphoblastic leukaemia**
C. **Chronic myeloid leukaemia**
D. **Chronic lymphocytic leukaemia**
E. **Hodgkin's lymphoma**

ANSWER:
Acute lymphoblastic leukaemia

EXPLANATION:
This is a frequent topic on PLAB 1. Be sure to know the differentiations between all the leukaemias and be able to classify them by the age groups. Acute lymphoblastic leukaemia (ALL) is the most common paediatric cancer. The differentiating factor between ALL and acute myeloid leukaemia (AML) is AML would present with massive splenomegaly on examination. ALL would just have lymphadenopathy.

But in actual fact, AML and ALL are usually indistinguishable clinically. This means you cannot determine the diagnosis only from the clinical presentation. ALL is more often associated with infiltration of other organs, but AML can do it as well. Acute lymphocytic leukaemia (ALL) is more common in children, and acute myelogenous leukaemia (AML) is more common in adults

It is very unlikely that the PLAB questions would ask you to differentiate the AML from ALL using specific test. However, if a child (young age) is given with signs and symptoms of pancytopenia, ALL would be the most likely as it is the commonest childhood leukaemia.

Q-41

A 72 year old man with a background of vascular dementia living alone has been brought in by his daughter to the Emergency Department for the third time this month for bruising around the head, face and forearms. His son in law has been stayingwith him recently as the patient has not been able to manage alone. He is on warfarin for atrial fibrillation and is otherwise not taking any other medications. His blood results done in the department show the following:

Haemoglobin 82 g/L
White cell count 6 x 10^9/L
Platelets 450 x 10^9/L
Serum urea 7.5 mmol/L
Serum creatinine 166 micromol/L
International normalized ratio (INR) 1.1

What is the SINGLE most likely cause for these symptoms?

A. **Non-accidental injury**
B. **Accidental falls**
C. **Heparin induced thrombocytopaenia**
D. **Increased prothrombin time**
E. **Side effect of warfarin**

ANSWER:
Non-accidental injury

EXPLANATION:

This elderly man is probably quite aggressive and difficult to manage. The presence of bruising on the forearms is reflective of him trying to defend himself and push someone away. The facial bruising is suspicious of abuse.

Option B. Accidental falls is incorrect. Most injuries in these cases involve hip joints or shoulder joints. There is no mention of hip or shoulder pains in this case.

Option C. Heparin induced thrombocytopaenia is incorrect. There is no history of use of heparin

Option D. Increased prothrombin time is incorrect. This disturbance of coagulation does not cause bruising but can make it so that bruising can persist for longer than normal.

Option E. Side effect of warfarin is incorrect. His INR is within normal limits. Furthermore, one would expect more generalised bruising over the entire body as opposed to the face and head.

Q-42

A11 year old boy has an upper respiratory tract infection followed by a low grade fever with erythematous macular rash, especially on the back of the legs. A few hours later, the macules evolve into purpuric lesions that are slightly raised and do not blanch on a glass test. He also complains of a headache and joint stiffness. His blood tests show:

Haemoglobin 123 g/L
White cell count 3.3 x 10^9/L
Platelets 211 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Meningitis**
B. **Sepsis**
C. **Henoch-Schonlein purpura**
D. **Idiopathic thrombocytopenic purpura**
E. **Thrombotic thrombocytopenic purpura**

ANSWER:
Henoch-Schonlein purpura

EXPLANATION:
The blood results are all normal. The rash in the legs that are non blanching and the arthritis are hints towards Henoch-Schönlein purpura.

The disease occurs mostly in the winter months. About 50-90% of patients have a preceding upper respiratory tract infection (URTI) which explains the cough in the given question.

The stem here gives a no history of fever. Generally, patients with Henoch-Schönlein purpura appear to be mildly ill, with low-grade fever. But having no fever does not exclude the diagnosis.

Q-43

A 26 year old man develops mild anaemia following a chest infection. A blood film shows Heinz bodies. What is the SINGLE most likely diagnosis?

A. **Hereditary spherocytosis**
B. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
C. **Alpha thalassaemia**
D. **Beta thalassaemia**
E. **Hereditary sideroblastic anaemia**

ANSWER:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency

EXPLANATION:
Heinz bodies are pathognomic for G6PD deficiency. In PLAB, if you see a question that has Heinz bodies on a blood film, you can almost be certain that this is G6PD deficiency.

Q-44

A 5 year old child has bleeding gums and sore throat for the last 3 months. He feels tired and lethargic all the time. On examination, splenomegaly was noted. Blood results show:

Hb 7.8 g/dL
WCC 3 x 10^9/L
Platelets 48 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Acute lymphoblastic leukaemia (ALL)**
B. **Acute myeloid leukaemia (AML)**
C. **Chronic myeloid leukaemia (CML)**
D. **Chronic lymphocytic leukaemia (CLL)**
E. **Hodgkin's lymphoma**

ANSWER:
Acute lymphoblastic leukaemia (ALL)

EXPLANATION:
The commonest leukaemia in children is Acute lymphoblastic leukaemia (ALL)

Bleeding gums (low platelet), feeling tired and lethargic, sore throat, splenomegaly are all well known features of Acute lymphoblastic leukaemia (ALL)

Q-45

A 29 year old man has back pain and abdominal pain following treatment of malaria. His urine has become dark and his eyes have a yellowish tinge. He has had gallstones in the past. His past medical history includes jaundice when he was a neonate. What is the SINGLE most likely diagnosis?

A. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
B. **Allergy to antimalaria medication**
C. **Steven-John syndrome**
D. **Peptic ulcer disease**
E. **Beta thalassaemia**

ANSWER:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency

EXPLANATION:
Haemolysis in G6PD deficiency patients can be elicited by treatment of malaria. Back pain and abdominal pain can be seen in severe haemolysis occurring in G6PD deficiency.

History of gallstones and neonatal jaundice support the diagnosis of G6PD deficiency.

Q-46

A 7 year old boy presents with epistaxis of 2 hour duration. The bleeding has been controlled. His blood tests show:

Platelets 219 x 109/L
Prothrombin time 13 seconds
Activated partial thromboplastin time 42 seconds
Bleeding time is normal

What is the SINGLE most likely diagnosis?

A. **Haemophilia**
B. **Von Willebrand disease**
C. **Idiopathic thrombocytopenic purpura**
D. **Vitamin K deficiency**
E. **Anatomical defect**

ANSWER:
Anatomical defect

EXPLANATION:

All his blood results are normal. Anatomical defect is the only possiblity.

Q-47

A 16 year old boy presents with a palpable rash on his buttocks and extensor surface of his arms and legs following a sore throat. He complains of joint stiffness, joint pains and crampy abdominal pain. On urine testing, microscopic haematuria and proteinuria are found. What is the SINGLE most probable diagnosis?

A. **Measles**
B. **Thrombotic thrombocytopenic purpura (TTP)**
C. **Meningococcal septicaemia**
D. **Idiopathic thrombocytopenic purpura (ITP)**
E. **Henoch-Schonlein purpura (HSP)**

ANSWER:
Henoch-Schonlein purpura (HSP)

EXPLANATION:
The purpuric rash found in HSP is typically over buttocks and extensor surfaces of arms and legs. Arthrlagia occurs in 80% of patients and gastrointestinal symptoms like abdominal pain occur in around 30% of patients. Renal involvement is usually seen in the older children which can be identified by microscopic haematuria or proteinuria.

Q-48

A 22 year old man is admitted to the hospital with lethargy. His medical history includes hereditary spherocytosis. His blood tests show:

Haemoglobin 51 g/L
Reticulocytes 0.4%

What is the SINGLE most likely cause of his low haemoglobin and low leukocytes?

A. **Parvovirus B19 infection**
B. **Autoimmune haemolytic anaemia**
C. **Splenic sequestration crisis**
D. **Haemolytic transfusion reactions**
E. **Recent antibiotic treatment**

ANSWER:
Parvovirus B19 infection

EXPLANATION:
Parvovirus B19 infection can cause an aplastic crises in patients with hereditary spherocytosis. This can be life-threatening and often requires blood transfusion.

