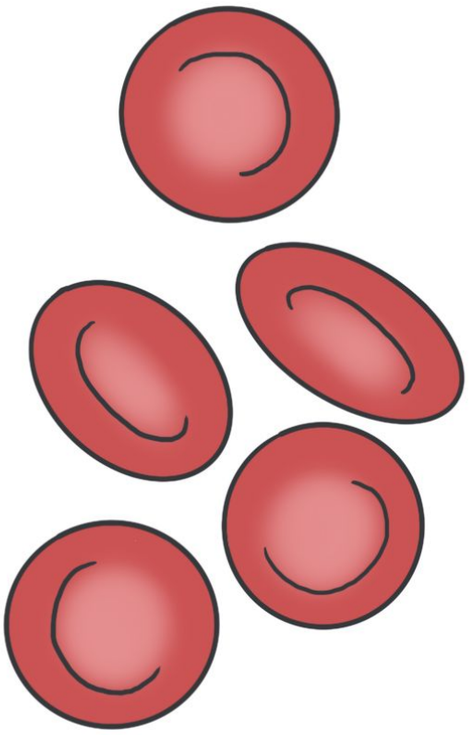
PLABABLE

GEMS

VERSION 2.8

HAEMATOLOGY



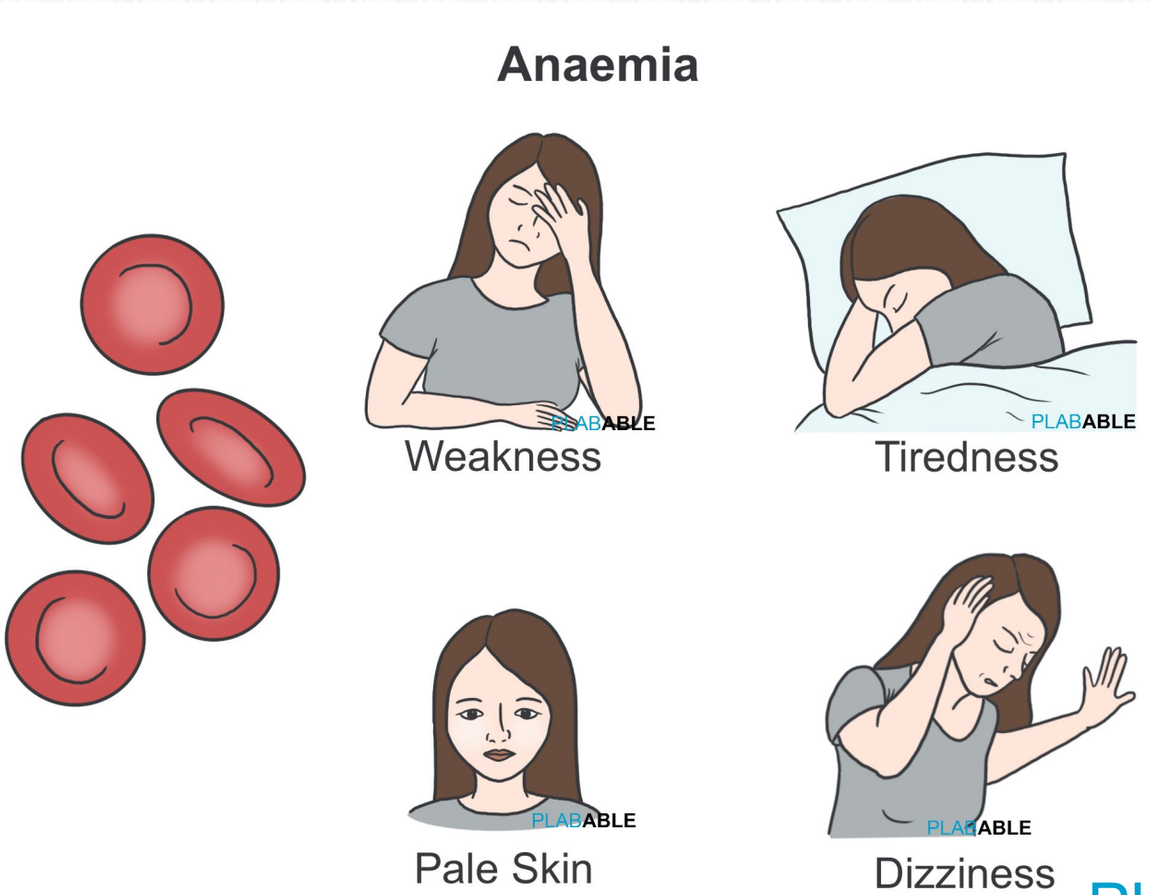
Anaemia Types

Microcytic anaemia MCV <80:

- **T**halassemia
- **A**naemia of chronic disease
- **I**ron deficiency anaemia
- **L**ead poisoning
- **S**ideroblastic anaemia

Macrocytic anaemia MCV >100:

- B12 deficiency
- Folate deficiency



Iron Deficiency Anaemia

Causes

- ↓ Iron intake
- Blood loss from GIT (GI malignancy)
- Menorrhagia

Labs

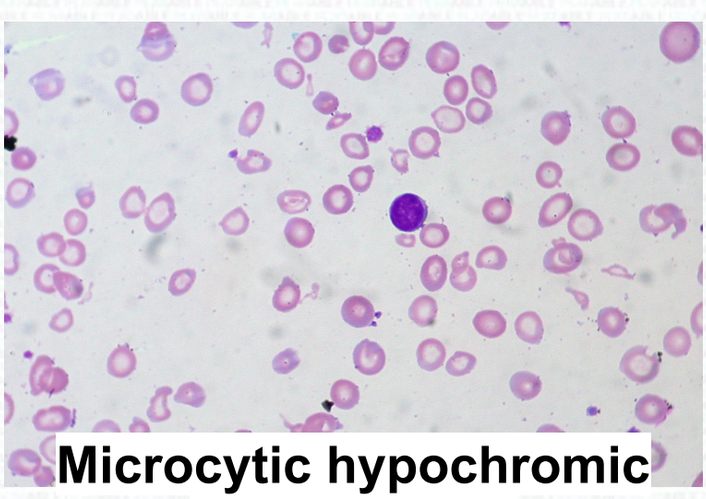
- ↓ Ferritin, MCV and haemoglobin
- ↑ TIBC and transferrin

Signs

- **Koilonychia** - spoon shaped nails
- Angular cheilitis
- Atrophic glossitis
- Pallor

Associated with **Plummer-Vinson syndrome** - oesophageal web in chronic cases

Treatment is specific for each cause and in most cases iron supplementation is necessary



Microcytic hypochromic blood picture

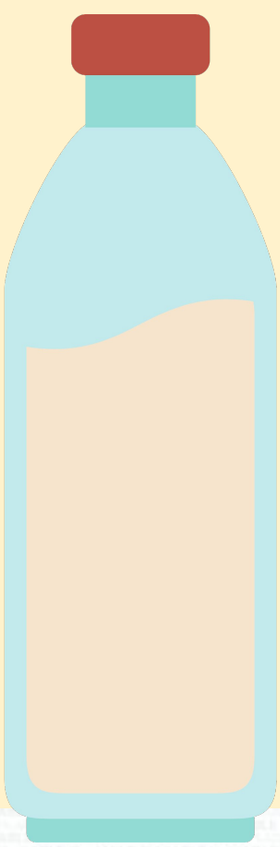
Iron Deficiency Anaemia

Brain trainer:

A 3 year old has microcytic hypochromic anaemia. He drinks mostly milk and eats very little solid food. What is the likely diagnosis?

