HAEMATOLOGY
T YEAR

SMALL INTRO

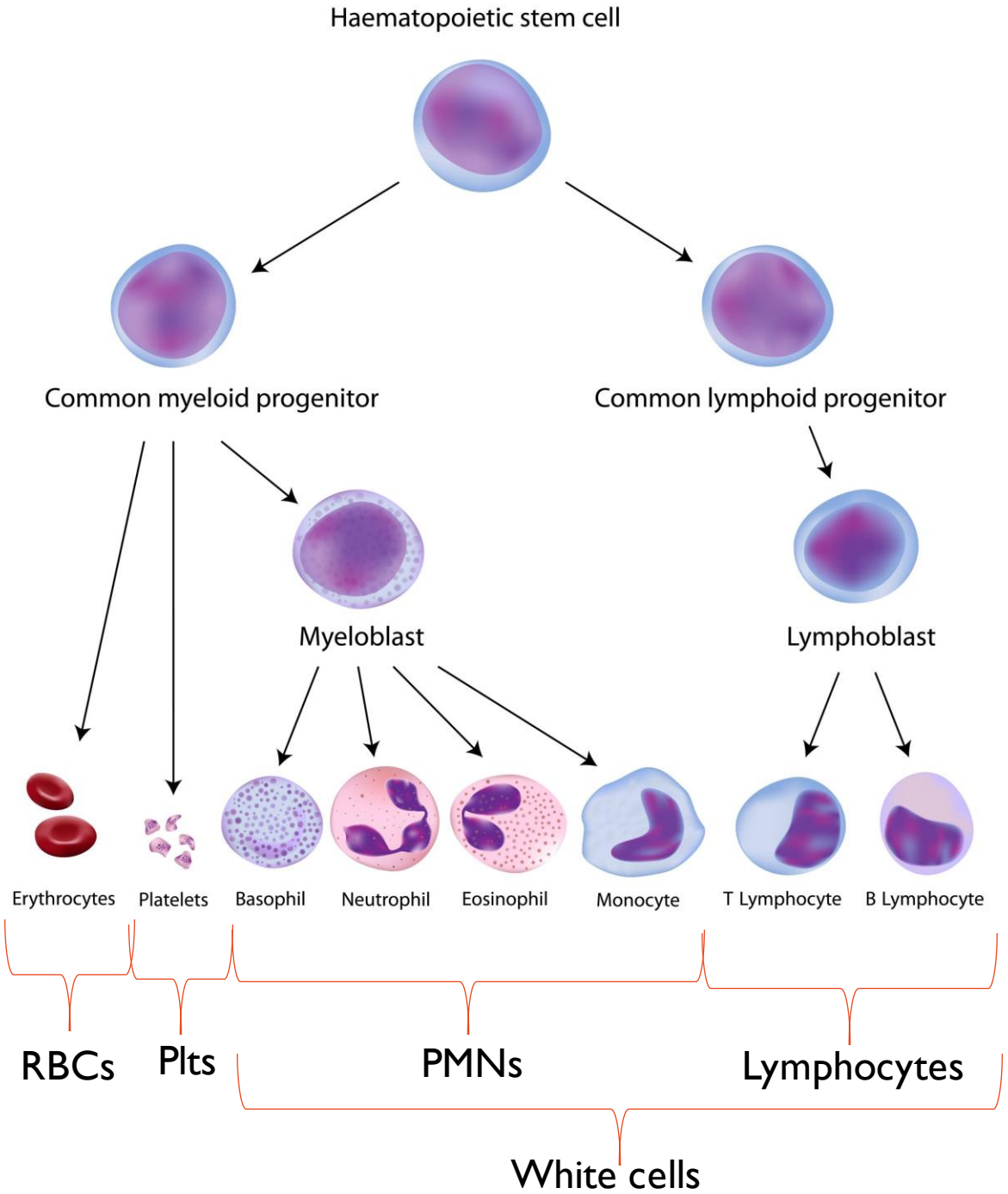
- Many people find haematology scary
- As a medical student you won't be expected to know the intricacies
- Only a haematologist really knows haematology
- Learn the important and serious ones

	Haematology		
113	Anticoagulation and related emergencies* (Bleeding, high INR, urgent surgery)	1*	
114	Transfusion	1*	
116	Diagnostic approach to anaemia	1	
117	Iron Deficiency Anaemia	1	
119	Bone Marrow Failure	2	
120	Macrocytic Anaemia and Macrocytosis	2	
121	Haematological aspects of systemic disease	2	
122	Approach to neutrophilia and neutropenia	2	
124	Lymphoma	2	
125	Leukaemia	2	
126	Haemoglobinopathies (Sickle Cell Disease and Thalassaemia))	2	
127	Inherited and acquired thrombotic disorders	2	
129	Haemolytic Anaemia	3	
130	MDS and myeloproliefrative disorders	3	

HOW PAINFUL IS HAEMATOLOGY TO LEARN?

a) 1-2
b) 3-4
c) 5-6
d) 7-8
e) 9-10

WHICH CELL?


Haematopoietic stem cell
Common myeloid progenitor
Common lymphoid progenitor
Myeloblast
Lymphoblast
Erythrocytes
Platelets
Basophil
Neutrophil
Eosinophil
Monocyte
T Lymphocyte
B Lymphocyte
RBCs
Plts
PMNs
Lymphocytes
White cells

BLOODY EMERGENCIES

Too much

Too few

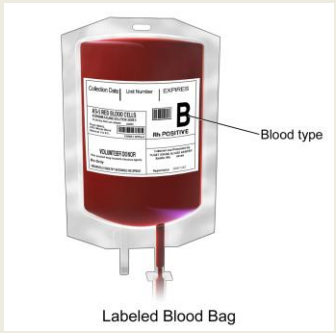
- Polycythaemia
- Hyperviscosity syndromes

- Sickle Cell Crises

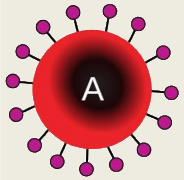
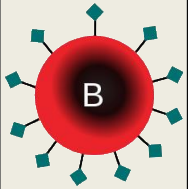
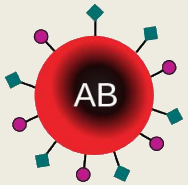
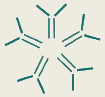
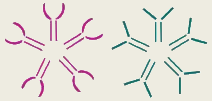
- Haemorrhagic shock
- Extreme anaemia
- High INR
- Neutropenia

RED CELLS

TRANSFUSION



Labeled Blood Bag

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	A antigen	 B antigen	 A and B antigens	None

- Wrongly identified patient
- Infections
- Emergency blood
- Code RED
- Transfusion reactions:
  - **Acute haemolytic**
  - Febrile non-haemolytic
  - Urticarial/anaphylaxis
  - TRALI
  - TACO
  - Acute hypotensive

- Delayed
  - Delayed haemolytic
  - Post-transfusion purpura
  - GVHD
  - Transmission of infectious diseases
  - Iron overload

ANAEMIA

- *Anaemia is the condition in which the number of red blood cells (and consequently their oxygen carrying capacity) is insufficient to meet the body's physiological needs.* – WHO

MICROCYTIC NORMOCYTIC MACROCYTIC

Which of the following would result in a normal MCV?

a) Iron deficiency anaemia
b) Thalassaemia
c) Coeliac's disease
d) CKD
e) Pernicious anaemia