Splenic sequestration crisis is a wrong answer. A patient with a sequestration crisis is also severely anaemic , but the reticulocyte count will be high, in contrast to the aplastic crisis where the reticulocyte count is low or zero. Splenic sequestration crisis is also usually seen in sickle cell.

Q-49

A 55 year old man complains of fatigue. A blood test shows:

Haemoglobin 82 g/L
Mean cell volume 107 fL

What is the most likely diagnosis?

A. **Folate deficiency**
B. **Thalassaemia major**
C. **Iron deficiency anaemia**
D. **Anaemia of chronic disease**
E. **Sickle cell anaemia**

ANSWER:
Folate deficiency

EXPLANATION:
The best option above is folate deficiency as it is a macrocytic anaemia (high MCV)

Q-50

A 45 year old man presents with a lump in the posterior triangle of his neck. It has been growing for the past few months. He also complains of having drenching night sweats, unexplained fever and weight loss. Lymph nodes are palpable at the supraclavicular region. What is the SINGLE most likely diagnosis?

A. **Tuberculosis**
B. **Lymphoma**
C. **Lipoma**
D. **Reactive lymph nodes**
E. **Virchow's nodes**

ANSWER:
Lymphoma

EXPLANATION:
This is quite the classical presentation of lymphoma.
• Drenching night sweats, fever, weight loss
• Enlarged but otherwise asymptomatic lymph node, typically in the lower neck or supraclavicular region
• Occasionally, findings on examination may reveal hepatomegaly or splenomegaly.

In this question thankfully you do not need to differentiate between Hodgkin's and non-Hodgkin's.

Q-51

A 51year old man complains of lethary, tiredness and pruritus. The pruritus is worse after he takes a hot shower. He also says that he feels a burning sensation in his fingers and toes. Splenomegaly was found during an abdominal examination. His medical history is significant for gout. What is the SINGLE most likely diagnosis?

A. **Polycythaemia rubra vera (PRV)**
B. **Myelofibrosis**
C. **Rheumatoid arthritis**
D. **Scleroderma**
E. **Systemic lupus erythematosus**

ANSWER:
Polycythaemia rubra vera (PRV)

EXPLANATION:
The signs and symptoms are consistent with polycythaemia rubra vera (PRV).

Gout can be seen in PRV. This is due to an increased cell turnover.

Q-52

A 51 year old male presents with malaise and tiredness. On physical exam, his spleen is noted to be approaching his right iliac fossa. No lymphadenopathy was noticed. What is the SINGLE most likely cell type to be seen on a blood smear?

A. **Helmet shaped cell**
B. **Sickle cell**
C. **Granulocyte without blast cells**
D. **Blast cells**
E. **Target red cells**

ANSWER:
Granulocyte without blast cells.

EXPLANATION:
The clincher here is the massive spleen that approaches the right iliac fossa. Although there are many causes of massive spleen, for the purpose of PLAB, massive spleen can only be caused by chronic myeloid leukaemia (CML) or malaria.

If you see a middle aged man/woman with a huge spleen → likely to be Chronic myeloid leukaemia (CML). Malaria would likely have a travel history of some sort.

Mnemonic: CML → Crazy Massive Large Spleen

Q-53

A 50 year old woman is investigated for anaemia. She has no past medical history of note. Clinical examination reveals massive splenomegaly associated with pale conjunctivae. A full blood count was requested and results show:

Haemoglobin 105 g/L
White cell count 62 x 10^9/L
Platelets 803 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Chronic lymphocytic leukaemia**
B. **Chronic myeloid leukaemia**
C. **Myeloma**
D. **Acute myeloid leukaemia**
E. **Malaria**

ANSWER:
Chronic myeloid leukaemia.

EXPLANATION:
Please see Q-53

Q-54

A 7 year old boy has recurrent epidoses of spontaneous bleeding into his knee and elbow joints. Mild joint deformity is noted. Factor VIII/IX assay shows a decrease in factor VIII. What is the SINGLE most appropriate management?

A. **Desmopressin**
B. **Recombinant factor IX**
C. **Heparin**
D. **Infusion of platelet concentrates**
E. **Vitamin K**

ANSWER:
Desmopressin

EXPLANATION:
Factor VIII deficiency is evidence of haemophilia A. Desmopressin is one of the treatment choices.

Q-55

A 28 year old man has sudden onset of bone pain. He also begins experiencing bleeding from his gums. Looking retrospectively, he notes a decreased energy

level over past weeks. He feels dizzy and has dyspnoea on exertion. He looks pale and has numerous ecchymoses seen over his body. Hepatosplenomegaly is noted. A full blood count shows WBC of 102 x 10^9/L. A bone marrow biopsy shows numerous blasts. What is the SINGLE most likely diagnosis?

A. **Mantle cell lymphoma**
B. **Infectious lymphocytosis**
C. **Waldenstrom's macroglobulinemia**
D. **Acute myeloid leukaemia (AML)**
E. **Acute lymphoblastic leukaemia (ALL)**

ANSWER:
Acute myeloid leukaemia (AML)

EXPLANATION:
This is actually an acute emergency. The leucocytosis is causing the bone pain. Bleeding from the gum is commonly seen in acute myeloid leukaemia (AML).
Note that gum bleeding can also be seen in ALL.

AML is the most common acute leukaemia in adults. Thus, majority of the acute leukaemia in children questions asked in the PLAB test would be acute lymphoblastic leukaemia (ALL) and not acute myeloid leukaemia (AML).

One needs to be careful with picking AML or ALL as there are often questions with a very similar stem. In reality, it is difficult to diagnose them clinically as well. Flow cytometry (immunophenotyping) is used to help distinguish AML from acute lymphocytic leukemia (ALL).

Acute myeloid leukaemia (AML)
This neoplastic proliferation of blast cells is derived from marrow myeloid elements. It progresses rapidly (death in about 2 months if untreated)

Children or young adults may present with acute symptoms over a few days to a few weeks.

Most AML subtypes show more than 30% blasts of a myeloid lineage in the blood, bone marrow, or both.

Presentation:
• Fatigue, pallor, dizziness and shortness of breath on exertion (symptoms of anaemia)
• Bleeding caused by thrombocytopenia. Thrombocytopenia often causes petechiae on the lower limbs. DIC may aggravate the situation and cause larger lesions
• Infection
• Gingivitis is common, with swollen, bleeding gums
• There can also be bone pain

• Hepatomegaly and splenomegaly may be found. Lymphadenopathy is less common.

Investigations
• FBC:
  • Total WBC count is often high. However, it may also be normal or even low
  • Neutrophils are usually depleted and blast cells are seen in their place
• Bone marrow aspiration is the diagnostic procedure. (The WHO classification requires more than 20% blasts in the peripheral blood, to make a diagnosis of AML)

Q-56

A 34 year old woman developed a purpuric rash on the back of her legs. She also reports frequent nose bleeds and menorrhagia. A blood count shows:

Haemoglobin 119 g/L
White cell count 6.8 x 10^9/L
Platelets 59 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Idiopathic thrombocytopenic purpura**
B. **Thrombotic thrombocytopenic purpura**
C. **Von Willebrand's diease**
D. **Antiphospholipid syndrome**
E. **Henoch-Schonlein purpura**

ANSWER:
Idiopathic thrombocytopenic purpura

EXPLANATION:
Idiopathic thrombocytopenic purpura is usually seen in children but that does not mean it can't happen in adults.

Chronic ITP which is mainly seen in women can run a fluctuating course of bleeding, purpura, epistaxis and menorrhagia.

The isolated thrombocytopenia in a well patient points to a diagnosis of idiopathic thrombocytopenic purpura.

Idiopathic thrombocytopenic purpura in adults
Unlike ITP in children, adult ITP does not normally follow an infection and usually has an insidious onset. It is more likely to follow a chronic course in affected adults than in children.

