D.PHARM • SECOND YEAR

Pharmacology

CHAPTER 6

Drugs Acting on Blood and Blood-Forming Organs



ENGLISH CHAPTER NOTES

DIPLOMA IN PHARMACY

HEMATINIC AGENTS: CLASSIFICATION

Hematinic agents improve red-blood-cell production or haemoglobin formation and are used for specific types of anaemia. The cause of anaemia must be identified before treatment.

1. IRON PREPARATIONS

ORAL



- ferrous sulfate
- ferrous fumarate
- ferrous gluconate

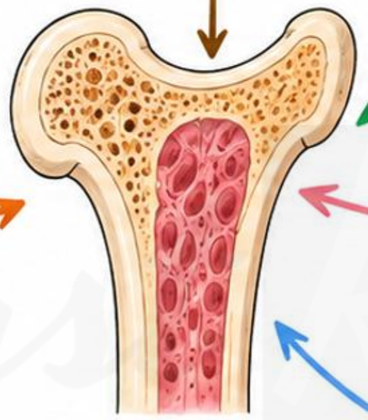
PARENTERAL, mainly IV



- iron sucrose
- ferric carboxymaltose
- iron dextran

Iron (from diet or supplements) → iron → haem component of haemoglobin

Bone marrow



Site of erythropoiesis (RBC production)

Mature red blood cells (RBCs)

2. VITAMIN B_{12} PREPARATIONS

- cyanocobalamin
- hydroxocobalamin

Routes depend on cause: oral therapy or injection.



Vitamin B_{12} + folate → normal DNA synthesis and RBC maturation

3. FOLATE PREPARATION

Folic acid, usually oral.



ESA (from kidney)



Kidney stimulates erythroid precursors in bone marrow

4. ERYTHROPOIESIS-STIMULATING AGENTS, ESAs

- epoetin alfa
- darbepoetin alfa

Usually given SC or IV under specialist monitoring.

ROLE MAP

iron ⟶ haem component of haemoglobin

vitamin B_{12} + folate ⟶ normal DNA synthesis and RBC maturation

ESA ⟶ stimulates erythroid precursors in bone marrow

MEMORY LINE

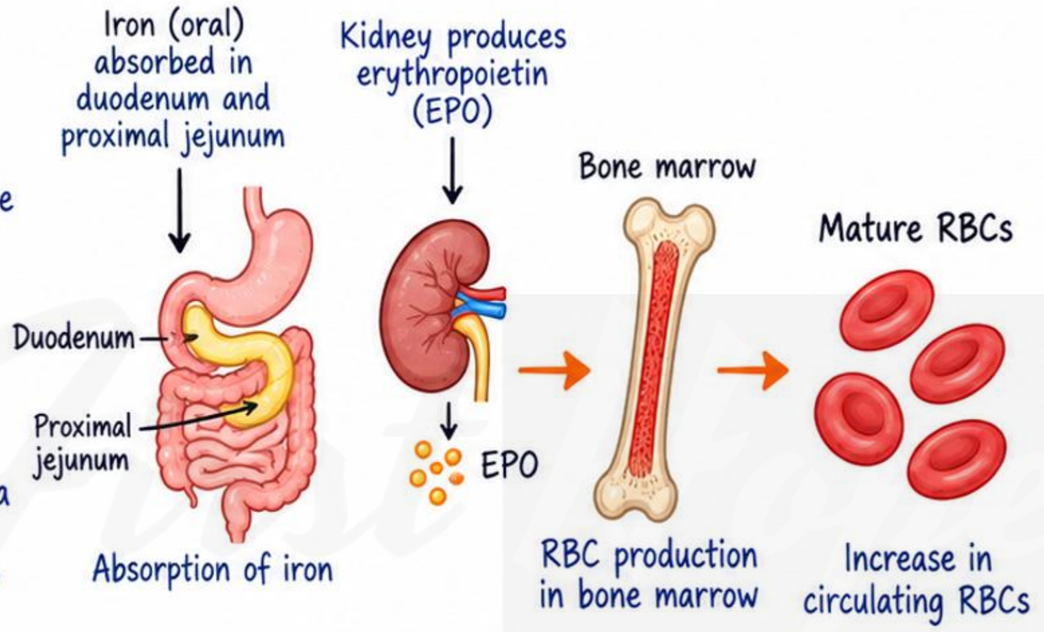
Build haemoglobin with iron, mature cells with B_{12} and folate, and stimulate marrow with ESA.