➔ **Iron deficiency anaemia**

Milk decreases iron absorption and also fills the stomach which leads to decrease space for solid foods where iron typically comes from



Megaloblastic Anaemia

B12 deficiency:

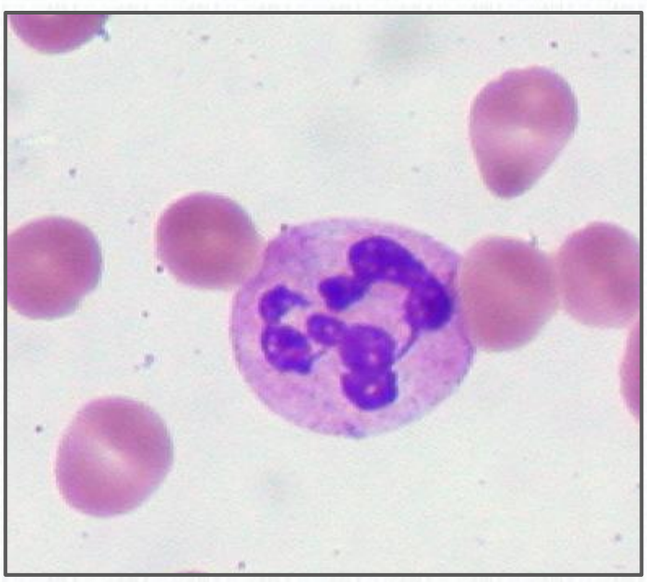
- Pernicious anaemia
- Gastrectomy and ileal resection
- Veganism
- Chronic pancreatitis

Folic acid deficiency:

- Dietary deficiency (e.g. lack of green leafy vegetables or fortified grains)
- Gastrointestinal disorders (coeliac, Crohn's disease)
- Alcoholism
- Pregnancy
- Jejunal resection *(proximal jejunum is main site of absorption)*
- Medications → Methotrexate, anticonvulsants, trimetoprim

Megaloblastic Anaemia

- ➔ Pins and needle sensations in the limbs and hyperlobulated neutrophils are common with **B12 deficiency**
- ➔ Neural tube defects are seen in infants born to women with **folate deficiency**



Hypersegmented neutrophils

Treatment of Megaloblastic Anaemia

ALWAYS CHECK B12 LEVELS BEFORE TREATMENT !!

Why

Folate masks symptoms and allows neurological deficit to develop

Treatment

1. Hydroxocobalamin (IM)
2. Folic acid (PO)

→ You must correct B12 levels before folate

We STRESS this point again!

Remember, you must check b12 levels in ALL patients with folate deficiency. If someone is deficient in both of them, replace B12 first!

Plabable's Tip

B (B12) comes before F (Folate)

B12 Deficiency

Keywords to remember

- History of gastrectomy
- History of vegan diet (inadequate dietary intake of B12
- Macrocytic anaemia
- Pins and needle sensations in the limbs
- Peripheral loss of vibratory sense and position
- Cognitive changes

Picking the Right Type Of Megaloblastic Anaemia

One quick tip in the exam with anaemia questions is to look for evidence of increased MCV. Once you have identified this, look for these ***keywords*** to guide you to the right diagnosis.

↓Hb + ↑MCV

- History of gastrectomy
- History of vegan diet (inadequate dietary intake of B12
- Pins and needle sensations in the limbs
- Peripheral loss of vibratory sense and position
- Cognitive changes

B12 deficiency

- Poor diet (lack of green vegetables)

Folate deficiency

Lastly, remember that this card is purely for exam purposes and has nothing to do with actual clinical practice since GPs would request for both serum folate and serum B12 levels in patients with megaloblastic anaemia.

What To Advice Patients To Eat In These Deficiencies

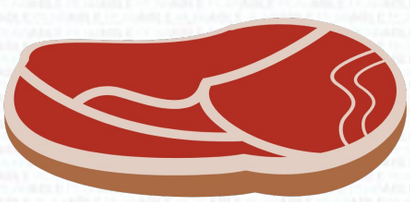
There are a lot of different foods with Vitamin B12 and folic acid but our goal is to make it easy for you and for your patients to remember.

What to eat?

B12 deficiency

Beef
Oily fish (like salmon)

***B**12 - **B**eef*



Folate deficiency

ABC's of folate deficiency

A → **A**sparagus
B → **B**roccoli or **B**rown rice
C → **C**itrus fruits or **C**hickpeas

***F**olate - **F**egetables*

Haemolytic Anaemia

Intrinsic causes	Extrinsic causes
Hereditary spherocytosis	Autoimmune haemolytic anaemia - idiopathic, SLE, etc.
Sickle cell anaemia	Prosthetic heart valve
Thalassaemia	SLE
Paroxysmal nocturnal hemoglobinuria	*Mycoplasma pneumoniae* - Cold agglutinins
G6PD deficiency	

- Hemolysis can happen either intravascularly or extravascularly (spleen)
- Decreased haptoglobin
- Increased reticulocytes
- Jaundice and increased bilirubin level
- Increased lactate dehydrogenase (LDH)
- Positive coombs in autoimmune hemolytic anaemia

Haemolytic Anaemia

It is important to know terms like **polychromasia**.

Polychromasia (“poly” which means many, and “chromasia” means color) is seen where there is a high turnover of immature red cells. It signifies a finding of haemolytic anaemia.

You might find this term in a patient with anaemia where the question would be asking about investigations. A **direct Coombs test** is usually perform to look for evidence of autoimmune haemolytic anaemia.

Haemolytic Anaemia

Tiredness + lethargy + increasing fatigability

↓

Low haemoglobin
Raised bilirubin
Raised/normal MCV

↓

Haemolytic anaemia

↓

Which diagnostic test to perform?

