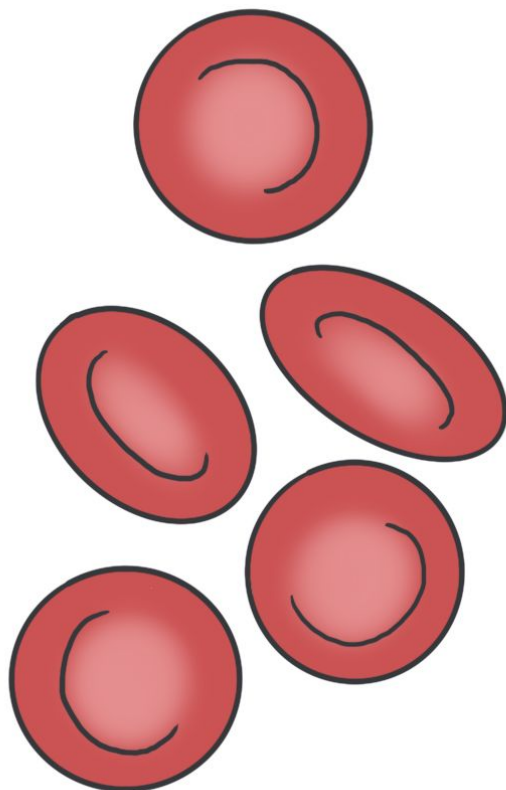


PLABABLE

GEMS 

VERSION 1.2

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
- Drugs (methotrexate and sulfasalazine)
- Chronic alcoholism

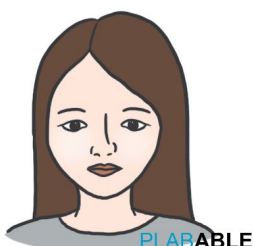
Anaemia



Weakness



Tiredness



Pale Skin



Dizziness

Iron Deficiency Anaemia

Causes

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

Labs

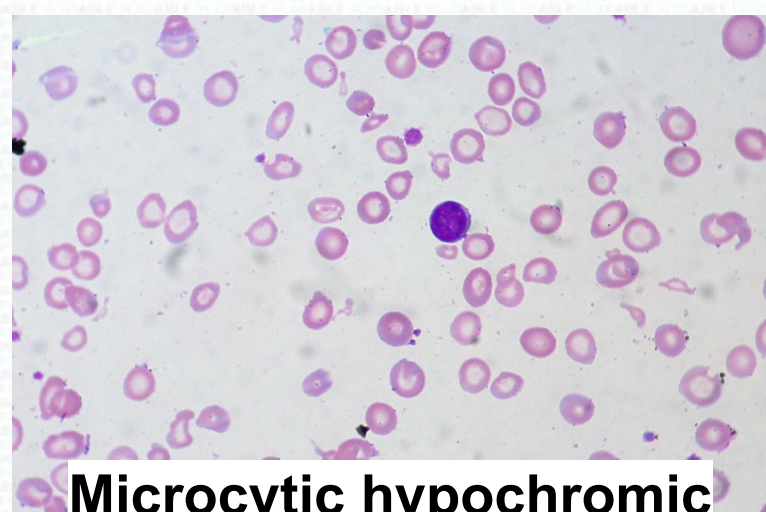
- ↓ Ferritin, MCV and haemoglobin
- ↑ TIBC and transferrin

Signs

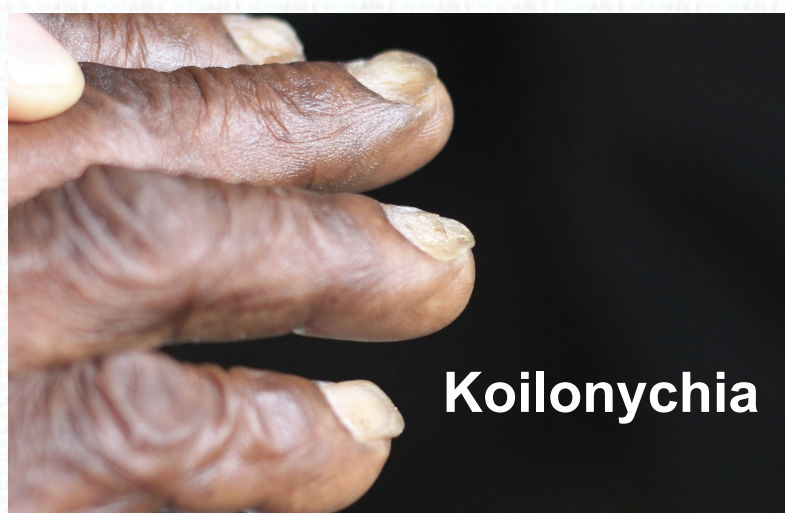
- **Koilonychia** - spoon shaped nails
- Angular cheilitis
- Atrophic glossitis
- Pallor

