PIPADOR REVISION

MRCOG Part 1 Revision Notes

Haematological Physiology

PHYSIOLOGY • LECTURE 134

VISUAL EXAMINATION REVISION NOTES

2026 Edition

MRCOG PART 1 REVISION NOTES | PHYSIOLOGY

134 Haematological Physiology

Haematopoiesis, red cells and haemoglobin, iron, B_{12} and folate, white cells and haemostasis

≈ 70 mL/kg	120–150 g/L	120 days	150–400
Blood volume (plasma ≈ 55%)	Hb (adult women)	Red cell lifespan	Platelets × 10^9/L (lifespan 7–10 days)

■ KEY FACTS: Learning objectives

- Describe haematopoiesis and its regulation.
- Describe red cell structure, metabolism, production and breakdown; haemoglobin structure and variants.
- Describe iron, vitamin B_{12} and folate metabolism and classify anaemia.
- Describe white cell types and functions.
- Describe primary haemostasis, coagulation, natural anticoagulants and fibrinolysis, and interpret coagulation tests.

134.1 Haematopoiesis

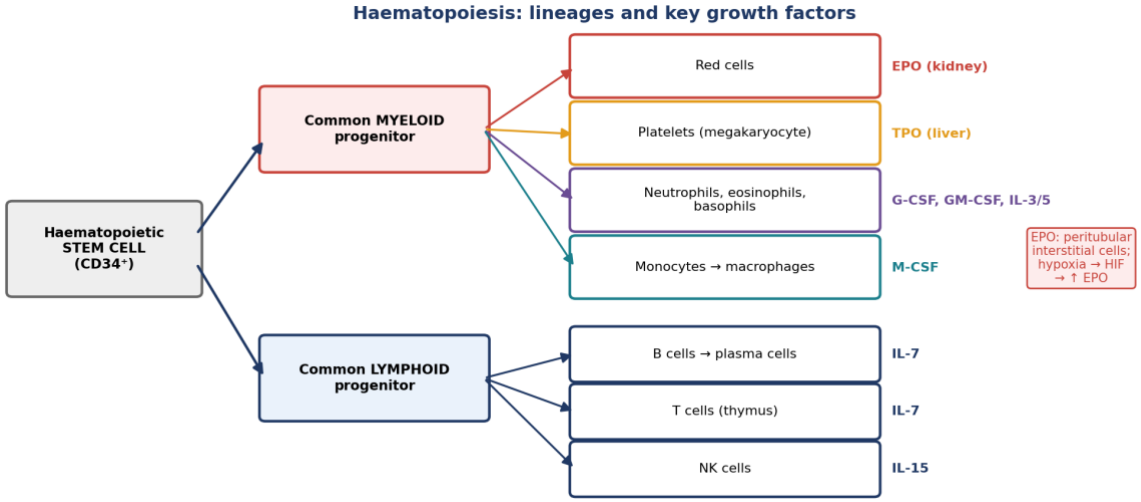


Figure 134.1 — Haematopoietic lineages and growth factors

Adult haematopoiesis occurs in the **red marrow of the axial skeleton** (pelvis, vertebrae, sternum, ribs, skull, proximal long bones). Fetal sites (yolk sac → liver → marrow) are covered in **Lecture 136**. Extramedullary haematopoiesis (liver, spleen) recurs in marrow failure or severe haemolysis (e.g. thalassaemia major).

134.2 Red cells

Pronormoblast ▶ Normoblasts (nucleus extruded) ▶ **Reticulocyte** (1–2 days in blood; 0.5–2.5%) ▶ Mature red cell (120 days) ▶ Removed by splenic **macrophages**

Feature	Physiology	Clinical link
Structure	Biconcave disc ≈ 7.5 µm; no nucleus or mitochondria; deformable spectrin–ankyrin cytoskeleton	Hereditary spherocytosis (membrane defects)

Feature	Physiology	Clinical link
Glycolysis (Embden–Meyerhof)	Sole ATP source (anaerobic)	Pyruvate kinase deficiency → haemolysis
Rapoport–Luebering shunt	Produces 2,3-DPG → right-shifts ODC	↑ in anaemia, altitude, pregnancy; ↓ in stored blood
Hexose monophosphate shunt	G6PD → NADPH → reduced glutathione protects against oxidants	G6PD deficiency (X-linked): haemolysis with fava beans, primaquine, nitrofurantoin, sulphonamides
Methaemoglobin reductase	Keeps iron as Fe^{2+}	Methaemoglobinaemia (local anaesthetics e.g. prilocaine, nitrites)

■ **DEFINITION**

Requirements for erythropoiesis: EPO, **iron, B_{12}, folate**, vitamin B_6, vitamin C, copper, amino acids, thyroxine, androgens.