ANAEMIA

- *Anaemia is the condition in which the number of red blood cells (and consequently their oxygen carrying capacity) is insufficient to meet the body's physiological needs.* – WHO

MICROCYTIC

- Iron deficiency anaemia
  - Increased demand or increased loss
  - E.g malabsorption, menstruation, growth,
  - GI Cancers
- Thalasaemia
- Anaemia of chronic disease
- Lead
- Sideroblastic anaemia

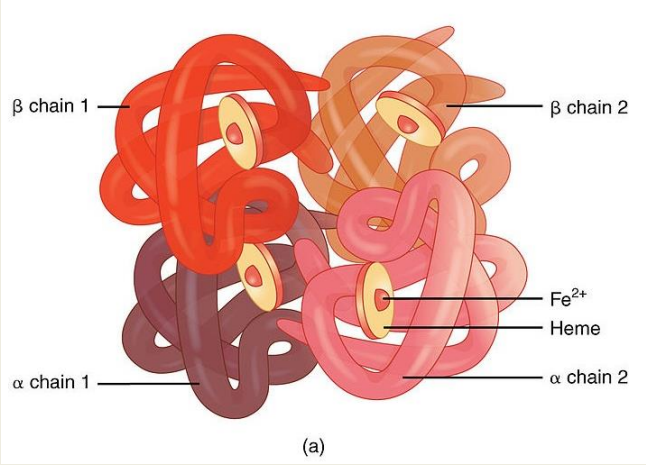
NORMOCYTIC

- Anaemia of chronic disease
- Bone marrow hypo/aplasia
- Sickle cell anaemia
- Chronic renal failure/low Epo

MACROCYTIC

- B12 deficiency
  - Alcohol
  - Pernicious anaemia
  - Nutritional (vegans)
  - Gastrectomy or ileal resection
  - Zollinger- Ellison syndrome
- Folate deficiency
  - Jejunal resection
  - Anti folate drugs e.g methotrexate, trimethorpim
- Myelodysplasia
- Drugs
- Liver disease
- Hypothyroidism

IRON DEFICIENCY ANAEMIA



- Most common cause of anaemia
- Absorbed in duodenum and proximal jejunum

Demand ⇆ **Loss**

- Causes:
  - Diet
  - Bleeding
  - Malabsorption
  - Cancer
  - Preganancy
  - Gut infestation (parasites)
  - Hepcidin

IRON DEFICIENCY	
FERRITIN	LOW
TF SATURATION	LOW
TIBC/Transferrin	HIGH
SERUM IRON	LOW / NORMAL

HAEMOLYTIC ANAEMIA

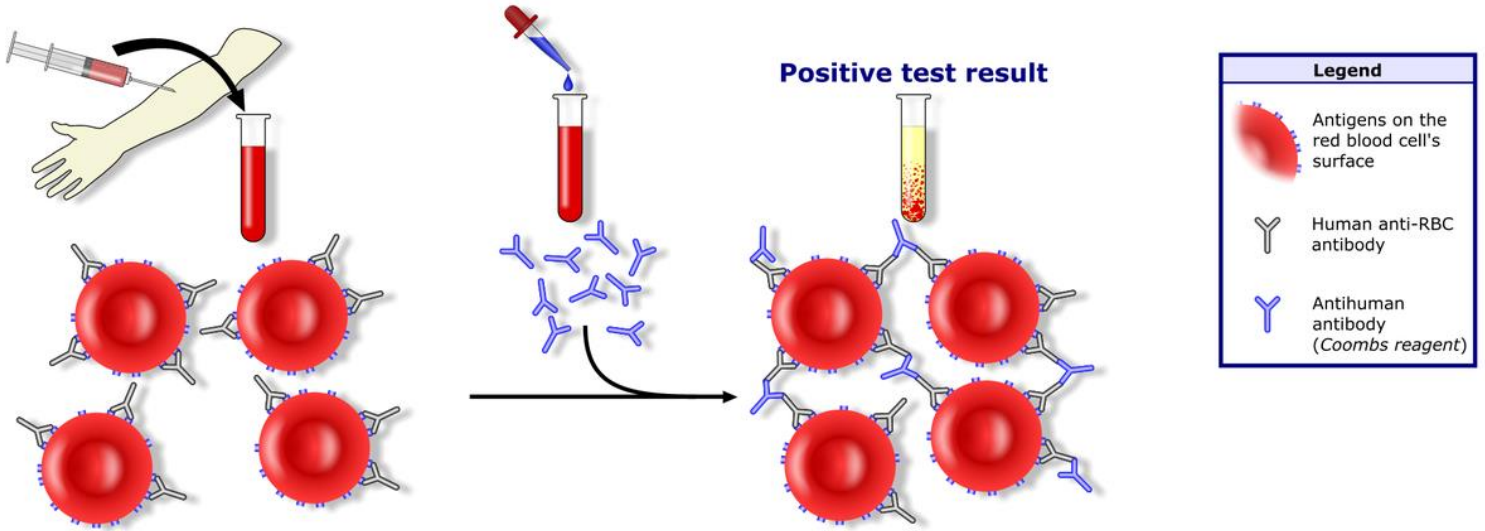
- Shortened lifespan of RBC due to increased peripheral destruction
- Intravascular vs extravascular
- Immune vs non immune

Intravascular	Extravascular
↑ unconjugated bilirubin	↑ unconjugated bilirubin
↑ LDH	↑ LDH
↑ Reticulocytes	↑ Reticulocytes
↓ haptoglobin	Normal haptoglobin
Haemoglobinuria	No haemoglobinuria
Haemoglobinaemia	No haemoglobinaemia
Hemosiderinuria	No hemosiderinuria

	Inherited	Acquired	
	Non-Immune	Non-Immune	Immune
Intravascular	G6PD deficiency Sickle Cell Disease	Paroxysmal nocturnal haemoglobuniria (PNH) Microangiopathic haemolysis (MAHA): TTP, DIC, HELLP Valve haemolysis Medications	Autoimmune: warm, cold, drug induced Alloimmune – transfusion reactions, HDFN
Extravascular (more common)	Membrane disorders e.g hereditary spherocytosis SCD		Autoimmune: warm, cold, drug induced