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**



Koilonychia

Megaloblastic Anaemia

B12 deficiency:

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

Folic acid deficiency:

- Alcoholism
- Pregnancy
- Jejunal resection
- Methotrexate

- 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 !!**



**Folate masks symptoms and allows
neurological deficit to develop**

Treatment

1. Hydroxocobalamin (IM)
 2. Folic acid (PO)
- You must correct B12 levels before folate

Plabable's Tip

B (B12) comes before F (Folate)

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	<i>Mycoplasma pneumoniae</i> - 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

HUS vs TTP

Haemolytic Uraemic Syndrome	Thrombotic Thrombocytopenic Purpura
<i>E.coli</i>	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

Hemolytic crisis caused by:

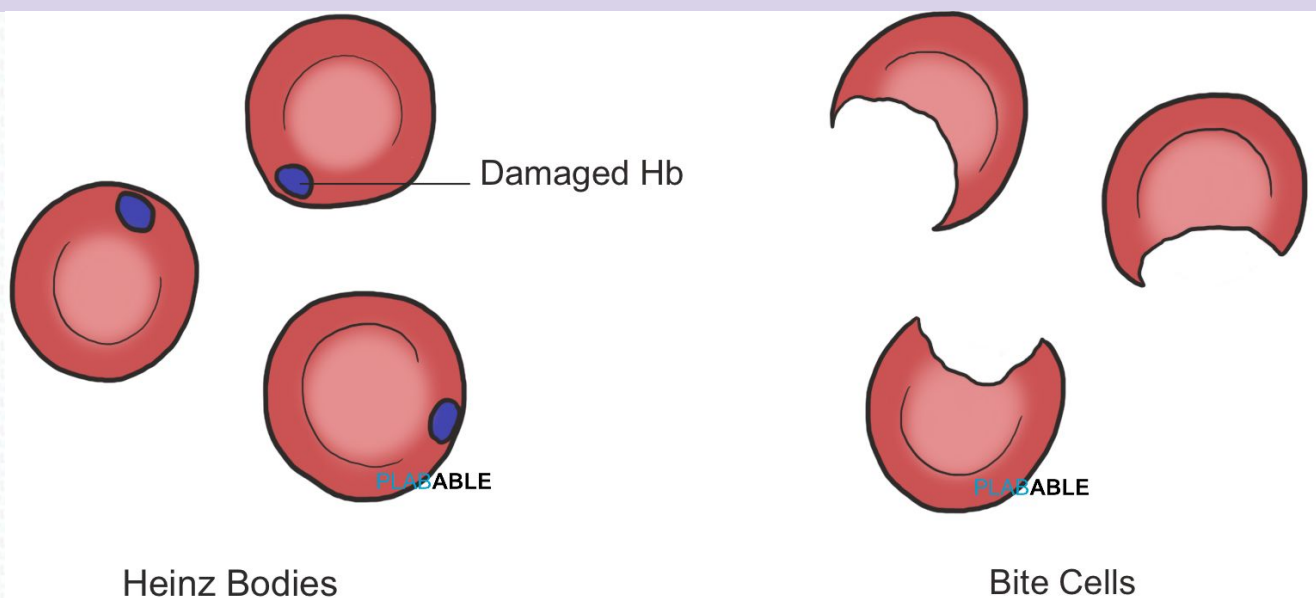
- Broad beans - favism
- Primaquine
- Nitrofurantoin
- Sulfonamides

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



Mode of Inheritance

Autosomal dominant

- Von Willebrand disease
- Hereditary spherocytosis

X-linked recessive

- Haemophilia
- G6PD deficiency

Autosomal recessive

- Thalassaemia
- 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 $\pm$ rigors
- Hypotension
- Feeling that “something is wrong”
- Dyspnea
- Chills
- Myalgia
- Pain at puncture site