Presentation:

• As in children, adults with ITP may demonstrate a range of symptoms from none at all through to severe haemorrhage
• Bleeding, purpura, epistaxis and menorrhagia

Laboratory diagnosis
• Isolated thrombocytopenia; blood count otherwise normal

Management:
• Prednisolone
• IV immunoglobulin
• Emergency platelet transfusion
  • Only in life threatening haemorrhage. (usually platelet less than 20 x 10^9/L)

Q-57

A 26 year old Greek man has recently recovered from a haemolytic episode 6 weeks ago. The haemolytic episode occurred a day after he ate a traditional Greek dish. Glucose-6-phosphate dehydrogenase deficiency is suspected. What is the SINGLE most definitive diagnostic test?

A. Osmotic fragility test
B. G6PD enzyme assay
C. Heinz bodies seen on blood film
D. Bite cells seen on blood film
E. Decreased haptoglobins and increased reticulocytes

ANSWER:
G6PD enzyme assay

EXPLANATION:
G6PD enzyme activity is the definitive test

Osmotic fragility test is to diagnose Hereditary spherocytosis. Heinz bodies and bite cells seen on blood film are important investigations that point towards G6PD but are not the definitive diagnostic test.

Q-58

A 67 year old woman with a history of rheumatoid arthritis presents to her GP's office with complaints of epigastric discomfort, especially after eating. She has been on long term methotrexate and NSAID therapy for her condition. On examination, she appears pale but seems otherwise well. A full blood count reveals the following:

Haemoglobin 105 g/L
MCV, MCH and MCHC are seen to be decreased

What is the SINGLE most likely diagnosis?

A. **Folate deficiency anaemia**
B. **Vitamin B12 deficiency anaemia**
C. **Haemolytic anaemia**
D. **Aplastic anaemia**
E. **Chronic gastrointestinal bleeding**

ANSWER:
Chronic gastrointestinal bleeding

EXPLANATION:
The blood values are indicative of a microcytic anaemia. It is true that methotrexate can cause a folic acid deficiency anaemia but since the blood results clearly show a microcytic anaemia (and folic acid deficiency anaemia is a macrocytic anaemia) the only correct conclusion that we can reach is that the long term NSAID therapy si the culprit for her anaemia.

Q-59

A 20 year old woman has had bruising and petechiae for a week. She also reports frequent nose bleeds and menorrhagia but is otherwise well. A blood count showed:

Haemoglobin 111 g/L
White cell count 6.3 x 10^9/L
Platelets 39 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Acute leukaemia**
B. **Aplastic anaemia**
C. **HIV infection**
D. **Idiopathic thrombocytopenic purpura**
E. **Systemic lupus erythematosus**

ANSWER:
Idiopathic thrombocytopenic purpura

EXPLANATION:
Idiopathic thrombocytopenic purpura is usually seen in children but that does not mean it can't happen in adults.

As the patient is otherwise well, acute leukaemia, HIV and SLE are unlikely. A normal WBC count excludes aplastic anaemia. Thus the likely diagnosis is ITP. Idiopathic thrombocytopenic purpura fits with her symptoms of bruising and petechiae. Older girls may have menorrhagia. Some experience nosebleeds.

The isolated thrombocytopenia in a well patient points to a diagnosis of idiopathic thrombocytopenic purpura.

Q-60

A 54 year old woman is diagnosed with deep vein thrombosis after taking a long haul flight. She is started on warfarin. What is the target INR for her?

A. < 1
B. 1-2
C. 2-3
D. 3-4
E. 2-5

ANSWER:
2-3

EXPLANATION:
INR is derived from the PT ratio and is a standardized method of reporting which permits comparability between laboratories.

The INR range of 2 to 3 is appropriate for:
• Prophylaxis or treatment of venous thromboembolism
• Reduction of the risk of systemic embolism for people with atrial fibrillation and valvular heart disease

For the purpose of PLAB, just remember that INR of 2 to 3 is the answer for majority of cases. The only cases where a higher INR is required, is in the cases of a mechanical heart valve replacement. Patients with metallic valves require lifelong anticoagulation with a target INR of 3 to 4.

Q-61

A 65 year old man presents with back pain. Abdominal examination shows splenomegaly

Blood report shows the following:

Haemoglobin 102 g/L
White cell count 122 x 10^9/L
Platelets 102 x 10^9/L
ESR 25

He has been found to have Philadelphia chromosome on cytogenetic analysis. What is the SINGLE most likely diagnosis?

A. Acute lymphoblastic leukaemia (ALL)
B. Acute myeloid leukaemia (AML)
C. Chronic myeloid leukaemia (CML)

D. **Chronic lymphocytic leukaemia (CLL)**
E. **Lymphoma**

ANSWER:
Chronic myeloid leukaemia (CML)

EXPLANATION:
Anaemia, raised WBC count, low platelet (platelet may be variable) are known features of Chronic myeloid leukaemia (CML)

Splenomegaly (particularly if massive) is very suggestive of Chronic myeloid leukaemia (CML) and Philadelphia chromosome is diagnostic of Chronic myeloid leukaemia (CML).

Q-62

A 55 year old HIV man presents with painless peripheral lymphadenopathy, fever, night sweats and weight loss. Abdominal examination reveals an enlarged spleen. What is the SINGLE most likely diagnosis?

A. **Hodgkin's lymphoma**
B. **Non-Hodgkin's lymphoma**
C. **Acute lymphoblastic leukaemia (ALL)**
D. **Acute myeloid leukaemia (AML)**
E. **Chronic myeloid leukaemia (CML)**

ANSWER:
Non-Hodgkin's lymphoma

EXPLANATION:
Although both Hodgkin's and Non-Hodgkin's lymphoma present in similar ways with lymphadenopathy, night sweats, fever, weight loss, non-Hodgkin's is more associated with HIV than hodgkin's disease. Non-Hodgkin's lymphoma (NHL) is known as AIDS-related lymphoma.

The most prevalent of the HIV-related lymphomas is diffuse large B-cell non-Hodgkin's lymphoma, followed by Burkitt's lymphoma.

Although not considered an AIDS-defining illness, Hodgkin's lymphoma is increasing in incidence in those with HIV infection and would be considered an answer to this question if NHL was not present as one of the answers.

There is a clear correlation between the degree of immunosuppression and the risk of developing NHL. The pathogenesis is rather the immunosuppression rather than the HIV itself.

Q-63

A 45 year old woman who is taking medication for the treatment of rheumatoid arthritis presents with dizziness, fatigability and lack of energy. Blood results show:

Haemoglobin 80 g/L
Mean cell volume (MCV) 106 fL

What is the SINGLE most likely cause of her anaemia?

- **A. Steroids**
- **B. Chronic disease**
- **C. NSAIDs**
- **D. Methotrexate**
- **E. Leflunomide**

ANSWER:
Methotrexate

EXPLANATION:
Methotrexate is a folate antagonist. It causes folate deficiency which is shown as a macrocytic anaemia like in the case above.

Anaemia of chronic disease would be considered as a cause if the MCV was normal or low. Rheumatoid arthritis leading to anaemia of chronic disease has red cells that are usually hypochromic, microcytic or normochromic, normocytic.

Q-64

A 30 year old woman presents with complaints of lethargy and frequent infections. On examination, her spleen is not palpable and there are no associated lymphadenopathy. A full blood count reveals the following:

Haemoglobin 85 g/L
White cell count 2.2 x 10^9/L
Platelets 26 x 10^9/L

What tissue biopsy will you do to prove the diagnosis?

- **A. Liver**
- **B. Lymph node**
- **C. Spleen**
- **D. Bone marrow**
- **E. Lung**

ANSWER:
Bone marrow

EXPLANATION:
According to her lab results, this woman appears to have a pancytopenia (reduction in all three haematopoietic cell lines). In order to prove a diagnosis of aplastic anaemia, a bone marrow biopsy must be done.

Please note that pancytopenia and aplastic anaemia are NOT interchangeable terms.