COOMBS TEST

Direct Coombs test / Direct antiglobulin test

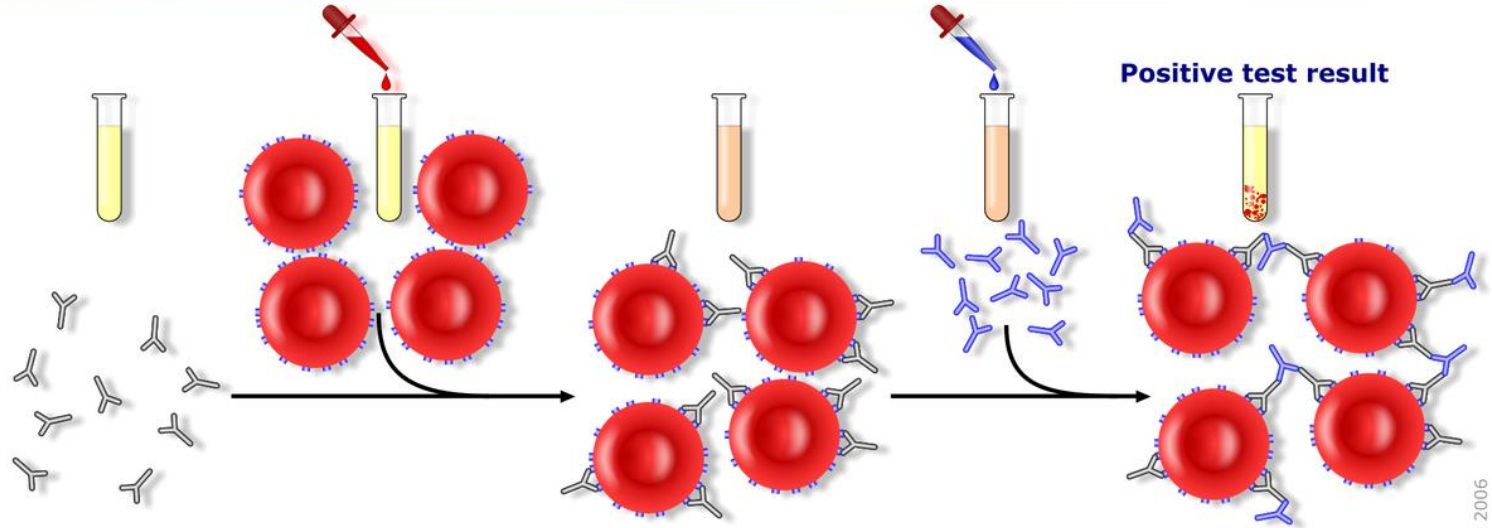


Blood sample from a patient with immune mediated haemolytic anaemia: antibodies are shown attached to antigens on the RBC surface.

The patient's washed RBCs are incubated with antihuman antibodies (*Coombs reagent*).

RBCs agglutinate: antihuman antibodies form links between RBCs by binding to the human antibodies on the RBCs.

Indirect Coombs test / Indirect antiglobulin test



Recipient's serum is obtained, containing antibodies (Ig's).

Donor's blood sample is added to the tube with serum.

Recipient's Ig's that target the donor's red blood cells form antibody-antigen complexes.

Anti-human Ig's (*Coombs antibodies*) are added to the solution.

Agglutination of red blood cells occurs, because human Ig's are attached to red blood cells.

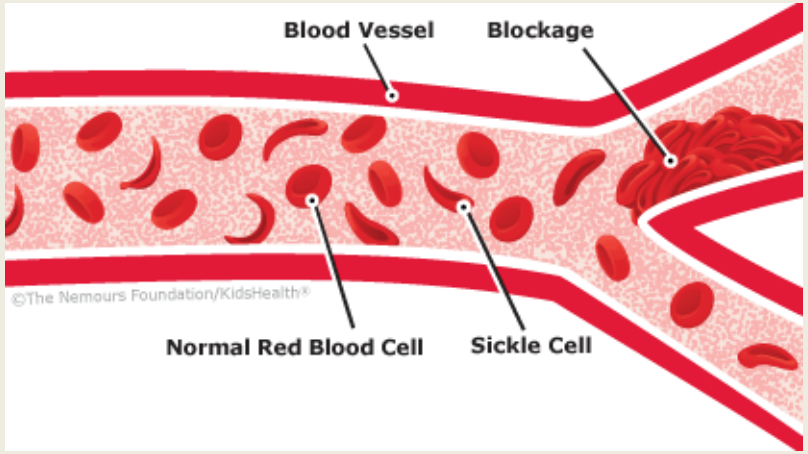
SBA

- 17 year old Shona presents to A&E with dysponea that progressed over the last three hours. She discloses a tightness in her chest as well. Shona says she was swimming with some friends earlier before the SOB started. Her Hb comes back as 50, with a high reticulocyte count. Shona tells you she has Sickle Cell Disease. What is most important management of this patient?

a) CXR and Analgesia
b) Aspirin and O2
c) O2 and Analgesia
d) CTPA
e) Exchange transfusion

INHERITED HAEMAGLOBINOPATHIES

- Sickle Cell Anaemia — **abnormal** globin chain structure
  - Vaso-occlusive crisis
  - Aplastic crisis
  - Splenic sequestration crisis
  - Acute chest syndrome
  - Haemolytic crisis
  - AVN
  - Stroke

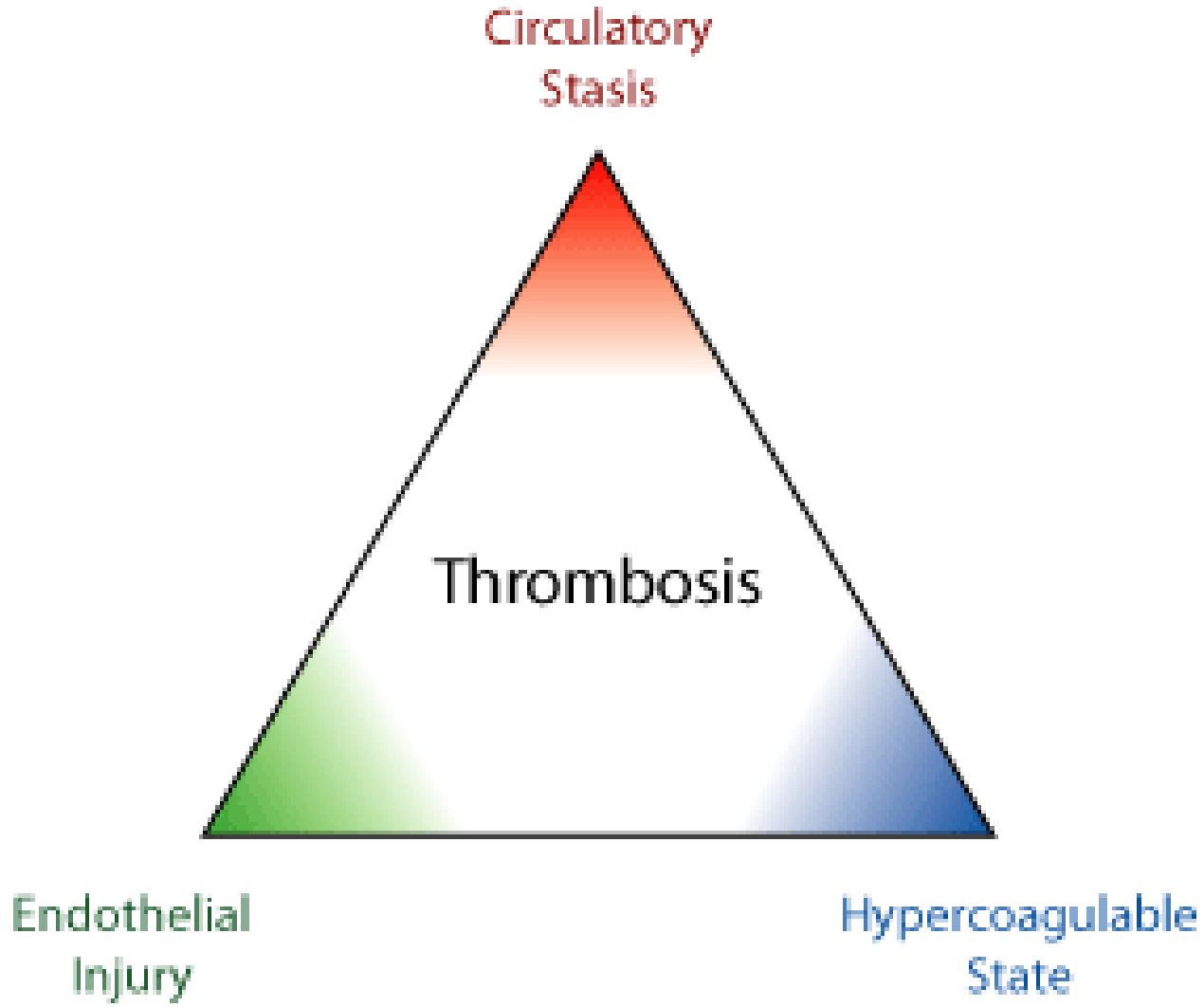


- Thalassaemia — **absent** or **reduced** production of globin chains

α0 homozygous	hydrops fetalis
α-/--	moderate
αa/-- or a-/a-	asymptomatic carrier
βo homozygotes	thalassaemia major → repeated transfusion extramedullary haematopoiesis, OP, iron overload
B+ heterozygotes	symptomless