↓

Direct antiglobulin test

Haemolytic anaemia → ↓ **Hb +** ↑ **bilirubin**

MCV can be raised in immunologically-mediated haemolytic anaemia

HUS vs TTP

Haemolytic Uraemic Syndrome	Thrombotic Thrombocytopenic Purpura
E.coli	ADAMTS13 gene mutation
Children	Adults
Prodrome of diarrhoea that turns bloody	Prodrome of flu-like illness
Microangiopathic haemolysis (schistocytes) Renal dysfunction Thrombocytopenia	
-	+ Neurological symptoms + Fever
10% mortality	90% mortality
Supportive: fluids, antihypertensives, dialysis	Plasmapheresis

- HUS has a triad, TTP has a pentad
- Do not give platelets as treatment as it can worsen the situation
- Do not give antibiotics for HUS

G6PD Deficiency

Haemolytic crisis caused by:

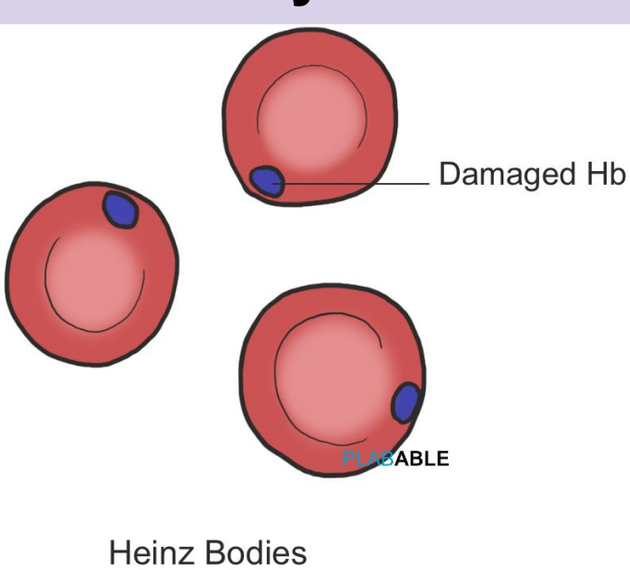
- Broad beans - favism
- Primaquine
- Nitrofurantoin
- Sulfinamides

Features

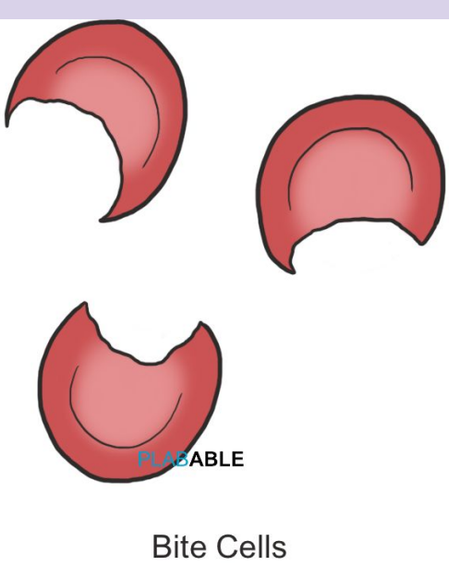
- X-linked recessive disease
- Common in male Mediterranean descendant
- Haemolysis and jaundice
- Heinz bodies and bite cells
- Negative coombs test
- Increased LDH and decreased haptoglobin

Treatment

- **Blood transfusion and dialysis (severe cases)**
- Folic acid supplementation
- Avoidance of triggers
- **Splenectomy** as last resort



Heinz Bodies



Bite Cells

Mode of Inheritance

Autosomal dominant

- Von Willebrand disease
- Hereditary spherocytosis

X-linked recessive

- Haemophilia
- G6PD deficiency

Autosomal recessive

- Thalassemia
- Sickle cell anaemia

Probability of inheritance to children

- Dominant → 50% (one parent affected)
- X-linked recessive → 50% male (if mother affected)
- Autosomal recessive → 25% (if both parents are carriers)

Remember

- Dominant diseases are present in each generation.
- Recessive diseases may skip a generation.

Febrile Transfusion Reactions

Presentation

- Fever ± rigors
- Hypotension
- Feeling that “something is wrong”
- Dyspnea
- Chills
- Myalgia
- Pain at puncture site

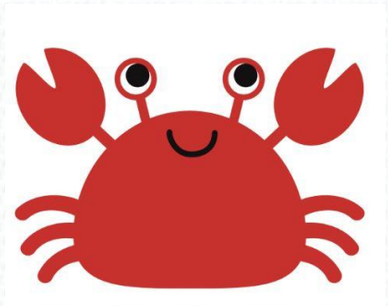
Management (if only feature is temp < 38.5°C)

- Paracetamol and antihistamine
- Slow transfusion rate
- Observe more frequently

Management

- Stop transfusion
- Oxygen and fluid support

Multiple Myeloma



C R A B

Hyper**c**alcemia

Renal Failure

Anaemia

Bone (pain)

The investigations that you MUST know

- **Urine protein electrophoresis → Bence Jones' protein**
- **Serum protein electrophoresis → increased monoclonal immunoglobulin spike**
- **X-ray → punched out lytic lesion**
- **Blood film → Rouleaux formation**
- **Bone marrow biopsy → Abundant plasma cells**

Treatment

- Likely not going to be asked as specialised

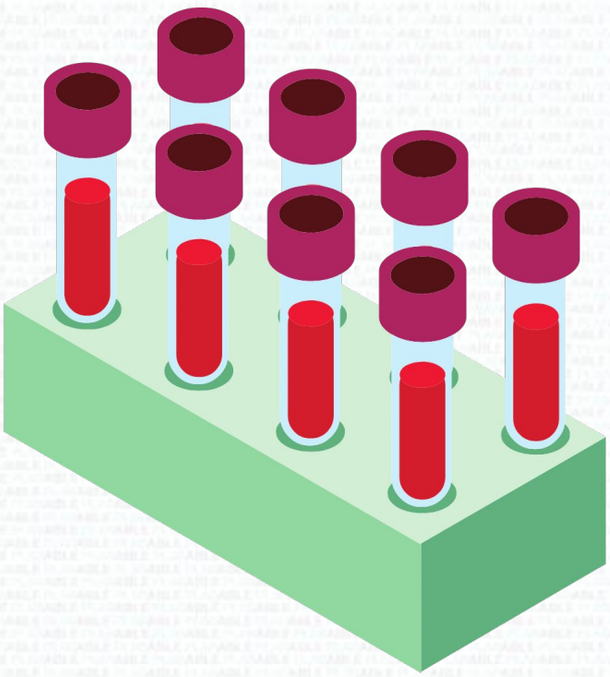
Multiple Myeloma

Must know symptoms

Firstly think of a patient that is over 60 years of age

- Bone pain (back or ribs)
- Fatigue
- Breathless
- Weight loss

Must know results of INITIAL investigations



- Haemoglobin ↓
- ESR ↑
- Calcium ↑

Multiple Myeloma Investigations

Break down the investigations to 3 groups

The **FIRST** usual test

- FBC → Hb ↓
- ESR ↑
- CRP ↑
- Renal profile → eGFR ↓, creatinine ↑
- Calcium ↑

If the blood test above look somewhat similar to this then get the next bunch of test

The next **SPECIAL** test

- Serum electrophoresis
- Serum-free light-chain assay
- Bence-Jones protein urine assessment