- Pancytopenia is a decrease in all three haematopoietic cell lines. Pancytopenia can be suspected from a full blood count with or without a peripheral blood smear.
- Aplastic anaemia is pancytopenia AND histological evidence of a hypoplastic bone marrow. It is a diagnosis of exclusion and can only be made by a bone marrow biopsy.

Q-65

A 25 year old lady has a chest infection which she is receiving antibiotics for. She has shortness of breath, feels tired and weak. On examination, she looks pale and purpura is seen on her legs. Blood results show the following:

Haemoglobin 76 g/L
White cell count 1.2 x 10^9/L
Neutrophils 0.3 x 10^9/L
Plaletets 19 x 10^9/L
Reticulocytes 1%

Blood film morphology was unremarkable. A bone marrow aspirate shows a reduction in haemopoietic cells. What is the SINGLE most likely underlying diagnosis?

A. Pernicious anaemia
B. Chronic myeloid leukaemia
C. Aplastic anaemia
D. Acute myeloid leukaemia
E. Acute lymphoblastic leukaemia

ANSWER:
Aplastic anaemia

EXPLANATION:
She has signs and symptoms of anaemia. The blood picture shows pancytopenia which rules out pernicious anaemia as an underlying cause.

Normal morphology rules out the possibility of acute myeloid leukaemia, and acute lymphoblastic leukaemia.

Chronic myeloid leukaemia usually has leucocytosis.

A bone marrow aspirate that shows a gross reduction in all haemopoietic tissue is seen classically in aplastic anaemia. Decrease reticulocytes support the diagnosis.

Q-66

A 30 year old woman complains of tiredness, lethargy and constipation. On inspection, she has dry coarse skin, hair loss and cold peripheries. On examination, a diffuse and lobulated goitre can be palpated on her anterior neck. A full blood count and peripheral smear is done which shows a macrocytic anaemia. What is the SINGLE most likely diagnosis?

A. **Cushing's syndrome**
B. **Hyperthyroidism**
C. **Crohn's disease**
D. **Addison's disease**
E. **Pernicious anaemia**

ANSWER:
Pernicious anaemia

EXPLANATION:
This is a multi-part question. Her symptoms are indicative of hypothyroidism. Her signs are indicative of Hashimoto's Thyroiditis (an autoimmune thyroid disorder). Since Hashimoto's is an autoimmune disease and her blood smear shows a macrocytic anaemia, a logical conclusion would be that she is suffering from pernicious anaemia (also an autoimmune disease).

Some points to remember for the PLAB 1 exam:

Growth patterns of goitres
• Iodine deficiency (rare in the developed world): diffuse
• Hashimoto's Thyroiditis: diffuse and lobulated
• Pituitary disease: diffuse
• Grave's Disease: diffuse
• Thyroid cancer and benign thyroid growths: uninodular

If you have difficulty remembering this long list just remember: all goitres grow diffuse except Hashimoto's (diffuse AND lobulated) and benign/malignant thyroid growths (uninodular).

Associations of hypothyroidism
• Obstructive sleep apnoea
• Carpal tunnel syndrome
• Galactorrhoea/hyperprolactinaemia

Q-67

A 20 year old man with sickle cell anaemia has shortness of breath, pallor,

headache and lethargy. He has been having flu-like symptoms for the past week. For the past few days, he has been having aches on his hands, knees and ankles. His initial blood tests show:

Haemoglobin 53 g/L

Infection with parvovirus B19 is suspected and further blood tests have been sent for specific IgM and IgG antibodies to parvovirus B19. What is the SINGLE most likely diagnosis?

A. **Aplastic crises**
B. **Haemolytic crises**
C. **Splenic sequestration crisis**
D. **Vaso-occlusive crises**
E. **Acute chest syndrome**

ANSWER:
Aplastic crises

EXPLANATION:
When you see parvovirus B19 in the exam, immediately think of sickle cell anaemia or hereditary spherocytosis with the diagnosis of aplastic crisis at hand.

Parvovirus is also a risk factor for splenic sequestration crisis however infection with parvovirus B19 is more commonly associated with aplastic crisis in patients with sickle cell anaemia.

In adults, parvovirus B19 can present with flu-like symptoms and symmetrical joint pain and stiffness involving joints of the hands, knees, wrists and ankles. This usually resolves in weeks.

Another group of people that you should be worried about parvovirus infections are pregnant women as they can affect the fetal red blood cells causing aplastic anaemia. The anaemia can be particularly severe due to the short life span of fetal erythrocytes.

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

There are four main types of crises:

Thrombotic crises (Vaso-occlusive crises)
- Most common type of crisis
- Caused by obstruction of the microcirculation by sickled red blood cells, causing ischaemia
- Precipitated by cold, infection, or dehydration – *Some patients would know their triggers and develop strategies to avoid them however majority of painful episodes*

have no identifiable cause.
• Occlusion causes pain which may be severe
• Infarcts occur in various organs
Commonly presenting scenarios in exams are
• Occlusion causing mesenteric ischaemia, mimicking an acute abdomen
• Avascular necrosis e.g. femoral head

Sequestration crises
• Is the sudden enlargement of the spleen, causing a decrease in haemoglobin concentration, circulatory collapse and hypovolaemic shock
• Occurs mainly in babies and young children
• Occurs mainly in babies and young children
• Reticulocyte count would be increased
• Recurrent splenic sequestration is an indication for splenectomy

Aplastic crises
• Characterized by a rapid drop in haemoglobin level caused by a transient cessation of erythropoiesis (production of red blood cells)
• Leads to a rapid reduction in red cell precursors in the bone marrow and a markedly reduced number of reticulocytes in the peripheral blood
• Caused by an infection with parvovirus B19
Most patients have a decrease of erythropoiesis (production of red blood cells) during parvovirus infection, however it is most dangerous in patients with sickle cell anaemia or hereditary spherocytosis, as they are heavily dependent on erythropoiesis due to the reduced lifespan of the red cells.

Haemolytic crises
• Rare thus uncommon to be asked in PLAB
• During painful crises there may be a marked increase in the rate of haemolysis with a fall in the haemoglobin level

Q-68

A 48 year old woman hasbecome increasingly fatigued over the past 10 months. Vitiligo of the hand was noted. Her blood tests show:

Haemoglobin 88 g/L
White cell count 8 x 10^9/L
Platelets 245 x 10^9/L
Mean cell volume 130 fL

What is the SINGLE most likely diagnosis?

A. Folate deficiency
B. Thalassaemia minor
C. Pernicious anaemia
D. Anaemia of chronic disease

E. **Sickle cell anaemia**

ANSWER:
Pernicious anaemia

EXPLANATION:
The mean cell volume is increased. This points towards either a B12 deficiency or folate deficiency

Pernicious anaemia is one of the causes of a B12 deficiency and it may coexist with other autoimmune disease such as vitiligo. Note that hypothyroidism is also another coexisting autoimmune disease to look out for.

Q-69

A 4 year old boy presents with recurrent episodes of self limiting spontaneous bleeding into his arms and legs that occurs with minimal trauma. His blood tests show:

Prothrombin time 11 seconds
Activated partial thromboplastin time 69 seconds
Bleeding time is normal

What is the SINGLE most likely diagnosis

A. **Haemophilia**
B. **Thalassaemia**
C. **Von Willebrand's disease**
D. **Idiopathic thrombocytopenic purpura**
E. **Thrombotic thrombocytopenic purpura**

ANSWER:
Haemophilia

EXPLANATION:
Activated partial thromboplastin time (APTT) that is prolonged with everything else being normal points towards haemophilia.

Factor VIII and IX levels should be offered to confirm the diagnosis.

Q-70

A 12 year old boy has sudden development of purpura 2 weeks after an upper respiratory tract infection. A blood count showed:

Haemoglobin 119 g/L
White cell count 6.8 x 109/L
Platelets 35 x 109/L

Prothrombin time 12 seconds
Activated partial thromboplastin time 41 seconds
Bleeding time 10 minutes

What is the SINGLE most likely diagnosis?