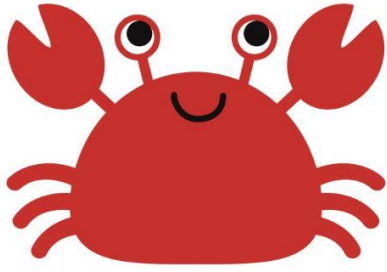
Management (if only feature is temp $< 38.5^{\circ}\text{C}$)

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

Management

- Stop transfusion
- Oxygen and fluid support

Multiple Myeloma



C

R

A

B

Hypercalcemia

Renal Failure

Anaemia

Bone (pain)

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

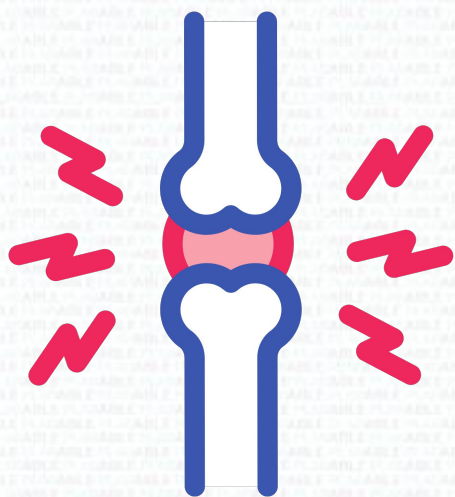
Treatment

- Bortezomib with dexamethasone
- Bisphosphonates to prevent fractures
- Symptomatic for hypercalcemia

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, bleeding time, and von Willebrand factor	
Treatment Factor VIII infusion Desmopressin (↑ factor VIII)	Treatment Recombinant factor IX



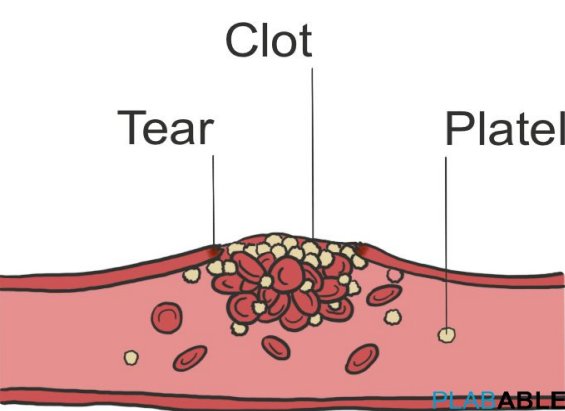
Hemarthrosis



Von Willebrand's Disease

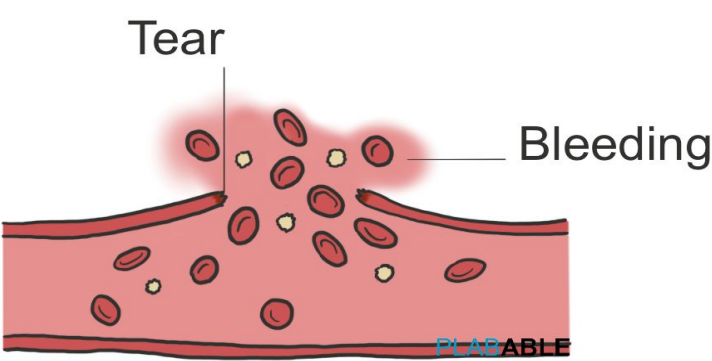
Deficiency or abnormal functioning of von Willebrand factor, which is necessary for platelet plug formation and preventing degradation of factor VIII.

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

- ↑ Bleeding time
- ↑ or normal aPTT
- Normal PT/INR
- Normal platelet count

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, PTT, 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