PLATELETS

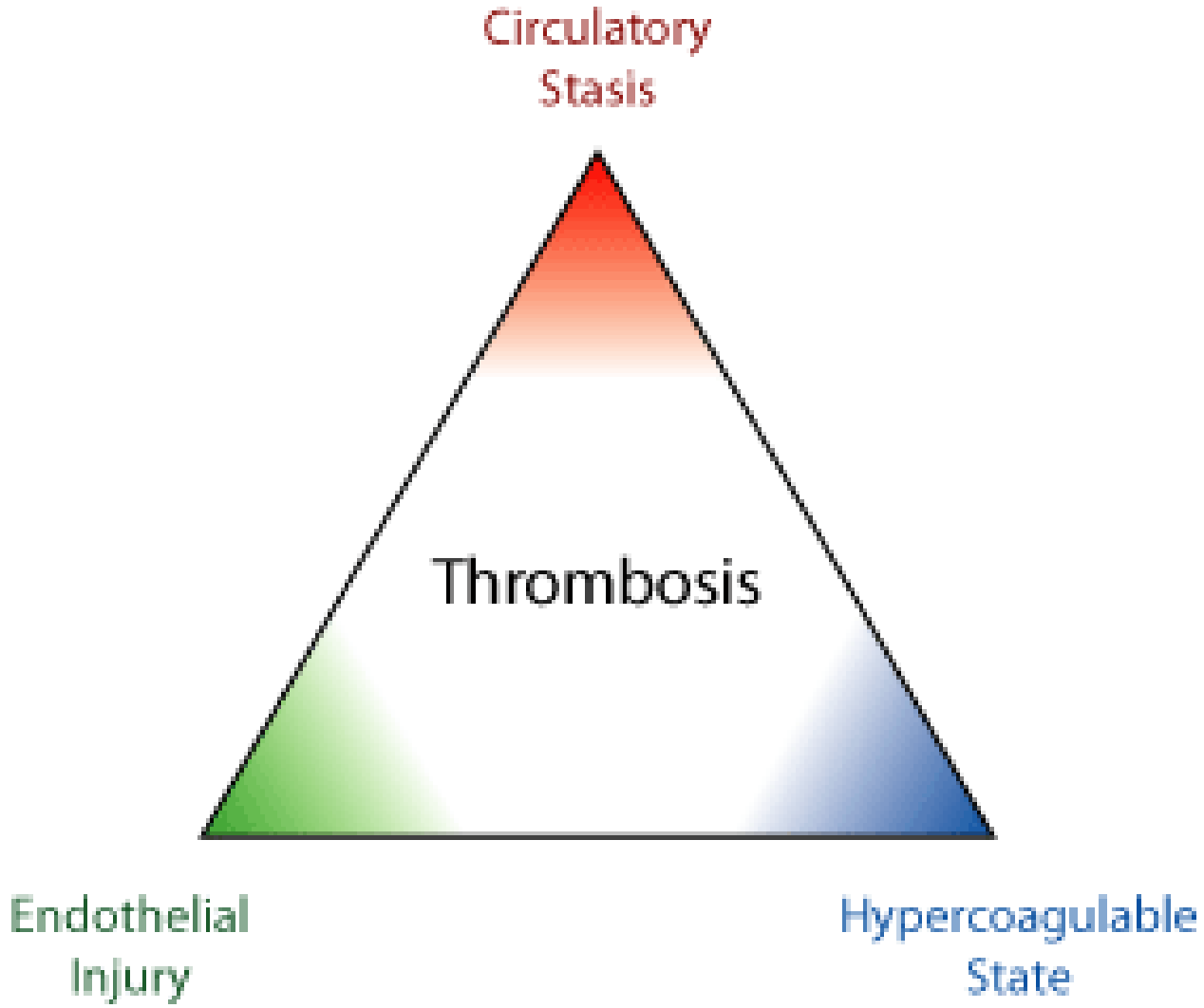
VIRCHOW'S TRIAD



Endothelial damage

Stasis

Hypercoagulable state



VIRCHOW'S TRIAD

A 40 year of female comes to the GP practice complaining of a swollen sore leg. She feels well in herself and denies any fever or recent travel. She says she went camping in the woods last week.

What in her history would make you less concerned about a DVT?