A. **Idiopathic thrombocytopenic purpura**
B. **Thrombotic thrombocytopenic purpura**
C. **Von Willebrand's disease**
D. **Haemophilia A**
E. **Haemophilia B**

ANSWER:
Idiopathic thrombocytopenic purpura

EXPLANATION:
The isolated thrombocytopenia and history of an upper respiratory tract infection with the development of purpura suggest idiopathic thrombocytopenic purpura.

In idiopathic thrombocytopenic purpura, bleeding time may be increased like the above.

Idiopathic thrombocytopenic purpura
Presentation:
• Follows viral infection or immunisation
• The most common presentation is petechiae or bruising. Petechiae mainly in arms and legs - sudden onset
• Up to a quarter present with nosebleeds
• Haematuria and gastrointestinal bleeds are less common.
• Older girls may have menorrhagia
• Otherwise the patient is well and physical examination is normal

Laboratory diagnosis
• Isolated thrombocytopenia; blood count otherwise normal

Management:
• Prednisolone
• IV immunoglobulin
• Emergency platelet transfusion
• Only in life threatening haemorrhage. (usually platelet less than 20 x 109/L)

Q-71

A 75 year old male presents with enlarged cervical nodes. He has several recurrrent infections over the year. His conjunctiva is pale and he feels weak. What is the SINGLE most likely cell type to be found on a blood smear of this patient?

A. **Granulocytes without blast cells**
B. **Myofibroblasts**
C. **Plasma cells**
D. **Mature lymphocytes**
E. **Sickling of cells**

ANSWER:
Mature lymphocytes

EXPLANATION:
The diagnosis here is Chronic lymphocytic leukaemia (CLL) which has mature lymphocytes on the blood film.

Factors that support the diagnosis of CLL in this question:
• His age (75 years old) - In the PLAB test, if you see an elderly patient (usually more than 65 years old) with symptoms of leukaemia, it is most likely CLL. However, read the whole question before you make a decision on the answer.
• Cervical lymphadenopathy
• Recurrent infections → dysfunctional WBC
• Pale conjunctiva → Anaemia

On blood film, B cell lymphocytosis will be seen often with smudge cells. They are mature but functionally impaired lymphocytes as they escape apoptosis.

Chronic lymphocytic leukaemia (CLL)
CLL can often present as an asymptomatic elevation of white cells found on routine evaluation of patients during investigations for other health problems. These patients are exclusively older (majority over 50 years old).

When patients do have signs and symptoms they are usually non-specific:
• Fatigue
• Lethargy
• Enlargement of lymph nodes

When should you suspect CLL?
When an older patient has marked elevation in white cell count with marked lymphocytic predominance. The marrow is often infiltrated with leukemic lymphocytes. “Smudge cells” are seen on smear.

Q-72

A 6 year old child has a history of recurrent mild jaundice that occurs a few days after the onset of a fever. Between the episodes he is well. 3 days ago, he had a chest infection and his blood results show:

Haemoglobin 106 g/L
Mean cell haemoglobin concentration 330 g/L

Bite cells are seen on blood film. What is the SINGLE most likely diagnosis?

A. **Hereditary spherocytosis**
B. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
C. **Thalassaemia**
D. **Sickle cell disease**
E. **Congenital storage disorder**

ANSWER:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency

EXPLANATION:
There are some precipitating factors of haemolysis causing jaundice in patients with G6PD deficiency. Among then include infection. Bite cells point towards the diagnosis of G6PD.

Q-73

A 13 year old boy presents complains of pins and needles sensation in his feet. He does not suffer from any medical conditions and takes no regular medication. He denies any palpitations, shortness of breath or lightheadedness. On examination, his tongue appears to be swollen and inflamed. He has a BMI of 15 kg/m^2. His FBC shows the following:

Haemoglobin of 80 g/L
Mean cell volume (MCV) 108 fL

A smear shows oval macrocytes and hypersegmented neutrophils. The patient mentions that he has recently become vegan and in the morning, only has time for a cup of tea before heading off to school. What is the SINGLE best treatment for this patient?

A. **Packed red cell blood transfusion**
B. **Parenteral iron**
C. **Pyridoxine**
D. **Vitamin C**
E. **Hycroxycobalamin and folic acid**

ANSWER:
Hydroxycobalamin and folic acid

EXPLANATION:
This patient has a vitamin B12 deficiency due to low intake.

Vegan diet patients such in the above stem is already a huge hint towards vitamin B12 deficiency. The fact that he has a low BMI is a hint that he has an improper diet.

The signs and symptoms are nonspecific – you cannot clinically differentiate between B12 deficiency anaemia and folic acid deficiency but for PLAB remember that patients with B12 deficiency often present with some form of neurological disturbance (peripheral neuropathy in this stem)

As there is no option for hydroxycobalamin alone, pick the one with the combination of hydroxycobalamin and folic acid.

Blood transfusion should NOT be considered if the patient has no symptoms of anaemia where the Hb is 80 g/L or more.

Usually, blood transfusions are considered if there are:

- Symptoms of anaemia and haemoglobin is less than 80 g/L
- Haemoglobin less than 70 g/L in an asymptomatic patient

Q-74

A 34 year old male patient with estbalished Burkitt's lymphoma is undergoing chemotherapy. He is currently at week two of treatment. He complains of only passing very little amounts of urine in the past 24 hours and feeling more lethargic than usual. Upon routine blood testing, he was found to have the following lab values:

Potassium 5.9 mmol/L
Urea 18 mmol/L
Creatinine 289 micromol/L
Serum calcium (total) 1.9 mmol/L

What SINGLE most appropriate investigation will you perform to aid in management of this patient?

A. **Serum urate**
B. **Serum alkaline phosphatase**
C. **C-reactive protein (CRP)**
D. **24 hour urinary calcium**
E. **Serum parathyroid hormone**

ANSWER:
Serum urate

EXPLANATION:
This patient is suffering from tumour lysis syndrome. Tumour lysis syndrome is a severe metabolic disturbance following the rapid lysis of malignant cells a short while after chemotherapy, radiotherapy, surgery or ablation procedures. It is an oncological emergency. It occurs most often in patients with acute lymphoblastic leukaemia (ALL) or Burkitt's lymphoma. In this stem, Burkitt's lymphoma was present.

Tumour lysis syndrome would result in the following blood results

- Hyperuricaemia
- Hyperkalaemia
- Hyperphosphataemia
- Hypocalcaemia

Although a full biochemical profile is needed to diagnose tumour lysis syndrome uric acid levels would help confirm the diagnosis of tumour lysis syndrome

TUMOUR LYSIS SYNDROME

Important key featuresto remember for tumour lysis syndrome

- *History of Leukaemia or Burkitt's lymphoma*
- *Chemotherapy*
- *Acute renal failure*
- *Hyperuricaemia, hyperkalaemia, hyperphosphataemia, hypocalcaemia*
- *IV fluids as part of management*

Tumour lysis syndrome involves a rapid tumour cell lysis leading to large amounts of potassium, phosphate and uric acid released into the bloodstream. In the exam, it usually follows a patient with malignancies who has recently been treated with chemotherapy.

It is considered a hematology and oncology emergency as it is life threatening and has associated renal, cardiac and neurological complications.

Seen in highly chemosensitive neoplasms such as leukaemia and non-Hodgkin's lymphoma (particularly Burkitt's lymphoma).

The following metabolic abnormalities develop rapidly

- Hyperuricaemia
  - Due to massive cell death and nuclear breakdown generating large amounts of nucleic acids of which the purines are converted into uric acid
  - Causes gout due to monosodium urate crystals and renal colic due to formation of renal stones
- Hyperkalaemia
  - Due to rapid cell lysis
  - Often the earliest sign of tumour lysis syndrome
  - Causes paraesthesia, muscle weakness and arrhythmias
- Hyperphosphataemia
  - Due to rapid cell lysis
  - Causes acute kidney failure due to deposition of calcium phosphate crystals in renal parenchyma
- Hypercalcaemia
  - Secondary to hyperphosphataemia (phosphates bind to calcium forming calcium phosphate crystals)
  - Causes tetany

Acute renal failure occurs due to uric acid nephropathy, acute nephrocalcinosis and precipitation of xanthine.