Breakdown: haem → biliverdin → **unconjugated bilirubin** (albumin-bound) → liver conjugation by **UGT1A1** → bile → urobilinogen/stercobilin; iron recycled; globin → amino acids. **Haptoglobin** binds free Hb (↓ in intravascular haemolysis).

Haemoglobin

Haemoglobin	Chains	Adult %	Notes
HbA	$\alpha_2\beta_2$	≈ 97%	Tetramer, each with haem (Fe^{2+}) — binds 4 O_2 cooperatively
HbA_2	$\alpha_2\delta_2$	2–3%	↑ (> 3.5%) in β-thalassaemia trait
HbF	$\alpha_2\gamma_2$	< 1%	Fetal; binds 2,3-DPG poorly → high O_2 affinity; ↑ in β-thal, hydroxycarbamide
HbS	$\alpha_2\beta^s_2$	—	β6 Glu → Val; polymerises when deoxygenated → sickle cell disease
Hb Bart's / HbH	γ_4 / β_4	—	α-thalassaemia major (hydrops) / HbH disease

Globin genes: **α on chromosome 16** (2 genes per chromosome, 4 total); **β, γ, δ on chromosome 11**. All are autosomal recessive — partner testing and prenatal diagnosis are central to antenatal haemoglobinopathy screening (Lecture 135).

134.3 Iron, vitamin B_{12} and folate

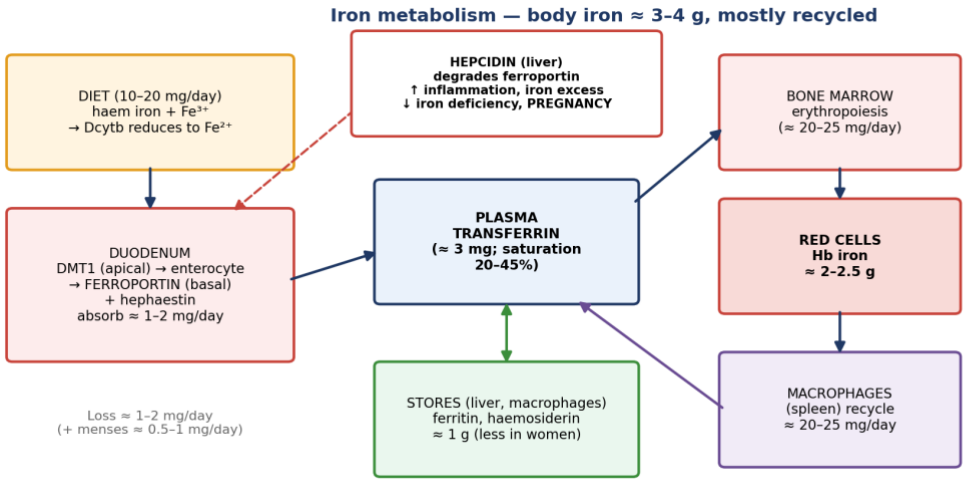


Figure 134.2 — Iron absorption, transport, use, storage and recycling

Test	Iron deficiency	Anaemia of chronic disease	Thalassaemia trait
MCV	↓	↔ / ↓	↓↓ (often with near-normal Hb)
Serum ferritin	↓ (< 30 µg/L)	↔ / ↑ (acute-phase)	↔
Transferrin saturation	↓	↓	↔
TIBC / transferrin	↑	↓	↔
Hepcidin	↓	↑	↔ / ↓
Other	↑ RDW, pencil cells	CRP ↑	↑ HbA_2 (β-trait); RBC count ↑

	Vitamin B_{12} (cobalamin)	Folate
Sources	Animal products only	Leafy vegetables, liver; fortified foods
Absorption	Binds intrinsic factor (gastric parietal cells) → terminal ileum	Duodenum / jejunum
Stores	3–5 years (liver)	≈ 4 months
Role	Cofactor: methionine synthase, methylmalonyl-CoA mutase	DNA synthesis (thymidylate); neural tube closure
Deficiency	Megaloblastic anaemia + neurological (subacute combined degeneration); pernicious anaemia, ileal disease, vegans, metformin	Megaloblastic anaemia; ↑ demand (pregnancy, haemolysis), anticonvulsants, methotrexate, trimethoprim