HEMATINIC ACTIONS, USES AND SAFETY

PHARMACOLOGICAL ACTIONS

- **iron:** supplies iron for haemoglobin synthesis; oral iron is absorbed mainly in the duodenum and proximal jejunum
- **parenteral iron:** replenishes iron when oral therapy is unsuitable, not tolerated or ineffective
- **vitamin B_{12}:** supports DNA synthesis and neurological function; deficiency causes megaloblastic anaemia and may cause neurological symptoms
- **folic acid:** supports purine and pyrimidine synthesis; deficiency causes megaloblastic anaemia
- **ESAs:** stimulate bone marrow to produce RBCs, especially in selected CKD-related anaemia

Erythropoiesis pathway



SAFETY AND CAUTIONS



- **oral iron:** nausea, abdominal discomfort, constipation and dark stools; avoid iron overload such as haemochromatosis



- **IV iron:** infusion reaction or hypersensitivity; give where observation and emergency treatment are available



- **vitamin B_{12}:** use care in Leber hereditary optic neuropathy



- **folic acid** alone can correct anaemia while neurological injury from untreated B_{12} deficiency progresses; check B_{12} when appropriate



- **ESAs:** hypertension and thromboembolic risk; haemoglobin target and dose must be individualized

MAIN USES

- iron-deficiency anaemia and pregnancy-related iron deficiency
- vitamin B_{12}- or folate-deficiency megaloblastic anaemia
- selected anaemia of CKD, chronic disease or chemotherapy

DOSE EXAMPLES, REGIMENS VARY

ferrous sulfate: 200 mg tablet, about 65 mg elemental iron, 1–3 times/day



iron sucrose IV: 100–200 mg per dose according to replacement plan



vitamin B_{12} IM: 1000 micrograms on a loading schedule, then maintenance according to cause



folic acid oral: 1–5 mg/day



epoetin alfa SC or IV: 50–150 IU/kg, commonly 3 times/week, individualized



PRACTICAL RULE

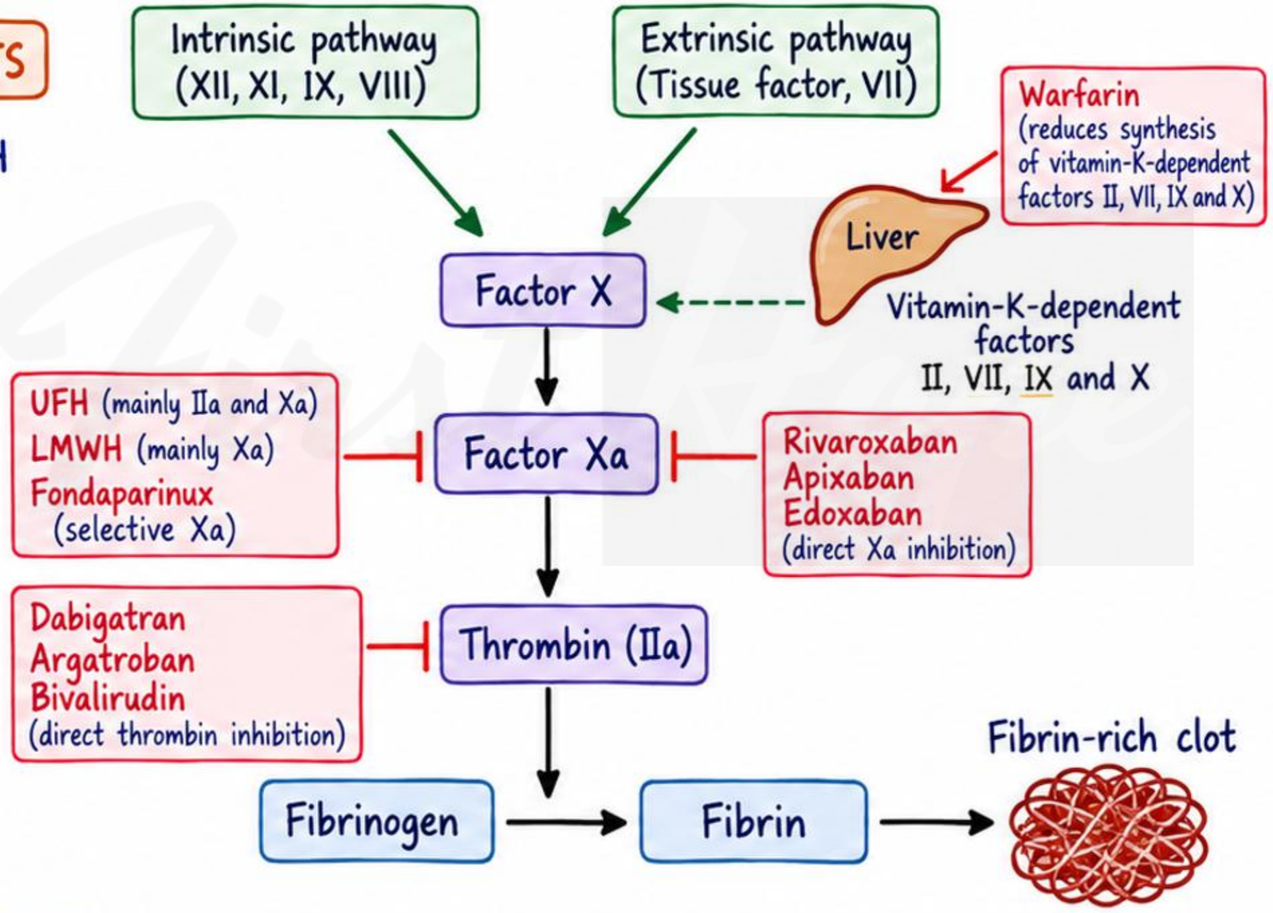
Treat the deficiency or cause; do not give a hematinic merely because haemoglobin is low.