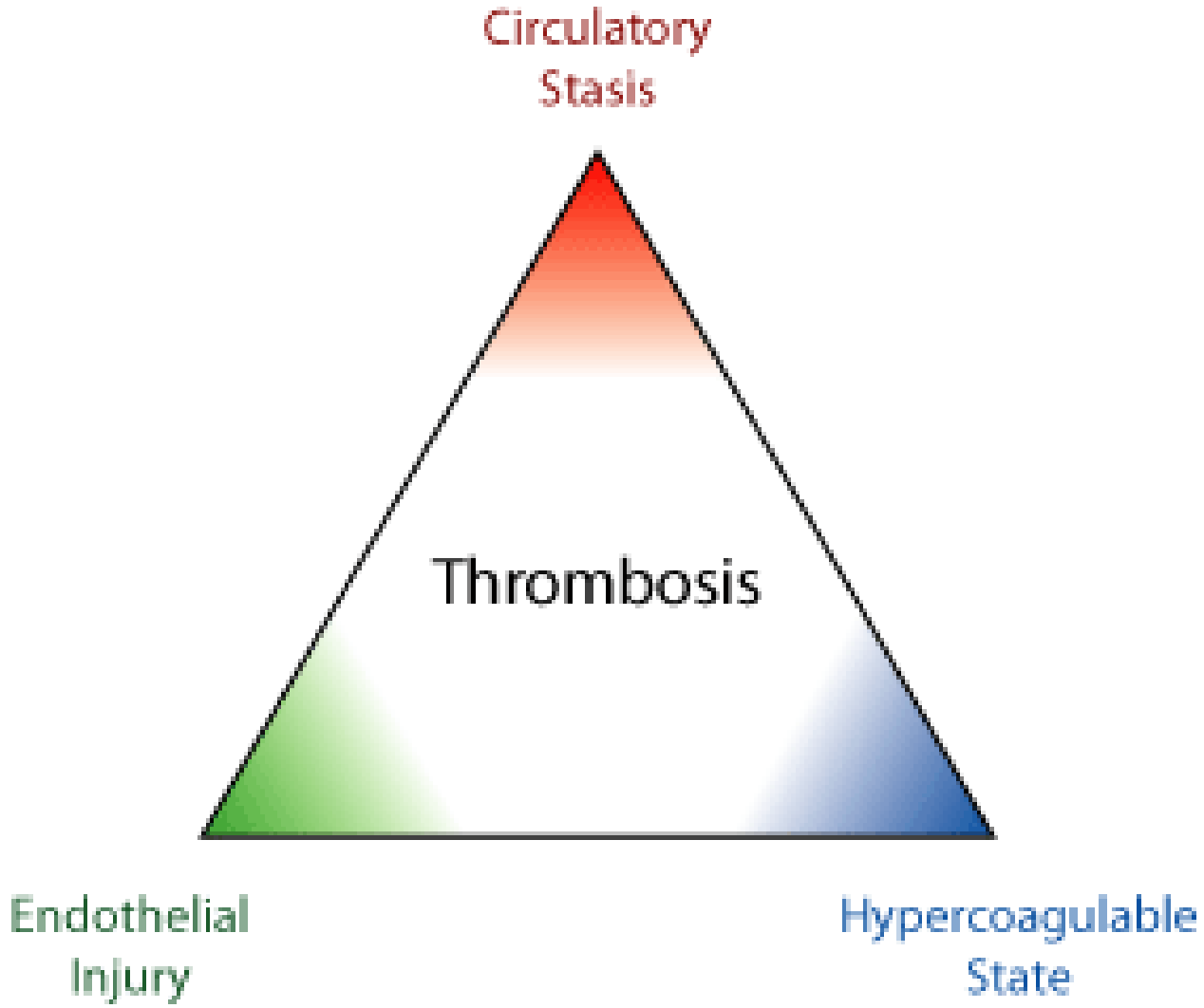
Previous history of cancer

Family history of Factor V Leiden

Works as a lorry driver

Has been bitten my an insect

Takes COCP



VIRCHOW'S TRIAD

Endothelial damage

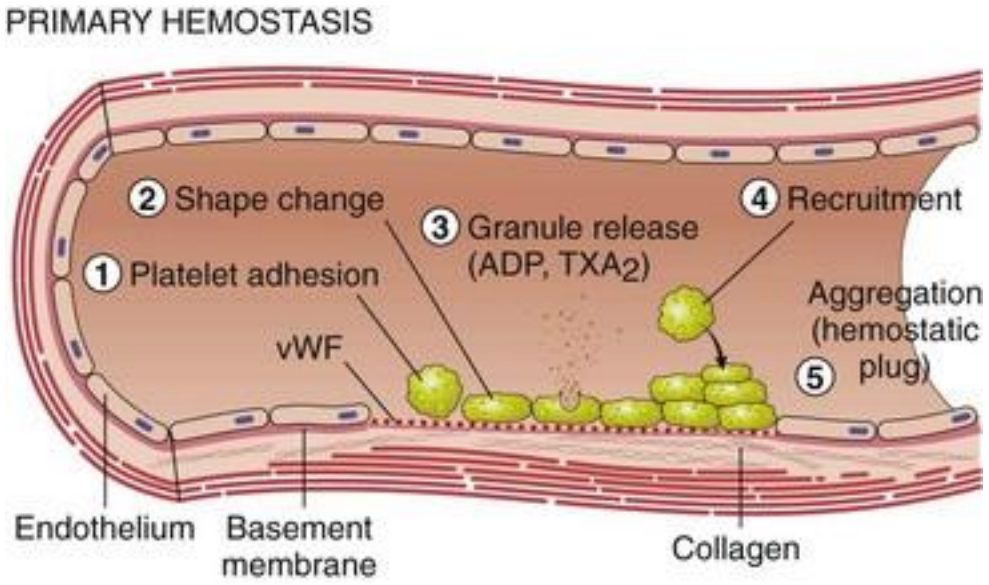
- Surgery
- Trauma
- Inflammation
- Sepsis
- Indwelling catheters
- Atherosclerosis

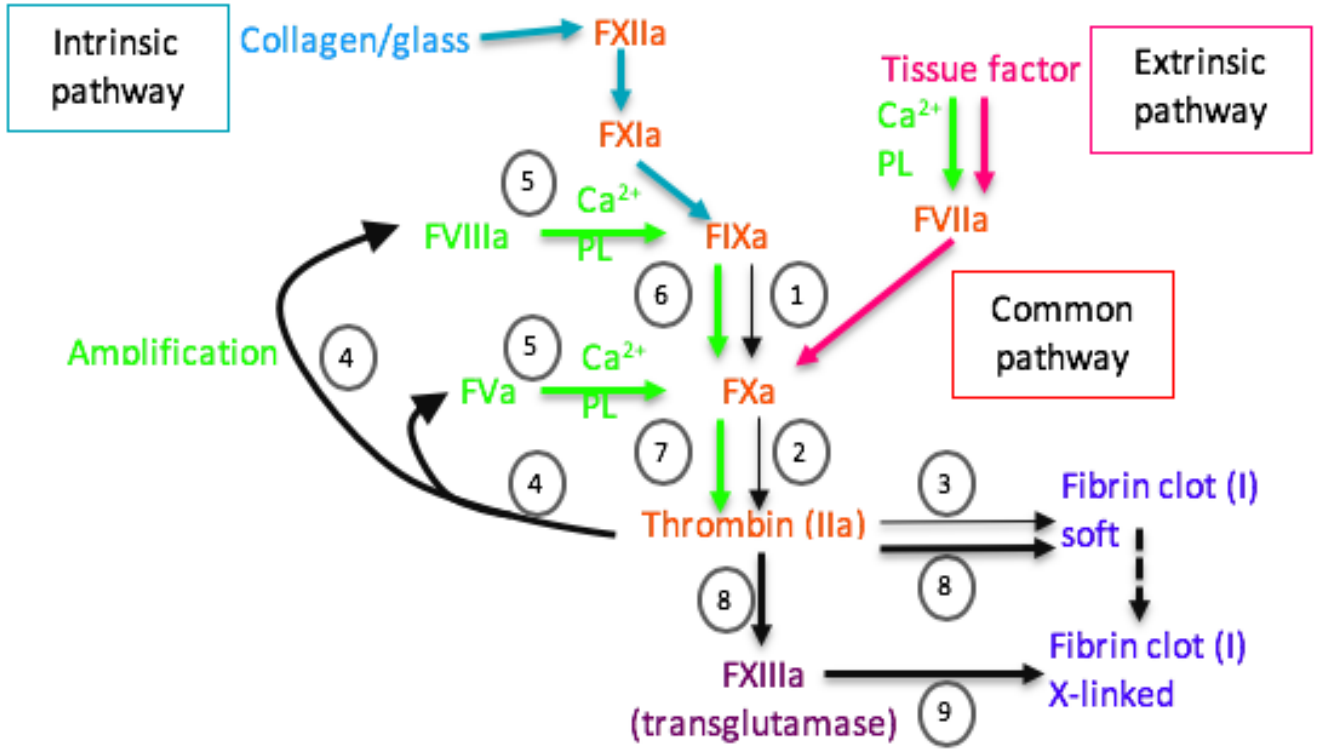
Stasis

- Immobility
- Post-op
- Venous insufficiency
- Atrial fibrillation
- LV dysfunction

Hypercoagulable state

- Thrombotic disorders
- Inflammation and sepsis
- Pregnancy
- Oestrogen
- Cancer
- Lupus
- CKD/Nephrotic syndrome
- Prosthetic heart valves