If the blood test above indicate myeloma then go to the next bunch of test

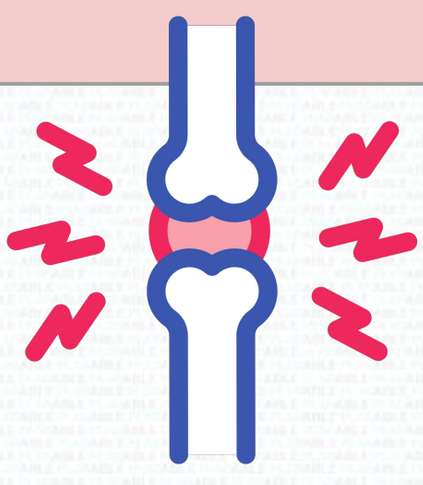
ESTABLISH THE DIAGNOSIS test

- Bone marrow biopsy
- Skeletal survey

Haemophilia

X-linked recessive disorder

Haemophilia A (Most common)	**Haemophilia B** (Christmas disease)
Factor VIII deficiency	Factor IX deficiency
Presentation: spontaneous bleeding into joints and intramuscular haemorrhage	
Labs ↑ APTT and normal PT, and von Willebrand factor *Bleeding time is also found to be normal but this is no longer a test done in the UK because it is difficult to standardise*	
Treatment Factor VIII infusion Desmopressin (↑ factor VIII)	**Treatment** Recombinant factor IX



Hemarthrosis

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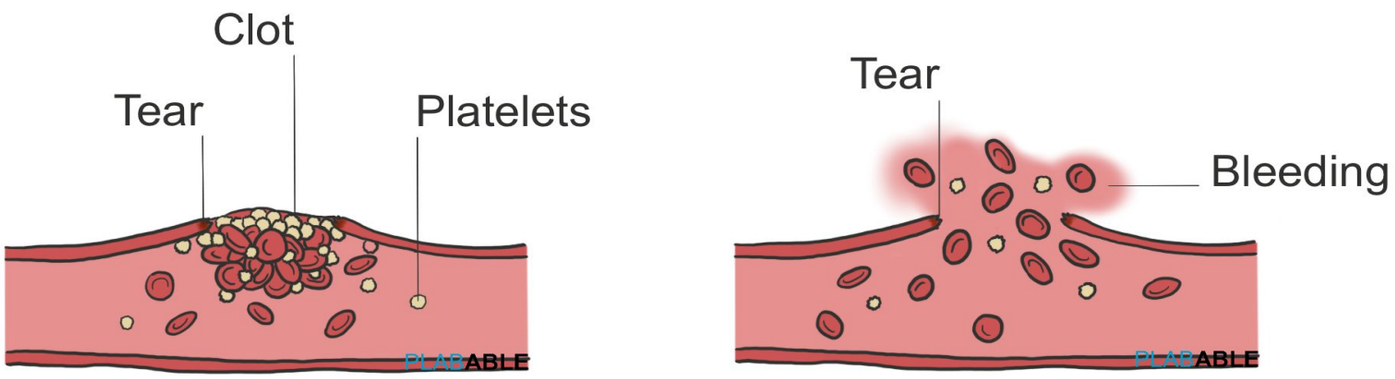
Von Willebrand's Disease

Deficiency or abnormal functioning of von Willebrand factor, which is necessary for platelet plug formation and preventing degradation of factor VIII.

Von Willebrand Disease



Normal Hemostasis

Normally, bleeding stops because platelets stick together and start a clot.

Von Willebrand Disease

With VWD, platelets don't stick together as they should.

Von Willebrand's Disease

Presentation

- Bleeding from mucosa: **epistaxis**
- Easy bruising
- Bleeding gums
- Menorrhagia

Labs

- ↑ or normal aPTT
- Normal PT/INR
- Normal platelet count
- ↑ Bleeding time → *Bleeding time may be high but this is no longer a test done in the UK because it is difficult to standardise*

Treatment

- Tranexamic acid - antifibrinolytic
- Desmopressin - releases vWF from endothelium

Coombs Test

Direct coombs test (direct antiglobulin test):

- Detects antibodies on RBC surface
- Diagnosis of autoimmune haemolytic anaemia

Indirect coombs test (indirect antiglobulin test):

- Detects antibodies in the serum
- Cross-matching of blood
- Antenatal antibody screen (detection of IgG antibodies in mother which can cross placenta)

Disseminated Intravascular Coagulation

Widespread activation of the coagulation cascade resulting in decreased clotting factors, blood clots in different organs and in the end bleeding

- **Causes:** Sepsis, major trauma, cancer and complications of pregnancy
- **Presentation:** Purpura, petechiae, GI bleeding, haematuria, etc.

Labs

- **Increased** PT, aPTT, INR, and fibrin degradation product (D-dimer)
- **Decreased** platelets and fibrinogen

Treatment

- Transfusion of **fresh frozen plasma** and **platelets**
- Treat underlying condition and supportive management

FFP platelets

Differentiation Bleeding Disorders

Haemophilia	↑aPTT Bleeding into joints
Von Willebrand disease	↑ aPTT ↑ Bleeding time Mucosal bleeding
Disseminated intravascular coagulation	↑ aPTT ↑ PT ↑ bleeding time ↑ D-dimer
Idiopathic thrombocytopenic purpura	↓ Platelets Bleeding or purpura History of URTI

*You may find some questions in the **exam** with **bleeding time** in the stem but these are usually old questions since bleeding time is no longer used in the UK because it is difficult to standardise*

Hereditary Spherocytosis

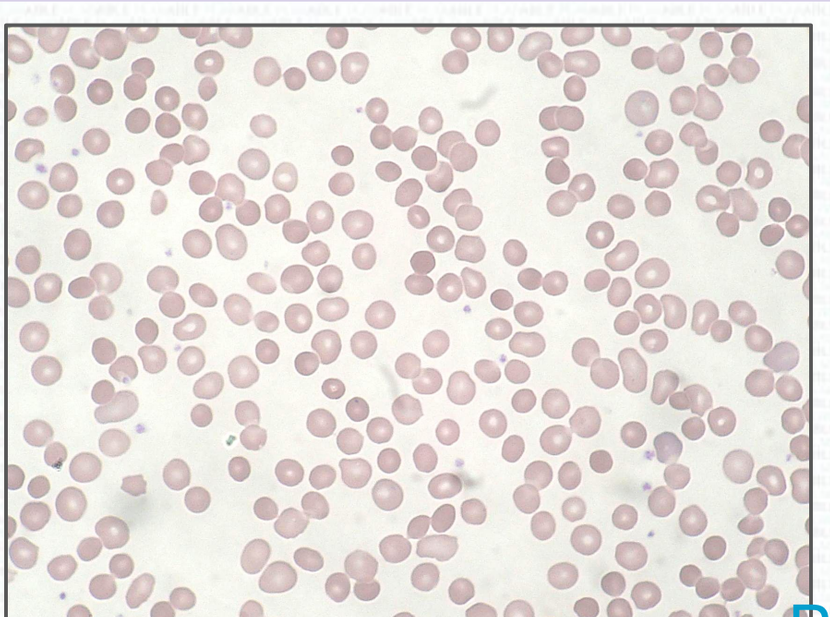
Autosomal dominant mutation → defect in RBC structural protein → spherocytes → haemolysis in the spleen → anaemia