Treatment
Rehydration with intravenous fluids
Management is complicated but for the exam, all that is required is the knowledge that this patient requires intravenous fluids

Q-75

A 15 year old boy is investigated after he bled excessively following a tooth extraction. He has always noted that he bruises easily with minimal trauma. His blood tests show:

Haemoglobin 120 g/L
White cell count 7 x 109/L
Platelets 168 x 109/L
Prothrombin time 13 seconds
Activated partial thromboplastic time 81 seconds
Bleeding time within normal ranges

What is the SINGLE most likely diagnosis?

A. **Haemophilia A**
B. **Haemophilia B**
C. **Von Willebrand's disease**
D. **Thrombotic thrombocytopenic purpura**
E. **Idiopathic thrombocytopenic purpura**

ANSWER:
Haemophilia A

EXPLANATION:
The prolonged aPTT supports the diagnosis of haemophilia.

Between both haemophilia A and B, haemophilia A is more common and it accounts for 90% of cases of haemophilia.

Q-76

A 52 year old lady has been suffering from chronic rheumatoid arthritis and is on methotrexate and naproxen. Her blood results show:

Haemoglobin 83 g/L
Mean cell volume (MCV) 70 fL

What is the SINGLE most likely cause?

A. **Haemorrhoids**
B. **Gastrointestinal haemorrhage**
C. **Menorrhagia**
D. **Folate deficiency**
E. **B12 deficiency**

ANSWER:
Gastrointestinal haemorrhage

EXPLANATION:
Gastrointestinal haemorrhage would be a cause of microcytic anaemia like in the given scenario and it fits with the history of prolonged use of NSAIDS.

Folate and B12 deficiency are in the category of macrocytic anaemias.

There should be no reason for menorrhagia. Besides, the patient is 52 years old. The average age of menopause in UK is 51. Blood loss from the gastrointestinal (GI) tract is the most common cause of iron deficiency anaemia in postmenopausal women.

There is also no relation with haemorrhoids

Q-77

A 39 year old pregnant woman who is 36 week gestation has acute abdominal pain and is rushed for immediate C-section. Her blood pressure was reported to be 110/60 mmHg. Her blood tests show:

Haemoglobin 101 g/L
White cell count 9.8 x 109/L
Platelets 60 x 109/L
Activated partial thromboplastin time 61 seconds
Prothrombin time 29 seconds
Fibrinogen 0.6 g/L
Bilirubin 22 micromol/L

What is the SINGLE most likely diagnosis?

A. **Pregnancy induced hypertension**
B. **Disseminated intravascular coagulation**
C. **HELLP syndrome**
D. **Acute fatty liver**
E. **Obstetric cholestasis**

ANSWER:
Disseminated intravascular coagulation

EXPLANATION:
Acute abdominal pain may indicate concealed abruptio placentae which may be a cause of disseminated intravascular coagulation.

The two top choices here are HELLP syndrome and disseminated intravascular coagulation (DIC). It is important to understand that HELLP syndrome may lead to disseminated intravascular coagulation. But the more specific answer in this question is DIC because in HELLP syndrome, the prothrombin time, activated partial thromboplastin time and serum fibrinogen levels are normal but are prolonged in DIC.

Bilirubin levels may be higher than normal due to bilirubin production secondary to haemolysis.

Q-78

A 55 year old man complains of headache and visual disturbances. He has a history of hypertension. He also reports itching after a hot bath and burning sensation in his fingers and toes. He is noted to have mass in the left upper quadrant. Blood report shows the following:

Haemoglobin 202 g/L
White cell count 19 x 10^9/L
Platelets 502 x 10^9/L
Eyrthropoeitin is normal

What is the SINGLE most likely diagnosis?

A. **Myelofibrosis**
B. **Polycythaemia rubra vera**
C. **Essential thrombocythemia**
D. **Chronic myeloid leukaemia**
E. **Chronhic lymphocytic leukaemia**

ANSWER:
Polycythaemia rubra vera

EXPLANATION:
The signs and symptoms are consistent with polycythaemia rubra vera (PRV)

Hypertension is found in 30% of patients with PRV. Splenomegaly is found in 75% of patients at the time of diagnosis.

The mass in the left upper quadrant represents the spleen (splenomegaly)

Burning sensation in fingers and toes, are characteristic.

PCV is usually associated with a low serum level of the hormone erythropoietin (EPO). However, everything else in this question points towards PRV.

Q-79

A 4 year old boy has a history of epistaxis. Prothrombin time, bleeding time, fibrinogen levels and von Willebrand factor are normal. Activated partial thromboplastin time (APTT) was found to be prolonged. His blood tests show:

Haemoglobin 112 g/L
White cell count 5 x 10^9/L
Platelets 250 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Haemophilia**
B. **Idiopathic thrombocytopenic purpura**
C. **Sickle cell anaemia**
D. **Haemolytic uraemic syndrome**
E. **Thalassaemia**

ANSWER:
Haemophilia

EXPLANATION:
Despite the fact that many people remember haemophilia presenting with bleeding into joints and muscles, you would need to know that epistaxis may occur in haemophilia

Activated partial thromboplastin time (APTT) that is prolonged with everything else being normal points towards haemophilia.

Factor VIII and IX levels should be offered to confirm the diagnosis.

Q-80

A 53 year old lady has been suffering from chronic rheumatoid arthritis and is on methotrexate. Blood results show:

Haemoglobin 83 g/L
Mean cell volume (MCV) 70 fL

What is the SINGLE most likely cause?

A. **Haemorrhoids**
B. **Anaemia of chronic disease**
C. **Menorrhagia**
D. **Folate deficiency**
E. **B12 deficiency**

ANSWER:
Anaemia of chronic disease

EXPLANATION:
The patient has microcytic anaemia which can fit with the diagnosis of anaemia of chronic disease. In anaemia of chronic disease, red cells are often normochromic, normocytic, but may be hypochromic, microcytic (as frequently seen in rheumatoid arthritis and Crohn's disease)

Folate and B12 deficiency are in the category of macrocytic anaemias.

There should be no reason for menorrhagia. Besides, the patient is 53 years old. The average age of menopause in UK is 51.

There is also no relation with haemorrhoids.

Q-81

A 36 year old woman has massive bleeding from a venipuncture site. Petechiae was noticed on her skin. Her blood tests show:

Haemoglobin 113 g/L
White cell count 9.8 x 10^9/L
Platelets 48 x 10^9/L

Prothrombin time, activated partial thromboplastin time and bleeding time are prolonged. Fibrin degradation products were elevated. What is the SINGLE most likely diagnosis?

A. **Haemophilia**
B. **Disseminated intravascular coagulation**
C. **Idiopathic thrombocytopenic purpura**
D. **Factor V Leiden**
E. **Warfarin overdose**

ANSWER:
Disseminated intravascular coagulation

EXPLANATION:
Please see Q-24

Q-82

A 40 year old man has a mild fever and feels generally tired. He has marked weight loss over the last 6 months and has a bilateral white, vertically corrugated lesion on lateral surfaces of the tongue. What is the SINGLE most likely diagnosis?

A. **C1 esterase deficiency**
B. **Crohn’s disease**

C. **HIV disease**
D. **Sarcoidosis**
E. **Sjogren's syndrome**

ANSWER:
HIV disease

EXPLANATION:
The white, vertical lesion described is called hairy leukoplakia which occurs primarily in HIV-positive individuals.

Hairy leukoplakia
Hairy leukoplakia is a condition that is characterised by irregular white patches on the side of the tongue and occasionally elsewhere on the tongue or in the mouth. It is a form of leukoplakia, which refers to white patches on the mucous membranes of the mouth often arising in response to chronic irritation. Hairy leukoplakia occurs primarily in HIV-positive individuals.