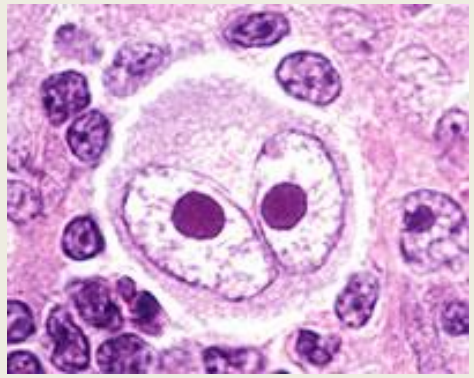
THROMBOTIC AND BLEEDING DISORDERS

- VW disease
  - Most common bleeding disorder
- Haemophilia A and B
  - X linked
  - A(8) B(9)
- ITP (immune thrombotic purpura)
- TTP (thrombocytopenic thombotic purpura)
- Factor V leiden

Immune thrombotic purpura	Thrombocytopenic thrombotic purpura
Platelets destroyed by auto-antibodies in the spleen Can be acute (self limiting purpura) or chronic (fluctuating course of bleeding and purpura , expistaxis, menorrhagia) Raised megakaryocytes in BM Anti-platelet antibodies present Mx Self limiting Steroids IvIg Definitive Rx: splenectomy or rituximab	**Thrombocytpenia, Fever , Renal failure, Confusion, MAHA** ↑Bili, LDH , creatinine; ↓plts Hb Microthombi Reduction in ADAMTS13 (breaks down vWF) due to IgG antibody, inflammation results in increased vWF multimers Platelets destroy RBCs in the vessels MEDICAL EMERGENCY Mx; plasma exchange, high dose steroids, blood transfusion

WHITE CELLS

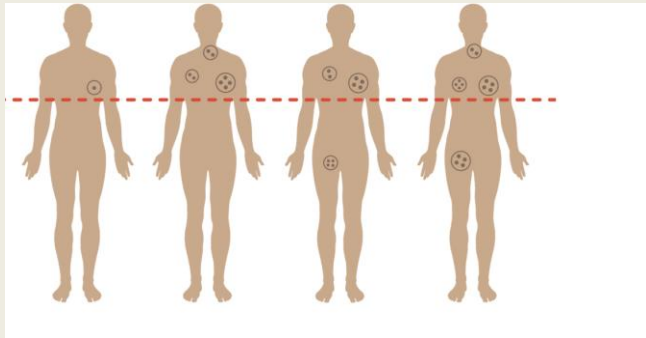
LYMPHOMA



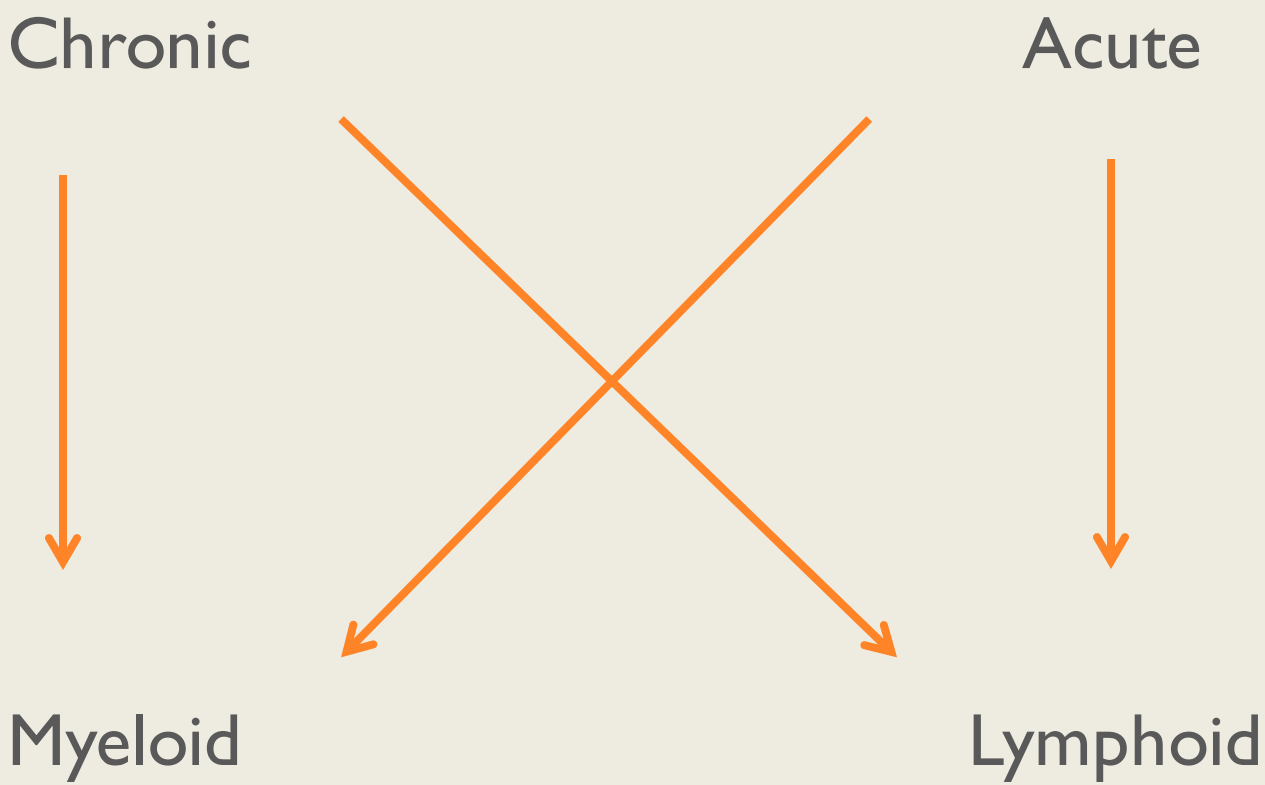
- Mutation in **lymphocytes** that has left the bone marrow and now reside in the **lymph node**
- Solid mass i.e enlarged lymph node
- 90% **B lymphocytes** due to **somatic hypermutation**

Hodgkin	Non-Hodgkin
33% Good cure rate Agressive Bimodal peak incidence (15-35; >55) RFs: EBV, Immunosuppression, FHx Painless Lymphadenopathy +/- B symptoms Alcohol induced pain, splenomegaly **Reed-Steinberg cell – histology**	66% B Cell NHL Indolent vs aggressive Diffuse B cell most common T Cell NHL Aggressive with poor response to treatment

- Ann Arbor



LEUKAEMIA



ACUTE LEUKAEMIA

Reduced differentiation (QUALITY)