Presentation

- **Haemolytic anaemia** and jaundice
- Gallstones (pigmented)
- Splenomegaly
- Peripheral smear - **spherocytes and Howell-Jolly bodies**
- +ve osmotic fragility and -ve direct coombs test
- **Parvovirus B19** can induce **aplastic crisis**
- Common in European people

Treatment

- Folate supplementation (due to increased turnover)
- Splenectomy



Sickle Cell Anaemia

Autosomal recessive mutation in beta globin gene resulting in sickling of RBCs under low oxygen tension

- Vaso-occlusive crisis → trigger (infection) → clumping of cells → block → ischaemic pain
- Sequestration crisis → vaso-occlusion in spleen → acute splenomegaly → recurrence → Treatment is splenectomy
- Acute chest syndrome → vaso-occlusion in the lungs → cough, tachypnoea, hypoxia, fever and chest pain
- Aplastic crisis → parvovirus B19 infection (↓reticulocytes)

Diagnosis

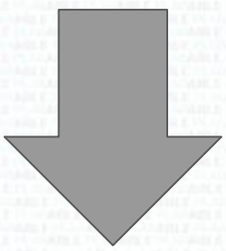
- Blood smear: High reticulocyte and sickled RBCs
- Haemoglobin electrophoresis for HbSS

Management

- Folic acid
- Blood transfusions
- Oral penicillin prophylaxis
- Avoiding situations causing crisis such as cold, dehydration and exhaustion

Tumour Lysis Syndrome

Massive cell death in chemotherapy



- Hyperkalemia
- Hyperphosphatemia
- Hyperuricemia
- Hypocalcemia

} **Intracellular contents**

Note: Excessive phosphate causes precipitation of calcium in the kidney and resultant hypocalcemia and renal failure

Treatment

- IV fluids and diuretics
- Rasburicase
- Hemodialysis if kidney failure
- Allopurinol (prevention)

Thalassaemias

Of all the Thalassaemia types, you want to concentrate on **Beta Thalassaemia major**

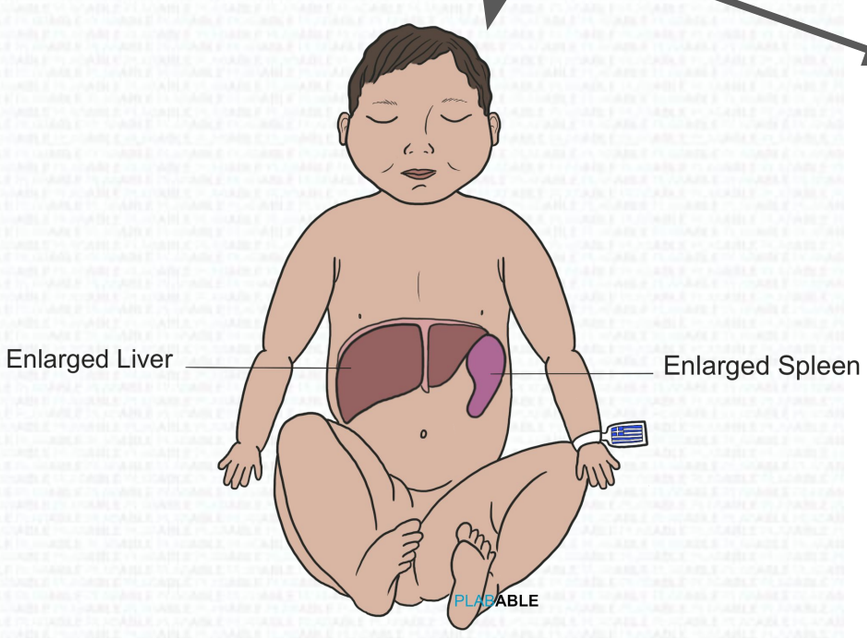
Why?

Because:

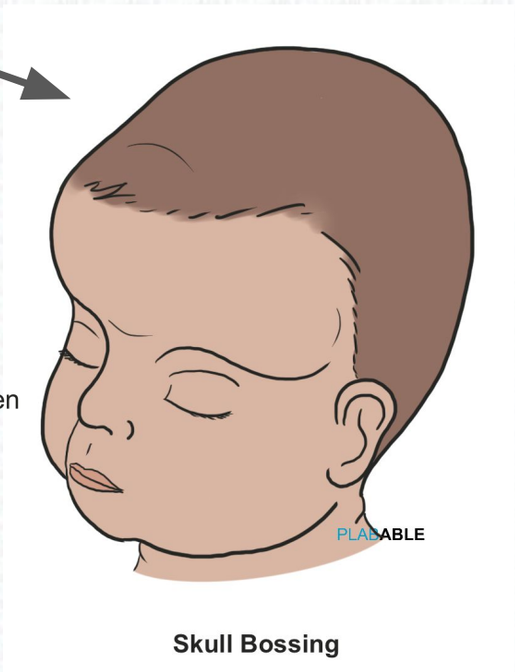
- Patients with Alpha Thalassaemia major usually die in utero
- Patients with Thalassaemia trait are usually asymptomatic or may have microcytic anaemia which do not require treatment

β thalassaemia major

Presents with anaemia in childhood and failure to thrive. If left untreated, can result in extramedullary haemopoiesis with



Hepatosplenomegaly



Skull Bossing

β thalassaemia major

Absent synthesis of beta chains of haemoglobin

Presentation

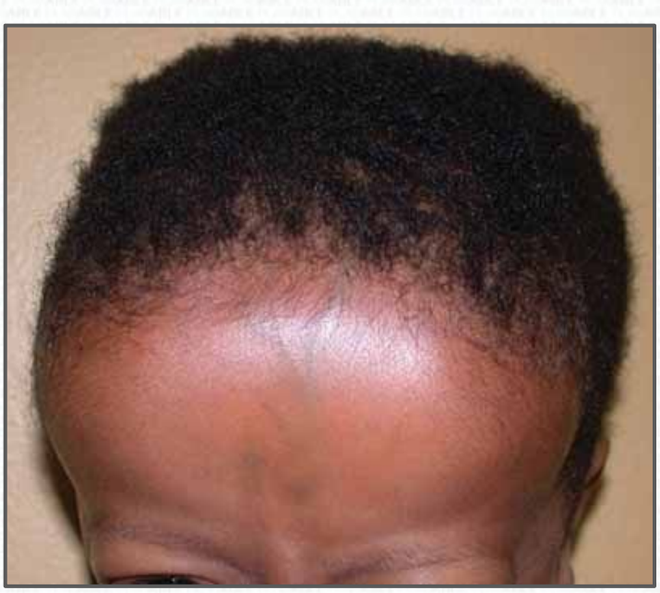
- Severe haemolytic anaemia
- Hepatosplenomegaly
- **Chipmunk facies: Frontal bossing**, prominent facial bones, and dental malocclusion
- Iron overload due to repeat blood transfusion