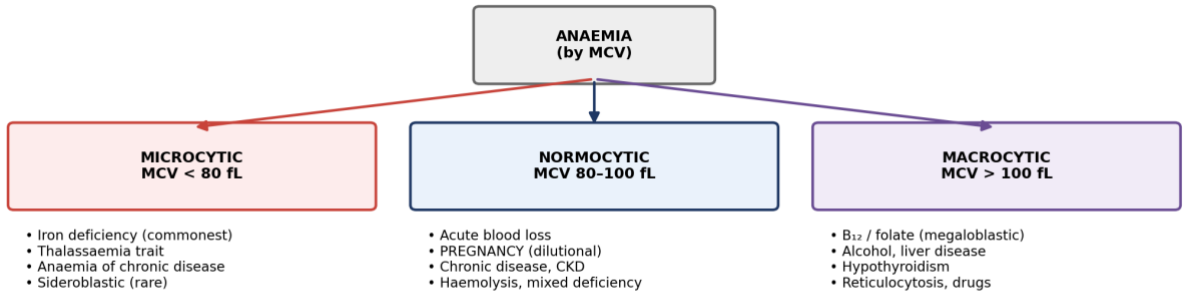


Figure 134.3 — Classification of anaemia by mean cell volume

134.4 White cells

Cell	Normal (× 10^9/L)	Key functions
Neutrophils	2.0–7.5	Phagocytosis, first responders; ↑ in infection, steroids, pregnancy and labour
Lymphocytes	1.5–4.0	B (antibodies via plasma cells), T (CD4 helper, CD8 cytotoxic), NK cells
Monocytes	0.2–0.8	Become tissue macrophages; antigen presentation
Eosinophils	0.04–0.4	Parasites, allergy
Basophils / mast cells	< 0.1	Histamine, heparin; anaphylaxis