Hereditary Spherocytosis

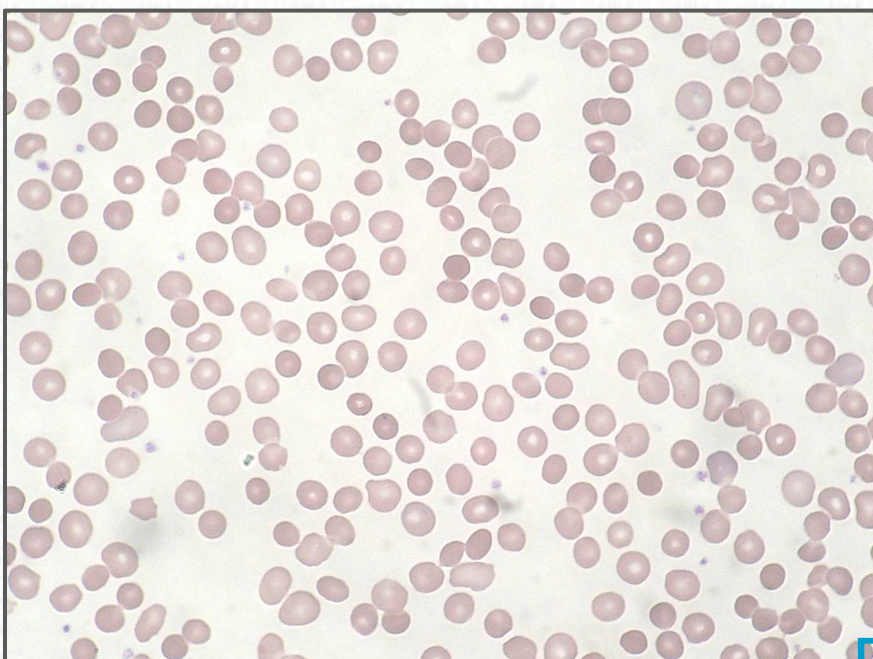
Autosomal dominant mutation → defect in RBC structural protein → spherocytes → haemolysis in the spleen → anaemia

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

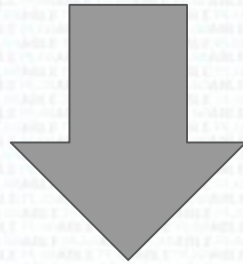
- Blood smear: High reticulocyte and sickled RBCs
- Haemoglobin electrophoresis for HbSS

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)

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

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

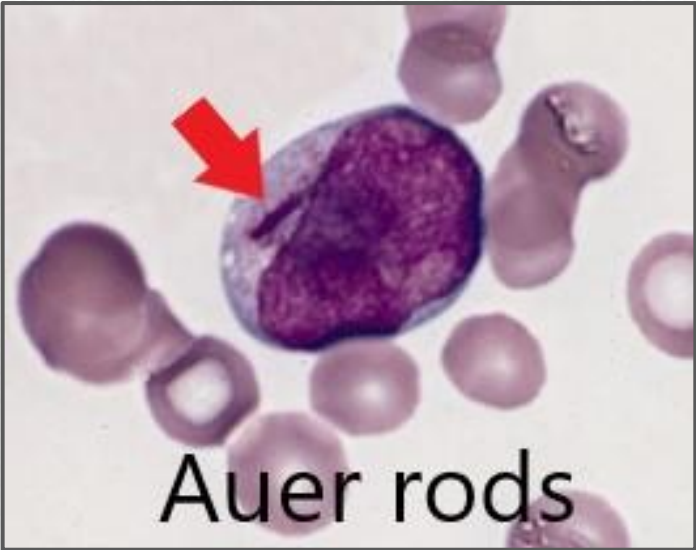
Treatment

- 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
Increased risk in patients with Downs syndrome	Auer rods are seen in peripheral smear
Presentation • Anaemia • Recurrent infections (low WBCs) • Bleeding (thrombocytopenia) • Bone marrow biopsy - numerous lymphoblasts	Presentation • Fatigue • Fever not responding to antibiotics • Gingivitis • Bleeding (thrombocytopenia) • Hepatosplenomegaly • 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?