Labs

- ↑ HbA2 on electrophoresis
- Microcytic hypochromic anaemia
- Elevated serum iron, saturation and ferritin
- **X-ray:** Hair on end appearance

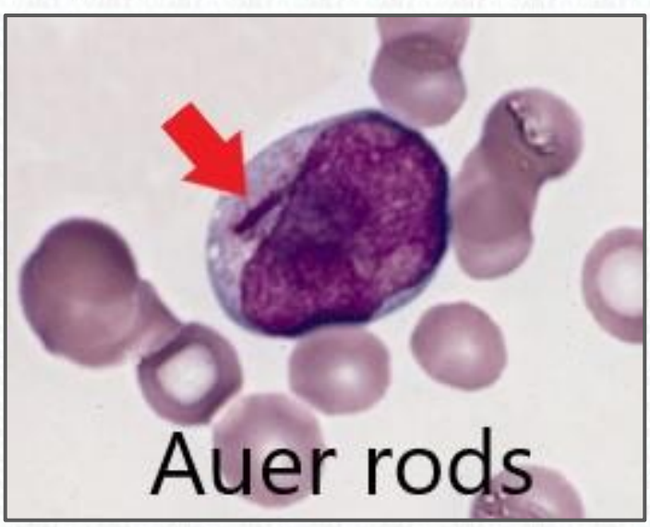
Treatment

- Life long blood transfusion
- Iron chelation to prevent overload



Acute Leukaemia

Acute lymphoblastic leukaemia (ALL)	**Acute myeloid leukaemia (AML)**
Seen in **children**	Seen in **adults**
Presentation ● Anaemia ● Recurrent infections (low WBCs) ● Bleeding (thrombocytopenia) ● Bone marrow biopsy - **numerous lymphoblasts**	**Presentation** ● Fatigue ● Fever not responding to antibiotics ● Gingivitis ● Bleeding (thrombocytopenia) ● Hepatosplenomegaly ● Peripheral smear - **Auer rods** ● Bone marrow biopsy - **numerous myeloblasts**



Pancytopenia

Brain trainer:

The stem has a patient who presents with pancytopenia. What clinical symptoms will allow you to choose acute leukaemia over aplastic anaemia?

➔ **Proliferative signs → lymphadenopathy or hepatosplenomegaly**

Non-Accidental Injury

Brain trainer:

An elderly man with bruises on his torso and arms. He has been cleared medically fit for discharge. What should you be suspicious of?

➔ **Non-Accidental Injury**

Anaemia In Pregnancy

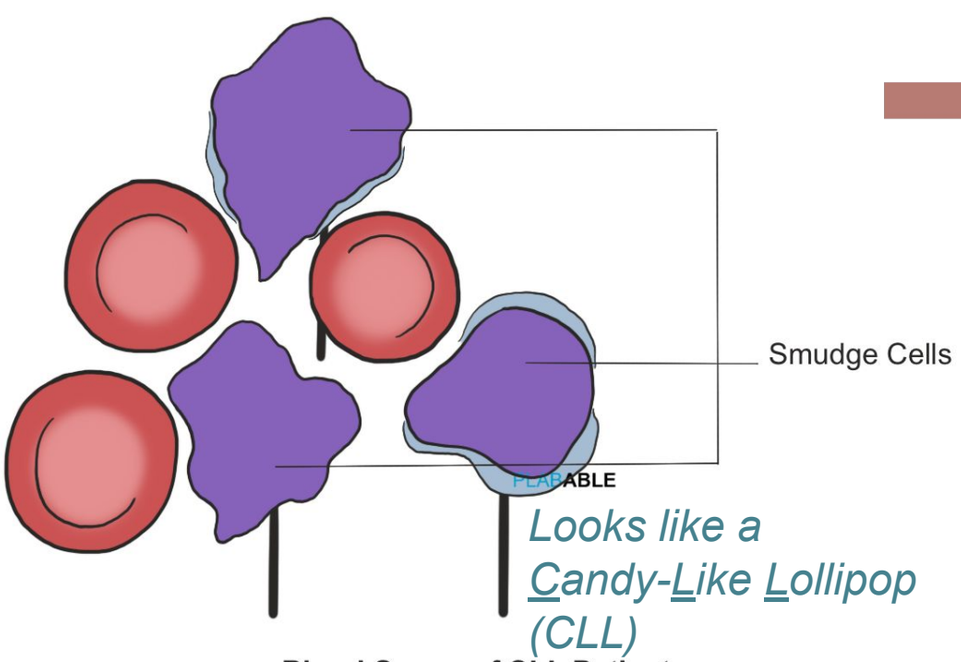
Brain trainer:

What laboratory values for anaemia in pregnancy must you know for the exam?

- ➔ **1st trimester → Hb < 11g/dL**
- ➔ **2nd/3rd trimester → Hb < 10.5g/dL**
- ➔ **Postpartum → Hb < 10 g/dL**

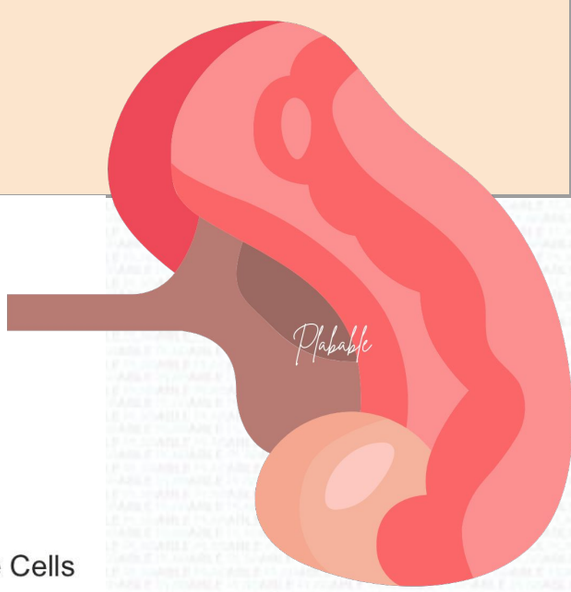
Chronic Leukaemia

Chronic lymphocytic leukaemia (CLL)	Chronic myelocytic leukaemia (CML)
Mostly age > 60	Average age onset = 50
Smudge cells (Smear cells)	Philadelphia chromosome **t(9;22)**
Presentation • **Symmetrically enlarged lymphocytes** • Bleeding due to thrombocytopenia • Anaemia • FBC shows B cell lymphocytosis	**Presentation** • **Massive splenomegaly** • Leukocytosis • Hyperviscosity syndrome • Treatment: **imatinib**



Looks like a Candy-Like Lollipop (CLL)

Blood Smear of CLL Patient



Crazy Massive Spleen (CML)

Chronic Myeloproliferative Disorders

Essential thrombocythaemia

- Thrombosis or bleeding
- ↑ PLT

Polycythemia vera

- ↑ HCT
- Erythromelalgia
- Itching (warm bath)
- Thrombosis or bleeding

CML

- Massive splenomegaly
- Ph chromosome
- Granulocytosis

Myelofibrosis

- Anaemia (severe)
- B-symptoms
- Hepato-splenomegaly

Polycythaemia

Brain trainer:

How do you distinguish primary from secondary polycythaemia?