134.5 Haemostasis

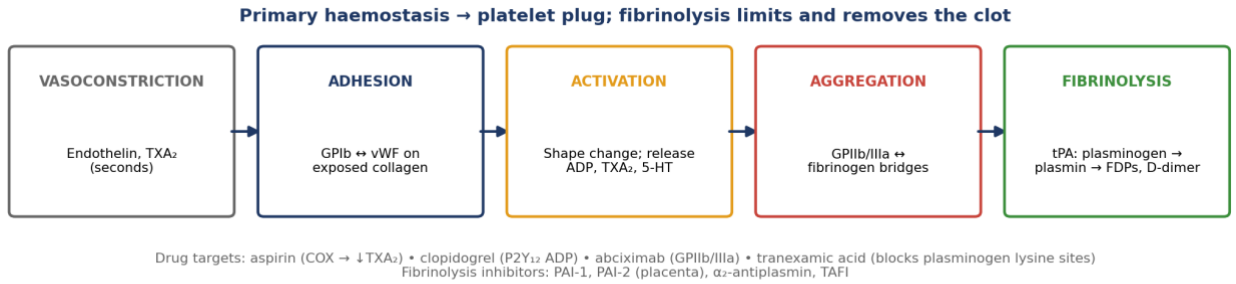


Figure 134.4 — Primary haemostasis and fibrinolysis

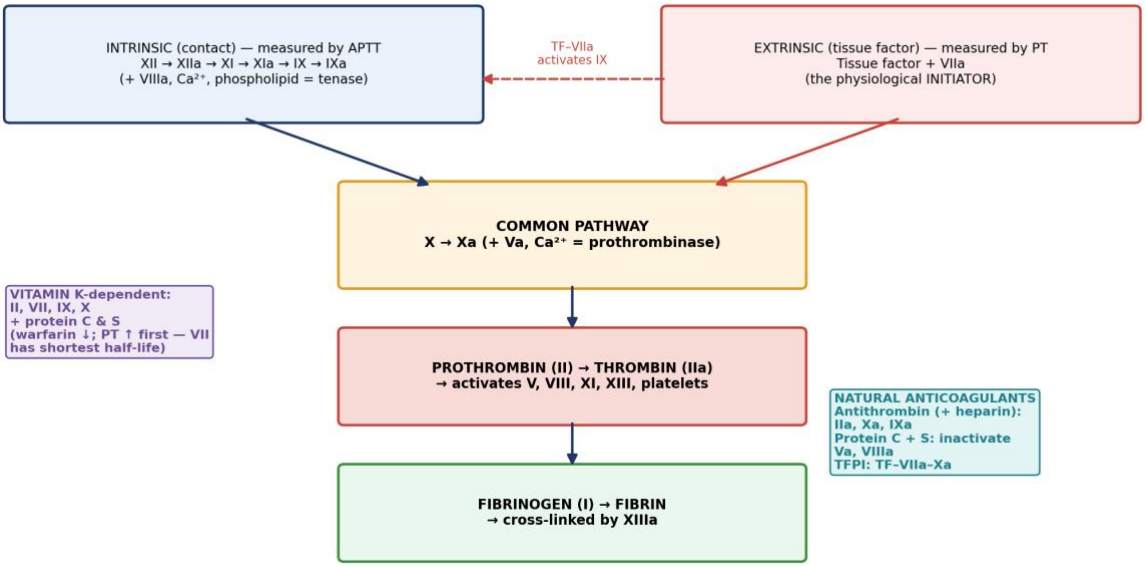


Figure 134.5 — Coagulation cascade (classical model) and its regulation

Cell-based model (physiological): **initiation** on tissue-factor-bearing cells (TF–VIIa generates a little thrombin) → **amplification** on platelets (thrombin activates V, VIII, XI, platelets) → **propagation** (tenase and prothrombinase complexes produce a **thrombin burst**). Factor XII deficiency prolongs the APTT but does **not** cause bleeding.

Test	Measures	Prolonged by
PT / INR	Extrinsic + common (VII, X, V, II, fibrinogen)	Warfarin, vitamin K deficiency, liver disease, DIC
APTT	Intrinsic + common (XII, XI, IX, VIII …)	Unfractionated heparin, haemophilia A/B, vWD (low VIII), lupus anticoagulant (paradoxically thrombotic), DIC
Fibrinogen (Clauss)	Fibrinogen concentration	DIC, dilution (major haemorrhage), abruption, AFE
Thrombin time	Fibrinogen → fibrin	Heparin, low/abnormal fibrinogen
Anti-Xa level	LMWH activity	Used for LMWH monitoring (renal impairment, extremes of weight, pregnancy)
D-dimer	Cross-linked fibrin breakdown	VTE, DIC, surgery, pregnancy (rises normally)

Bleeding disorder	Inheritance	Defect / features
von Willebrand disease	Autosomal (type 1 dominant)	Commonest inherited bleeding disorder; mucosal bleeding, menorrhagia, PPH; ↓ vWF ± VIII
Haemophilia A / B	X-linked recessive	FVIII / FIX deficiency; joint and muscle bleeds; carriers may have low levels
Factor XI deficiency	Autosomal	Variable bleeding; level does not rise in pregnancy

Factor V Leiden	Prothrombin G20210A	AT, PC, PS deficiency	Antiphospholipid
Commonest inherited thrombophilia (APC resistance)	↑ prothrombin levels	AT deficiency = highest VTE risk	Acquired; LA, aCL, anti-β2GPI

134.6 Must-know summary

■ EXAM TIP

- EPO comes from renal **peritubular interstitial cells** in response to hypoxia (HIF); reticulocytes reflect marrow response.
- Iron is absorbed in the **duodenum**; **hepcidin** blocks ferroportin. **Ferritin < 30 µg/L** confirms iron deficiency; ferritin is an acute-phase protein.
- B_{12}: intrinsic factor, terminal ileum, stores 3–5 years; folate: jejunum, stores ≈ 4 months.
- Vitamin K-dependent: **II, VII, IX, X, protein C and S**. PT tests extrinsic (VII); APTT intrinsic (VIII, IX, XI, XII).
- **vWD** is the commonest inherited bleeding disorder; **factor V Leiden** the commonest inherited thrombophilia.

■ MNEMONIC / MEMORY AID

Vitamin K factors — '1972': factors 10, 9, 7, 2 (+ proteins C and S). **'WEPT'** = Warfarin → Extrinsic → PT; **'HIP'** = Heparin → Intrinsic → aPtt.