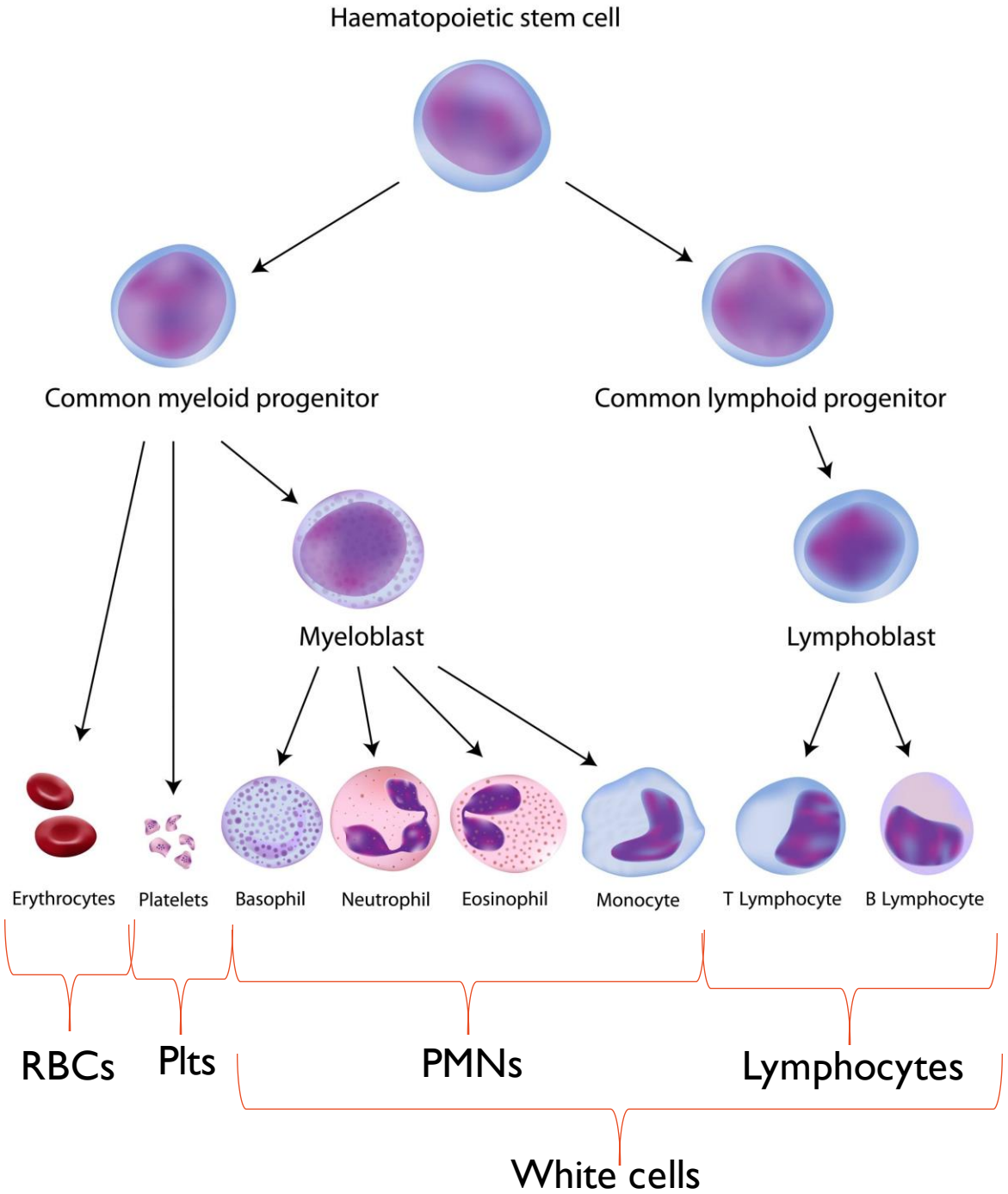
Immature cells

Highly proliferative (QUANTITY)

Overwhelming accumulation in BM

Bone marrow failure

Spill over into blood



CHRONIC LEUKAEMIA

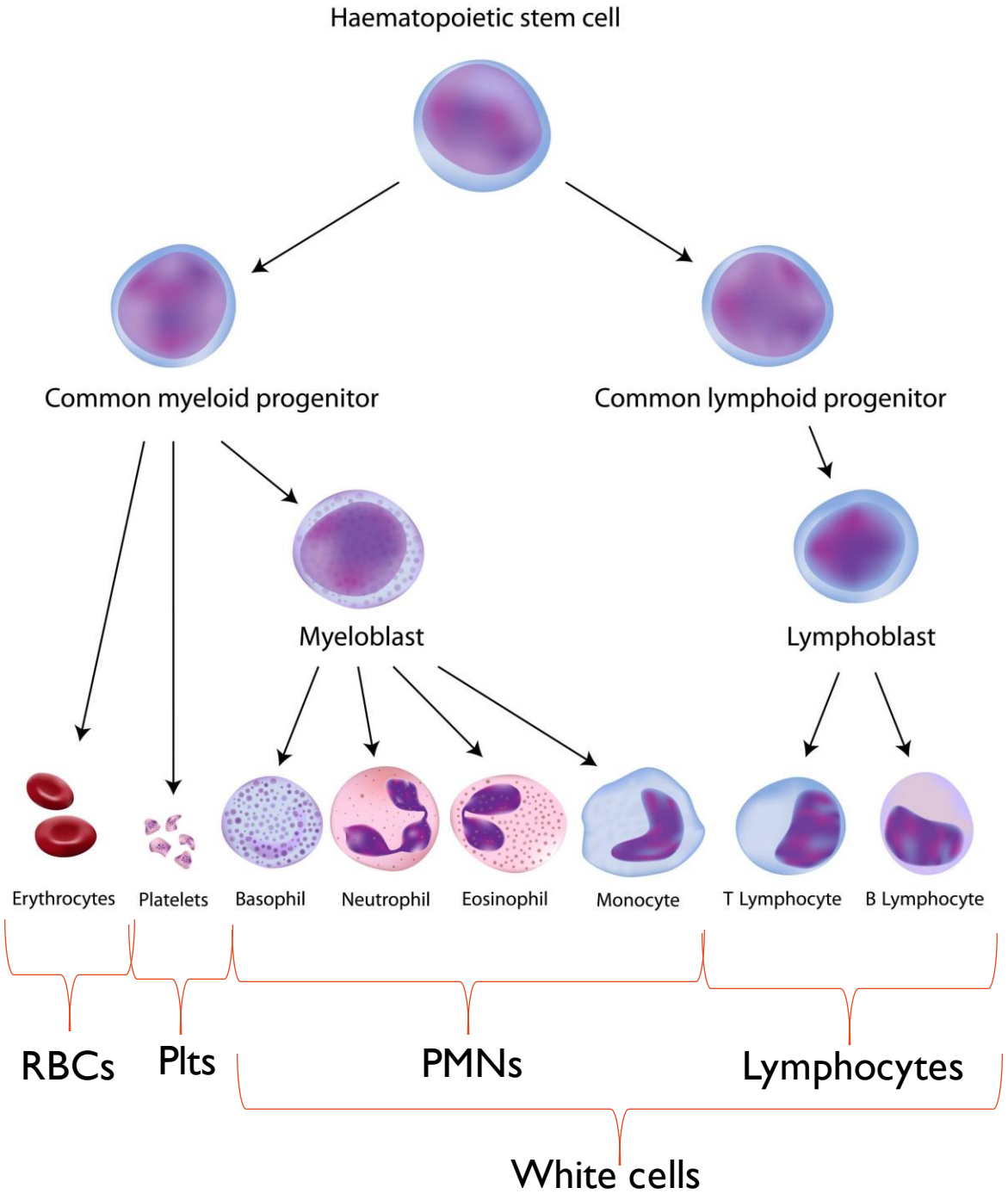
Increased differentiation (QUALITY)

Mature cells

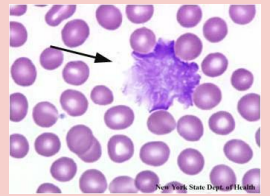
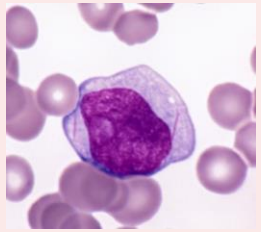
Lower proliferative capacity (QUANTITY)