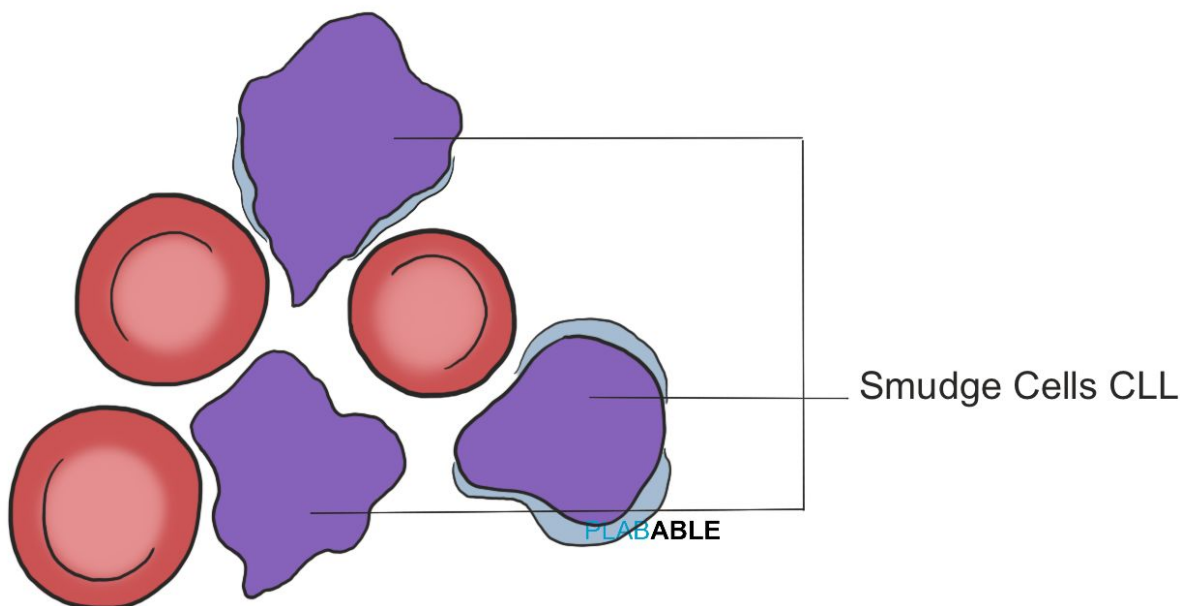
→ 1st trimester → Hb < 11g/dL

→ 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	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



Chronic Myeloproliferative Disorders

Essential thrombocytopoenia

- 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 $\pm$ hepatomegaly $\pm$ B symptoms

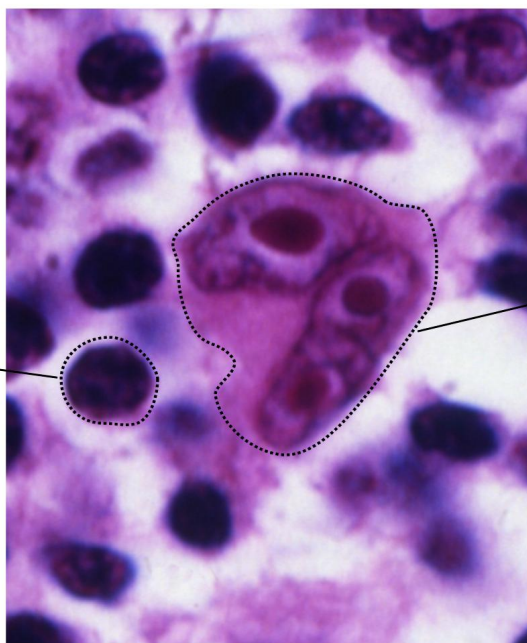
B symptoms

- Unexplained weight loss
- Night sweats
- Low-grade fever
- 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:** HIV, immunosuppression and smoking
- Treatment is by chemotherapy and is based on histological type and staging

Normal lymphocyte



Reed-Sternberg Cell

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

Warfarin - INR Management

INR

8+

Stop

Give oral or IV vitamin K1

6

Stop

Re-start when < 5

5

Reduce or stop

Re-start warfarin when < 5

**If above target range,
reduce or omit 1-2 doses
Re-check INR in 2-3 days**

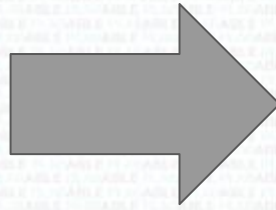
Major Bleed

Stop warfarin

**Give IV Vitamin K $\pm$ Prothrombin complex
concentrate. If unavailable $\rightarrow$ 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