➔ **Primary → EPO is low to normal**
➔ **Secondary → EPO is high**

Lymphoma

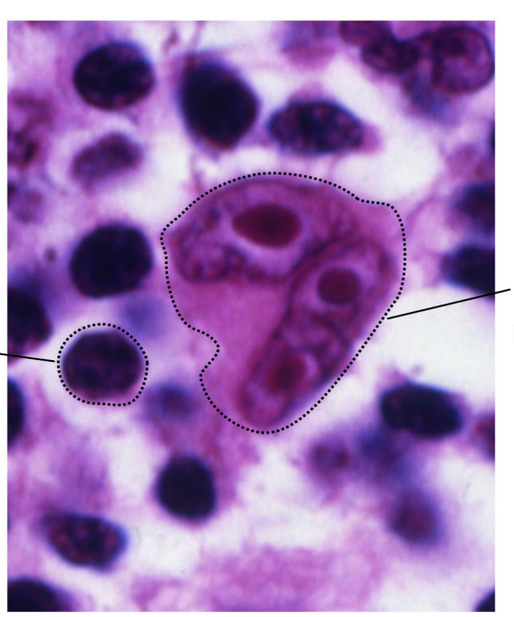
Painless lymphadenopathy + splenomegaly + weight loss ± hepatomegaly ± B symptoms

B symptoms

- Unexplained weight loss
- Night sweats
- Fever (38+)
- Fatigue

Hodgkin's lymphoma

- Bimodal distribution (age <25 and >55)
- Associated with Epstein-Barr virus infection
- **Histology:** Reed-Sternberg cells (multilobulated giant cells)
- **Risk factors:** Immunosuppression and smoking
- Treatment is by chemotherapy and is based on histological type and staging



Lymphoma

Non-Hodgkin's lymphoma

- Follicular and Diffuse large B cell lymphoma are most common
- Absence of Reed-Sternberg cells
- Extranodal presentation is more common
- Bone marrow infiltration causing cytopenia

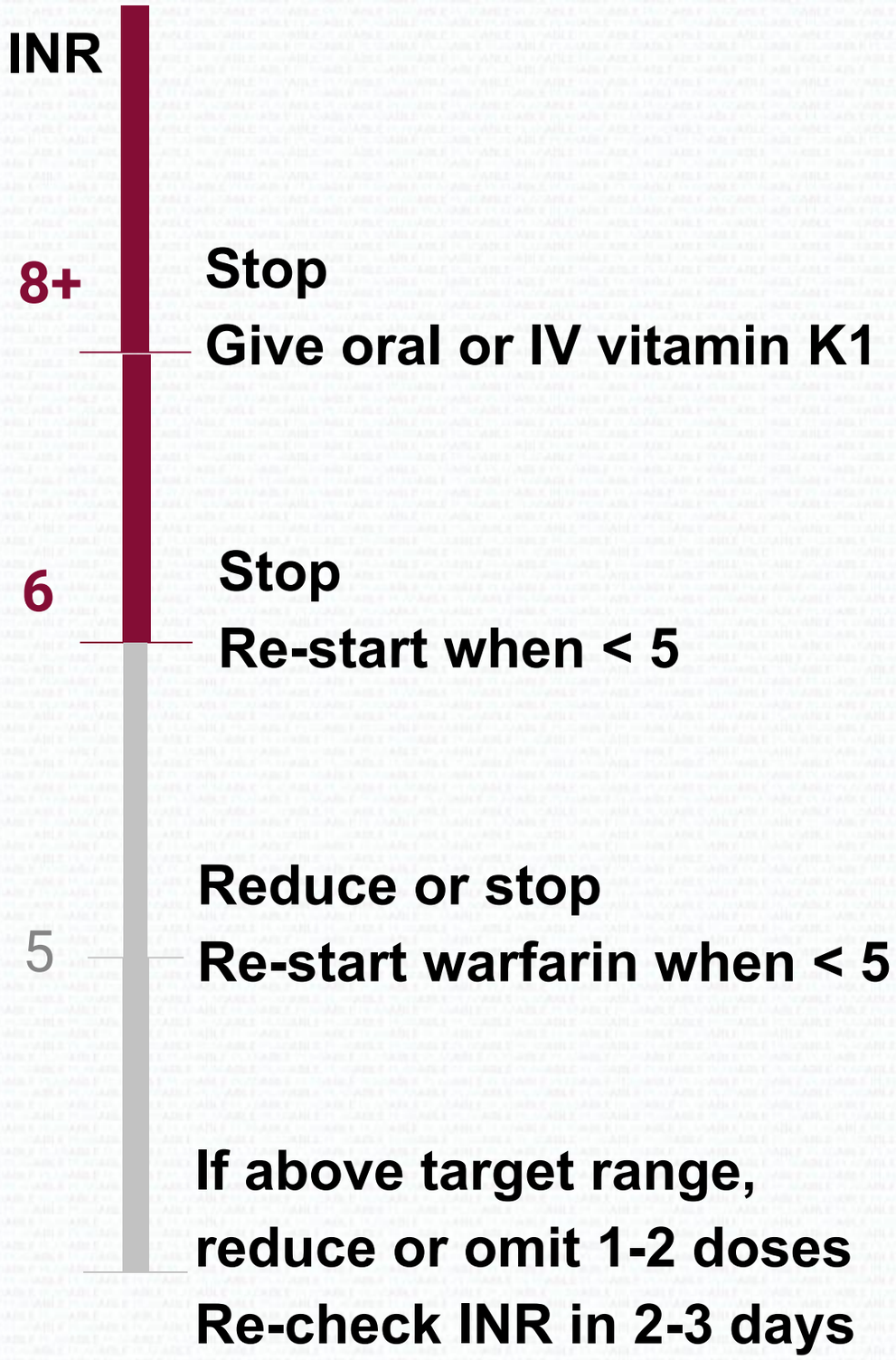
Lymphoma

Brain trainer:

A patient with HIV presents with painless peripheral lymphadenopathy, fever, night sweats, weight loss and splenomegaly. What is the most likely diagnosis?