This white lesion cannot be scraped off. The lesion itself is benign and does not require any treatment.

Q-83

A 14 year old child has recurrent throat infections. He feels tired and lethargic all the time. Blood results show:

Hb 7.2 g/dl
WCC 6 x 10^9/L
Platelets 95 x 10^9/L

Blood film shows blast cells. What is the SINGLE most likely diagnosis?

A. **Acute lymphoblastic leukaemia (ALL)**
B. **Acute myeloid leukaemia (AML)**
C. **Chronic myeloid leukaemia (CML)**
D. **Chronic lymphocytic leukaemia (CLL)**
E. **Hodgkin's lymphoma**

ANSWER:
Acute lymphoblastic leukaemia (ALL)

EXPLANATION:
Please see Q-3

Q-84

A 26 year old businessman travelled from New York to the UK. He presented to A&E three weeks later complaining of drenching night sweats, fever and lymphadenopathy in the neck since returning from his business trip. What is the

SINGLE most likely diagnosis?

A. **Tuberculosis**
B. **Lymphoma**
C. **Aplastic anaemia**
D. **Hereditary spherocytosis**
E. **Infectious mononucleosis**

ANSWER:
Lymphoma

EXPLANATION:
The two main contenders for an answer to this question are tuberculosis and lymphoma.

Tuberculosis is improbable because New York City (USA) is not a tuberculosis prone area. The main TB prone areas that you have to take note of for the PLAB exam is a patient travelling to or from South Asia or sub-Saharan Africa.

While it is true that the signs and symptoms of tuberculosis and lymphoma are very similar, the following table makes is easy to differentiate between tuberculosis and lymphoma if you are having difficulty choosing either as an answer:

Tuberculosis	**Lymphoma**
Fatigue, malaise, fever, weight loss, anorexia	Drenching night sweats, fever, weight loss
Hilar, paratracheal or superficial node involvement. Palpable nodes may be initially tender, firm and discrete	Enlarged but otherwise asymptomatic lymph node, typically in the lower neck or supraclavicular region
Chronic, productive cough with purulent +/- bloodstained sputum	Patients might complain of chest discomfort with a cough or dyspnoea
May result in lobar collapse, bronchiectasis, pleural effusion and pneumonia	Mediastinal masses are frequent and are sometimes discovered on a routine CXR
Erythema nodosum	Findings on examination include lymphadenopathy, hepatomegaly, splenomegaly, and superior vena cava syndrome

Q-85

A 54 year old man has fatigue. A recent blood report shows the following:

Haemoglobin 90 g/L
Mean cell volume 70 fL
Mean cell haemoglobin concentration 290 g/L
Serum ferritin 9 micrograms/L

Total iron-binding capacity 75 micromol/L

What is the SINGLE most likely diagnosis?

A. **Thalassaemia trait**
B. **Hypoparathyroidism**
C. **Hereditary sideroblastic anaemia**
D. **Anaemia of chronic disease**
E. **Iron deficiency anaemia**

ANSWER:
Iron deficiency anaemia

EXPLANATION:
Iron-deficiency anaemia
Aetiology
• Blood loss from the gastrointestinal (GI) tract is the most common cause of iron-deficiency anaemia in adult men and postmenopausal women
• Blood loss due to menorrhagia is the most common cause of iron deficiency in premenopausal women
• In tropical countries, infestation of the gut may cause irondeficiency anaemia , especially with hookworm and schistosomiasis
• *Common causes of blood loss include:*
    • Non-steroidal anti-inflammatory drug (NSAID) use
    • Colonic carcinoma
    • Gastric carcinoma
    • Gastric or duodenal ulceration
• Dietary inadequacy
• Failure of iron absorption: Malabsorption conditions such as coeliac disease
• Excessive requirements for iron: Pregnancy

Laboratory tests
• Low Haemoglobin
• Low Mean cell volume (MCV)
• Low Mean cell haemoglobin concentration (MCHC)
• High Red cell distribution width (RDW)
• Low serum ferritin
• High Total iron-binding capacity

The above laboratory tests are important to remember for PLAB as they may be asked

Q-86

A 15 year old girl was admitted with chest infection. She was treated and her symptoms had regressed. She was brought again with fever and the same symptoms a few days later. It was found that all her blood works done in the hospital showed a mild anaemia and thrombocytopenia. What is the SINGLE most likely diagnosis?

A. **Acute myeloid leukaemia (AML)**
B. **Acute lymphoblastic leukaemia (ALL)**
C. **Aplastic anaemia**
D. **Chronic myeloid leukaemia**
E. **Chronic myeloid leukaemia (CML)**
F. **Chronic lymphocytic leukaemia (CLL)**

ANSWER:
Acute lymphoblastic leukaemia

EXPLANATION:
The age is th3e only factor that support the diagnosis of acute lymphoblastic leukaemia (ALL) along with the given picture. The same picture can happen in aplastic anaemia but there is not a single factor mentioned in favour of it. So acute lymphoblastic leukaemia (ALL) can be taken as best option in the given scenario.

Q-87

A 36 year old female presents with a petechial rash and menorrhagia. Her physical examination is completely normal and she has no other complaints. A full blood count was done and reveals:

Hb 13.3 g/dL
WBC 9 x 10^9/L
Platelets 90 x 10^9/L

What is the SINGLE most likely diagnosis?

A. **Polycythaemia rubra vera**
B. **Thrombocytopenia**
C. **Thrombocytosis**
D. **Chronic myeloid leukaemia**
E. **Hyposplenism**

ANSWER:
Thrombocytopenia

EXPLANATION:
This woman has an isolated decrease in platelets with no other complaints (other than menorrhagia). The presence of petechiae is an additional clue to thrombocytopaenia.

Q-88

A 33 year old man complains of lethargy tiredness and pruritus. A diagnosis of polycythaemia vera was made. What is the SINGLE most appropriate management?

A. **Phlebotomy**

B. **Splenectomy**
C. **Indomethacin**
D. **Heparin**
E. **Warfarin**

ANSWER:
Phlebotomy

EXPLANATION:
Venesection is the most appropriate.

Splenectomy is something to consider in the management of PCV. But it is usually down the line when there is painful splenomegaly or there are repeated episodes of splenic infarction.

Q-89

A 25 year old Greek man presents with dark red urine hours after eating fava beans. He is now very ill and has signs of shock. Spherocytes and red blood cell fragments are seen on blood film. What is the SINGLE most likely diagnosis?

A. **Hereditary spherocytosis**
B. **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**
C. **Alpha thalassaemia**
D. **Beta thalassaemia**
E. **Hereditary sideroblastic anaemia**

ANSWER:
Glucose-6-phosphate dehydrogenase (G6PD) deficiency

EXPLANATION:
Spherocytes are usually seen in hereditary spherocytosis and autoimmune haemolytic anaemias. However, they may be seen in G6PD deficiency as well in severe haemolysis. The history of consumption of fava beans followed by rapid deterioration points towards G6PD deficiency. Otherwise, in the exam, if you see spherocytes, it is almost always either hereditary spherocytosis or autoimmune haemolytic anaemias.

Q-90

A 59 year old smoker who recently underwent a hip replacement surgery 2 days ago, has a swollen and tender left leg. The diameter of his left calf is higher than the right calf. Passive movements cause pain. The calf is tender to touch. What is the SINGLE most likely diagnosis?

A. **Deep vein thrombosis**
B. **Lymphoedema**
C. **Peripheral vascular disease**
D. **Cellulitis**

E. **Superficial thrombophlebitis**

ANSWER:
Deep vein thrombosis

EXPLANATION:
One calf having a larger diameter than the other is one one of the known signs of a DVT. The risk factors (smoker, immobile, major surgery) that are given also point clearly towards the likely diagnosis of deep vein thrombosis.

Q-91

A 35 year old man has fatigue, night sweats and a mild fever for the last month. Examination reveals painless cervical lymphadenopathy. Splenomegaly is noted on abdominal examination. He has signficant weight loss. What is the SINGLE most likely diagnosis?