Accumulation in BM

Spill over into blood



LEUKAEMIA

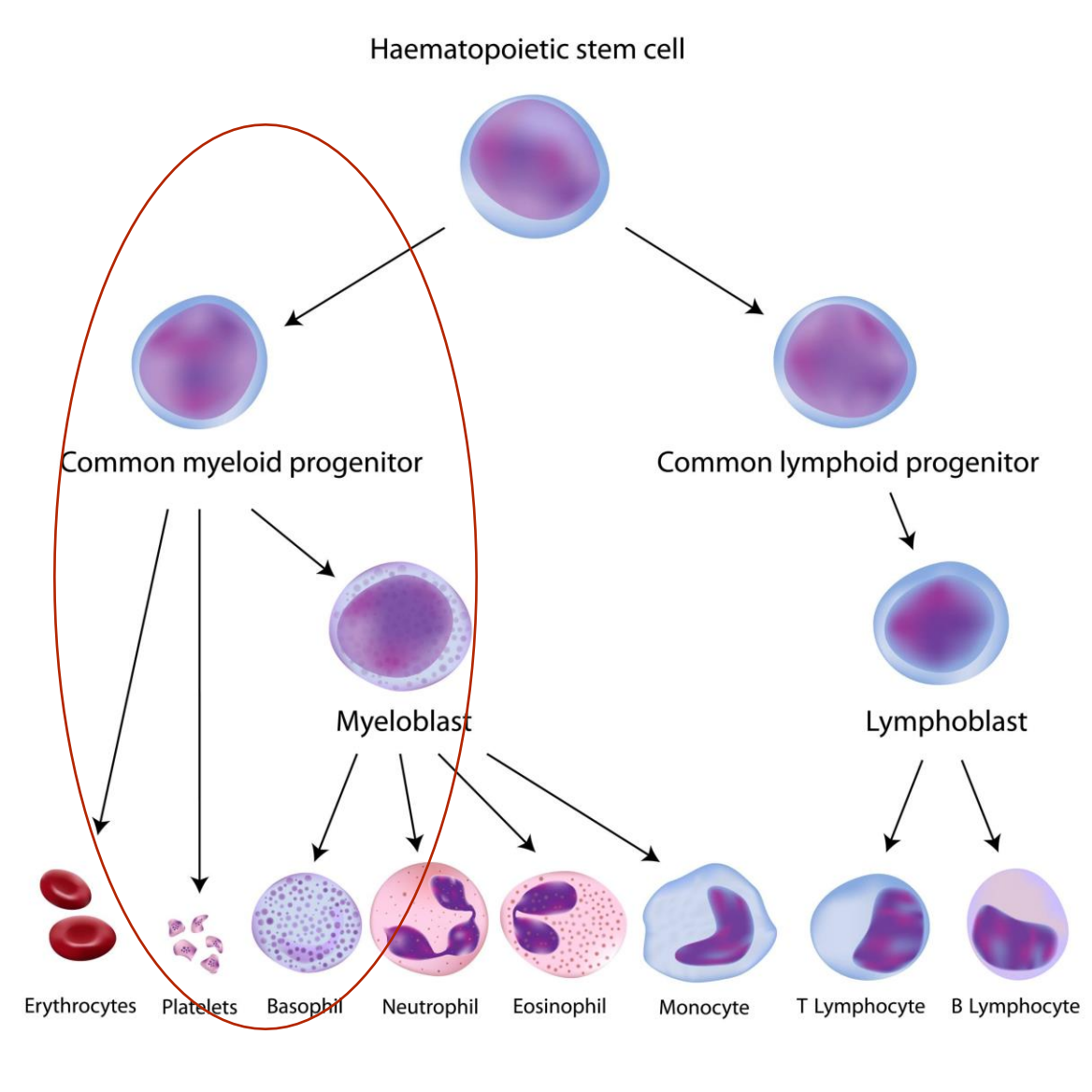
	Acute	Chronic
Lymphoid	ALL **Children** Bleeding Anaemia Increased atypical infections Lymphadenopathy Hepatosplenomegaly CNS involvement Bone pain **Ph chromosome 9:22** ☒ **↑WCC (> 20% blasts) + Pancytopenia**	CLL (Ineffective B Cells) **Elderly** **Asymptomatic and indolent** Bleeding Infections Constitutional symptoms Hepatosplenomegaly AIHA (warm) Hypo Ig Hyperviscosity **↑WCC (leuk), ↓ Hb, plts, neut** **Smudge cells** 
Myeloid	AML **Adults** Associated with MDS Bleeding Anaemia Increased atypical infections Lymphadenopathy Hepatosplenomegaly Gum hypertrophy **↑WCC (> 20% blasts) + Pancytopenia** **Auer rods** 	CML Myeloproliferative disorder **Adults** Constitutional symptoms Gout Bleeding Hepatosplenomegaly (MASSIVE) Hypervisocity **Ph chromosome 9:22** ✓ **↑WCC (myeloid), ↓ Hb, plts**

MDS AND MYELOPROLIFERATIVE DISORDERS

- QUANTITY PROBLEM
  - Myeloproliferative
  - High blood count
  - Table 8.10 Classification of myeloproliferative disorders

By proliferating cell type		
RBC	→	Polycythaemia vera (PRV)
WBC	→	Chronic myeloid leukaemia (CML, p[link])
Platelets	→	Essential thrombocythaemia
Fibroblasts	→	Myelofibrosis

- QUALITY AND QUANTITY PROBLEM
  - Myelodysplastic
  - Low blood count
  - Transformation to AML
  - Marrow failure
    - Hyperplasia and hypercellular



BONE MARROW FAILURE

SYSTEMIC DISEASE

- RBC
  - Anaemia of chronic disease
    - Cancers
    - Chronic inflammatory (incl infections)
    - Autoimmune
    - Chronic organ dysfunction
- WBC
  - Leukocytosis
    - Neutophilia - bacterial
    - Lymphocytosis - viral
  - Leukopenia – infection e.g pertussis
    - Neutropenia – drug induced, immunosuppression, chemo
- Plts
  - Thromboytosis
    - Acute phase response
  - Thrombocytopenia
    - Immune
    - Drug mediated
    - Consumption in hypersplenism and DIC
    - Splenic infection

SYSTEMIC DISEASE

- Connective tissue disorder
  - Cytopenia
- Malaria
  - Anaemia
  - Thrombocytopenia
  - Haemolysis
  - Splenomegaly
- Cancer
  - Anaemia from haemolytic changes
  - Pancytopenia
- HIV
  - Cytopenia
  - Poor production
  - Drugs
- CKD
  - Low EPO
- Lupus
  - Thrombocytopenia
  - Haemolytic anaemia
  - Leucopenia
  - ITP
- Polyarteritis nodosa
  - eosinophilia
- Parasitic infections
  - eosinophilia
- Medication effects!!!
- DIC
  - Low fibrinogen and D dimers
  - Elevated PT, APTT
  - Sepsis

HOW PAINFUL IS HAEMATOLOGY TO LEARN?

a) 1-2
b) 3-4
c) 5-6
d) 7-8
e) 9-10

SBA

- 50 year old Simon Lee presents to A&E with a profuse nosebleed. On questioning, he says he gets nosebleeds quite often for the last 5/12. Simon has been feeling unwell the last 3/7 but assumed it was Covid so he stayed home. On examination he has a distended abdomen stony dull to percussion and you note a swollen MTP joint. You suspect he has something serious and send off FBC, U+E, LFT bloods.
- What do you suspect Simon has?
    a) ALL
    b) AML
    c) CLL
    d) CML
    e) Liver failure