➔ **Non-Hodgkin lymphoma**

Warfarin - INR Management



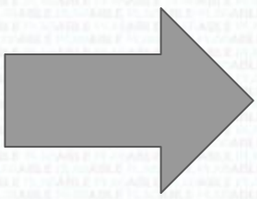
Major Bleed

Stop warfarin

Give IV Vitamin K ± Prothrombin complex concentrate. If unavailable → fresh frozen plasma

Immune Thrombocytopenic Purpura

Platelet / mucosal bleeding



Easy bruising (purpura)

Epistaxis

Child

- Acute
- Viral prodrome
- Typically lasts a few weeks and fully recovers

Adult

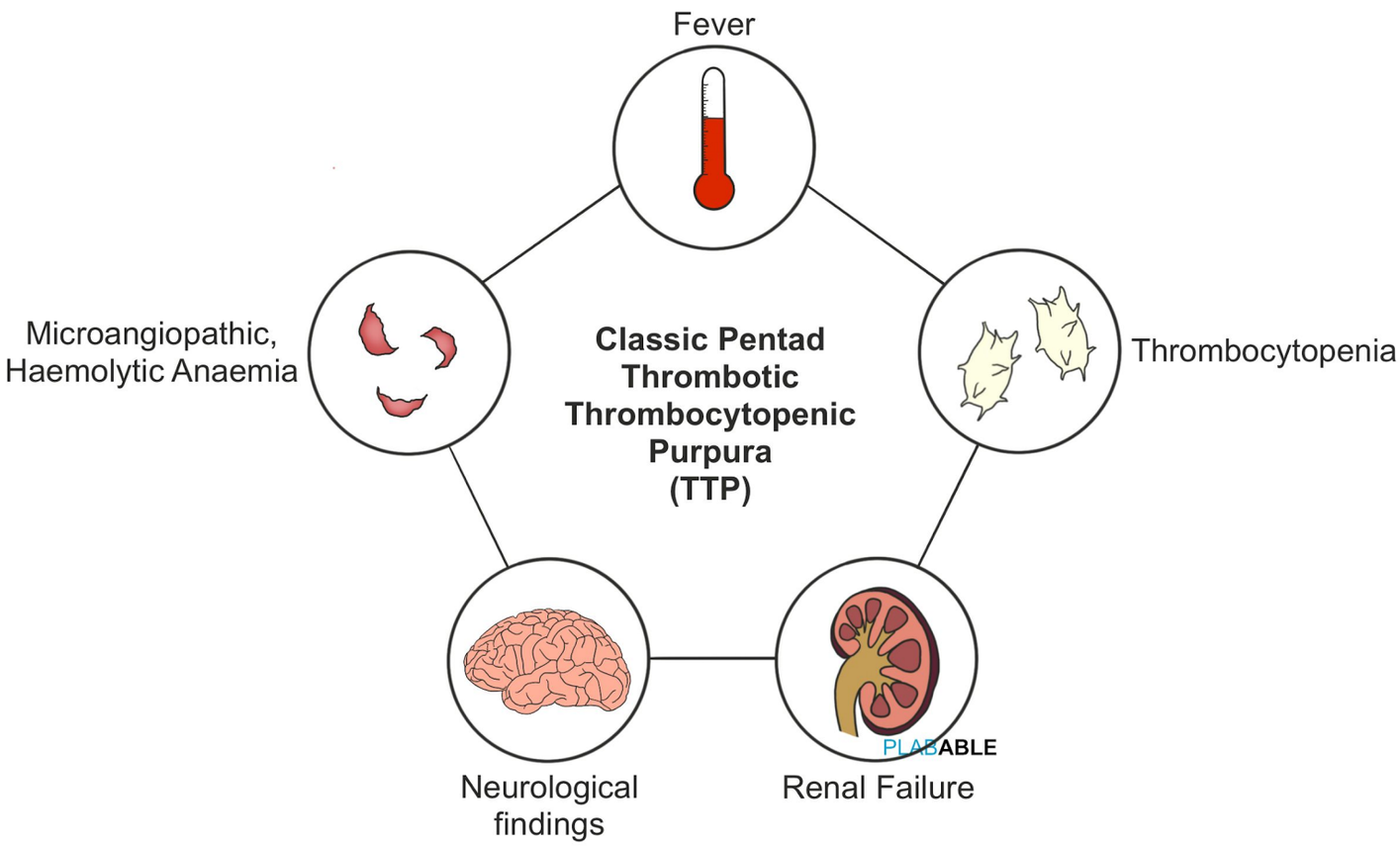
- Chronic
- No viral prodrome
- Gradual onset
- Platelet count does NOT return to normal

Treatment

- Steroids
- Immunoglobulins
- Splenectomy

Thrombotic Thrombocytopenic Purpura

Due to the deficiency of **ADAMTS13** which normally cleaves von Willebrand factor



Labs

- Blood smear - Fragmented RBCs
- Elevated creatinine
- Elevated LDH
- Urinalysis - Microscopic haematuria
- **Low ADAMTS13 level**

Treatment

- Plasma exchange
- Steroids
- Rituximab (relapse)

Polycythaemia Rubra Vera

Haematological malignancy due excessive proliferation of RBCs, WBCs and platelets

Symptoms

- **Pruritus especially after hot shower**
- Fatigue
- Splenomegaly
- Burning sensation of fingers and toes (Erythromelalgia)
- Headache and facial plethora
- Hyperviscosity leading to increased risk for MI, DVT, PE and stroke

Investigation

- Hb >18.5 in males and > 16.5 in females
- **JAK2 mutation**
- **Low erythropoietin** and ferritin level
- **Hypercellularity** in bone marrow biopsy
- Thrombocytosis & leukocytosis

Treatment

- Intermittent long-term phlebotomy
- Low dose aspirin
- Chemotherapy with hydroxycarbamide and interferon

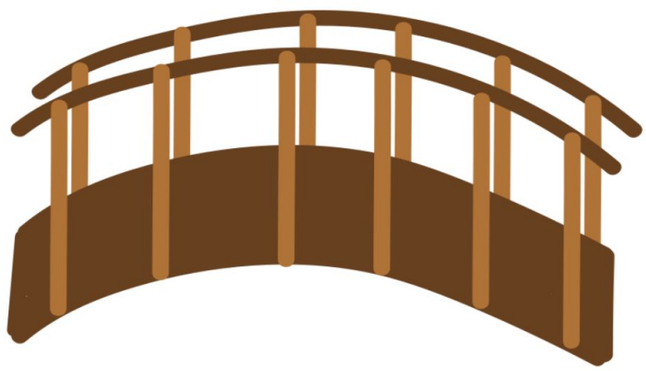
Warfarin and Surgery
Anticoagulation bridging

This card is specific for elective surgeries

Stop warfarin 5 days before elective surgery.

Bridge with heparin if high risk of thomboembolism, e.g.

- Venous thromboembolic event in the last 3 months
- Atrial fibrillation with a previous stroke
- Atrial fibrillation with a CHA_2DS_2-VASc score of 5 or more
- Recent transient ischemic attack
- Patients with mechanical heart valves



Remember, if patient is only having warfarin with a CHA_2DS_2-VASc score less than 5 and has no previous stroke, he would just need to stop warfarin (no heparin bridging required)

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