A. **Non-Hodgkin lymphoma**
B. **Polycythemia**
C. **Iron deficiency anaemia**
D. **Toxoplasmosis**
E. **Cytomegalovirus infection**

ANSWER:
Non-Hodgkin lymphoma

EXPLANATION:
There are two major points mentioned here: cervical lymphadenopathy and splenomegaly.

This combination makes Non-Hodgkin lymphoma as the most likely cause Toxoplasmosis although uncommon, may have cervical lymphadenopathy and splenomegaly as well. But weight loss is not seen in toxoplasmosis hence non-hodgkin's lymphoma remains the top choice.

Q-92

A 52 year old female has lost a few litres of blood during a hysterectomy. She is due for a blood transfusion. What is the SINGLE most likely test involved in the preparation of blood transfusion?

A. **Indirect Coomb's test**
B. **Direct Coomb's test**
C. **Sickle cell solubility test**
D. **G6PD enzyme assay**
E. **Osmotic fragility test**

ANSWER:

Indirect Coomb's test

EXPLANATION:
An indirect Coombs test would test patient's serum rather than red blood cells. This is appropriate as we would like to identify antigenicity. By doing the indirect Coombs test we are able to detect antibodies against RBC that are present unabound in the patient's serum.

Q-93

A 63 year old man presents with extreme thirst that despite drinking fluids he still feels thirsty. He has been having a back ache for the last 4 months that is getting worse and feels tired all the time. During this time, he has noticed weight loss and mild breathlessness. His serum calcium was found to be elevated. A blood film was taken. What is the SINGLE most likely finding to be seen on a blood film?

A. Basophilic stippling
B. Howell Jolly bodies
C. Heinz bodies
D. Trophozoites
E. Rouleaux formation

ANSWER:
Rouleaux formation

EXPLANATION:
The signs and symptoms along with the hypercalcaemia point towards multiple myeloma. Breathlessness occurs due to anaemia found in multiple myeloma. Rouleaux formation can be seen on the blood film in multiple myeloma.

Q-94

A 50 year old man presents to his GP with the complaint of shortness of breath. He describes his shortness of breath as increasing in severity over the past few months. He is also noted to have a persistent cough. The patient also complains of lethargy and tiredness which he says started around three months ago. The patient's past medical history is signficant for migraine headaches which he takes non-steroidal anti-inflammatory medications for. He works as a production manager for a medium sized company and reports no undue stress in his personal or professional life. He drinks socially and smokes around 20 cigarettes a day for the past 30 years. A blood test done and the results are as follows:

Haemoglobin 198 g/L
Platelets 250 x 10^9/L
White cell count (total) 9.8 x 10^9/L
Haematocrit 58%

What is the SINGLE most useful hormone level to test for to help establish a diagnosis?

A. **Aldosterone**
B. **Cortisol**
C. **Erythropoeitin**
D. **Thyroxine**
E. **Insulin**

ANSWER:
Erythropoietin

EXPLANATION:
This stem shows a diagnosis of secondary polycythaemia due to chronic hypoxia. Patients who are long term smokers who have an underlying chronic obstructive pulmonary disease may have polycythaemia as a complication. The long term hypoxia triggers an increased production of erythropoietin by the kidneys so that it stimulates the bone marrow cells to produce more red blood cells to transport oxygen to tissue.

Patients can present with non-specific symptoms such as lethargy, tiredness and headaches.

Other important causes of secondary polycythaemia due to hypoxia include:
- High altitudes
- Cyanotic congenital heart disease

Q-95

A 4 year old boy has a cough and arthritis followed by rash on legs which are non-blanching on glass test. He has no history of a fever. His blood tests show:

Haemoglobin 120 g/L
White cell count 6.3 x 10^9/L
Platelets 259 x 10^9/L
Prothrombin time 13 seconds
Activated partial thromboplastin time 35 seconds

What is the SINGLE most likely diagnosis?

A. **Meningitis septicaemia**
B. **Haemophilia**
C. **Henoch-Schonlein purpura**
D. **Idiopathic thrombocytopenic purpura**
E. **Thrombotic thrombocytopenic purpura**

ANSWER:
Henoch-Schonlein purpura

EXPLANATION:
The blood results are all normal. The rash in the legs that are non blanching and the arthritis are hints towards Henoch-Schönlein purpura.

The disease occurs mostly in the winter months. About 50-90% of patients have a preceding upper respiratory tract infection (URTI) which explains the cough in the given question.

The stem here gives a no history of fever. Generally, patients with Henoch-Schönlein purpura appear to be mildly ill, with low-grade fever. But having no fever does not exclude the diagnosis.

Q-96

A 65 year old man has a routine full blood count which results are as follows:

Haemoglobin 195 g/L
Platelets 390 x 10^9/L
White cell count (total) 7.8 x 10^9/L

He is a chronic smoker. What is the SINGLE most likely diagnosis?

A. **Secondary polycythaemia**
B. **Polycythaemia rubra vera**
C. **Essential thrombocythaemia**
D. **Myelofibrosis**
E. **Chronic lymphocytic leukaemia**

ANSWER:
Secondary polycythaemia

EXPLANATION:
Secondary polycythaemia (more accurately secondary erythrocytosis) is the answer. Erythrocytosis has many causes which include primary (polycythaemia rubra vera) or secondary (living at high altitudes, smokers, patients with COPD). The fact that platelets and white cell counts are within the normal range suggest a secondary cause rather than polycythaemia rubra vera. Chronic smokers are at risk of developing secondary erythrocytosis due to chronic hypoxemia which triggers increased production of erythropoietin by the kidneys.

If repeated haemoglobin is still high in 2 months time, further investigations would be warranted.

Q-97

An INR result of a 64 year old man was found to be 6.3. The local haematology laboratory highlighted this finding and informed the clinic. The patient takes

warfarin for atrial fibrillation. He is otherwise well with no active bleeding. What is the SINGLE most appropriate diagnosis?

A. **Start oral phytomenadione**
B. **Inform patient to present to the nearest A&E department**
C. **Stop warfarin and arrange for a repeat INR the following day.**
D. **Reduce dose of warfarin and repeat INR the following day**
E. **Reduce dose of warfarin and repeat INR in a week**

ANSWER:
Stop warfarin and arrange for a repeat INR the following day

EXPLANATION:
This patient has an INR between 6 and 8 without bleeding. He needs his warfarin stopped until his INR is less than 5. Cases like these are usually managed in an anticoagulation clinic. A telephone call to the patient to inform him of his INR result is appropriate. He does not need to present to A&E.

Phytomenadione is also known as vitamin K1. It is used when the INR is more than 8 or if the patient has a major bleed in the context of warfarin use.

Q-98

An 18 year old boy presents with a lump on his neck which has been enlarging in size over the few weeks. He feels fatigued and describes frequent night sweats. He has been told by his family members that he looks thinner over the past month. He denies recent travels abroad. On examination, he has a 3 cm non-tender lump in the right side of the neck and an enlarged spleen on abdominal examination. He has a temperature of 38.4 C. What is the SINGLE most likely diagnosis?

A. **Infectious mononucleosis**
B. **Lipoma**
C. **HIV**
D. **Thyroglossal cyst**
E. **Hodgkin lymphoma**

ANSWER:
Hodgkin lymphoma

EXPLANATION:
This lump is concerning and with the systemic symptoms of night sweats, fever and weight loss are termed B symptoms. Hodgkin's lymphoma can occur in the paediatric population (usually older children). Splenomegaly is seen in 30% of all cases of Hodgkin's lymphoma.

"B" symptoms

- ***Weight loss*** *of more than 10% of body weight during the previous 6 months*
- *Unexplained* ***fever***
- *Drenching* ***night sweats***

Another take home point from this question is that Hodgkin's lymphoma has a bimodal age distribution. It has two incident peaks. One peak around age 20 to 29 years of age and another at 60 years of age.