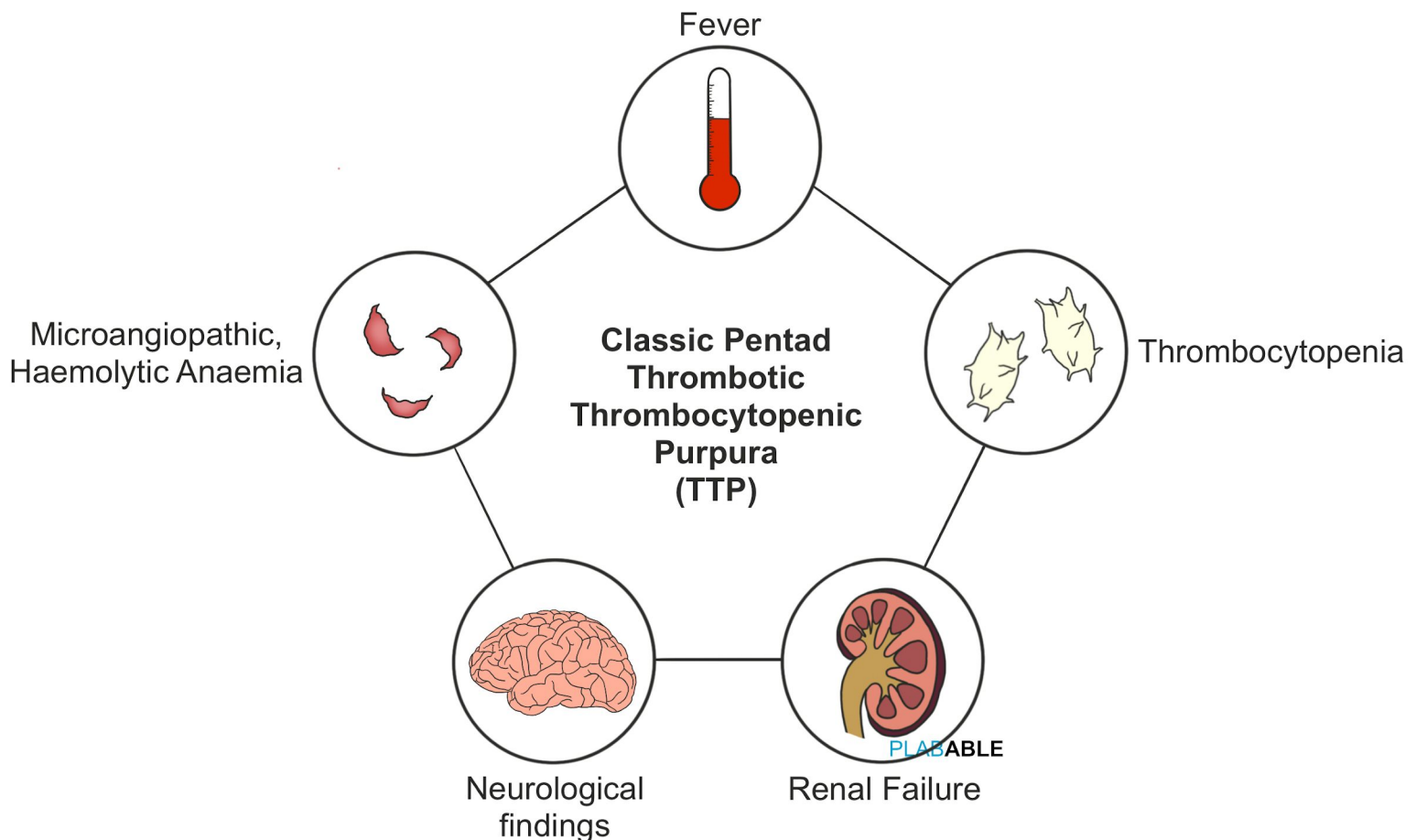
- Chronic
- No viral prodrome
- Gradual onset
- Platelet count does NOT return to normal

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

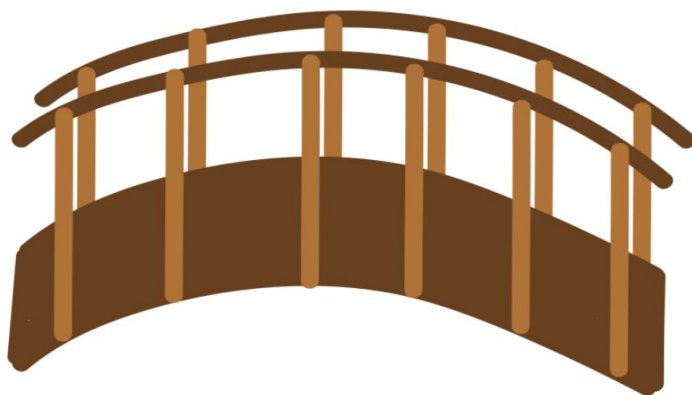
Anticoagulation bridging

This card is specific for elective surgeries

Stop warfarin 5 days before elective surgery.

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

- Venous thromboembolic event in the last 3 months
- Atrial fibrillation with a previous stroke
- Atrial fibrillation with a CHA₂DS₂-VASc score of 5 or more
- Recent transient ischemic attack
- Patients with mechanical heart valves



Remember, if patient is only having warfarin with a CHA₂DS₂-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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