ANTICOAGULANTS: CLASSIFICATION

Definition: Anticoagulants reduce formation or extension of fibrin-rich clots by inhibiting steps in the coagulation cascade. They prevent new clot growth; they do not directly dissolve an existing clot.

A. PARENTERAL ANTICOAGULANTS

1. **UNFRACTIONATED HEPARIN, UFH**
   - Heparin.
2. **LOW-MOLECULAR-WEIGHT HEPARINS, LMWHs**
   - Enoxaparin, dalteparin.
3. **INDIRECT FACTOR Xa INHIBITOR**
   - Fondaparinux.
4. **DIRECT THROMBIN INHIBITORS**
   - Argatroban, bivalirudin.



B. ORAL ANTICOAGULANTS

1. **VITAMIN K ANTAGONISTS**
   - Warfarin, acenocoumarol.
2. **DIRECT ORAL ANTICOAGULANTS, DOACs**
   - direct thrombin inhibitor: dabigatran
   - direct factor Xa inhibitors: rivaroxaban, apixaban, edoxaban

Memory line: Heparins work through antithrombin; DOACs directly block IIa or Xa; warfarin reduces factor synthesis.

ANTICOAGULANT ACTIONS, MONITORING AND SAFETY

UFH / LMWH

- **UFH**: binds antithrombin and rapidly inactivates thrombin, IIa, and factor Xa; short half-life
- **LMWH**: predominantly inhibits factor Xa through antithrombin; response is more predictable than UFH

Antithrombin → Thrombin (IIa) ↓
Antithrombin → Factor Xa ↓

Warfarin

- inhibits vitamin K recycling → reduced synthesis of factors II, VII, IX and X; delayed onset, so INR-guided dosing is essential

Vitamin K recycling ✕ → ↓ Synthesis of factors II, VII, IX and X

Direct thrombin inhibitor

- **DOACs**: dabigatran directly inhibits IIa; rapid onset

Thrombin (IIa) ⊣ Dabigatran

Direct Xa inhibitor

- **DOACs**: rivaroxaban and apixaban directly inhibit Xa; rapid onset

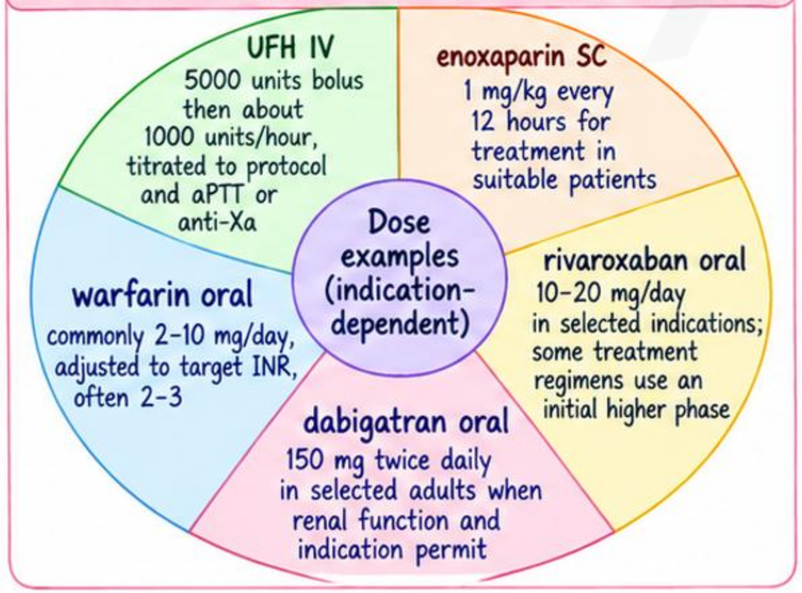
Factor Xa ⊣ Rivaroxaban, Apixaban



PROTECTED BLOOD VESSEL

Less clot formation → maintained blood flow

DOSE EXAMPLES, INDICATION AND RENAL FUNCTION MATTER



MAIN USES

- DVT, pulmonary embolism, stroke prevention in atrial fibrillation, thromboprophylaxis after selected surgery, and selected acute coronary care.
- Mechanical heart valves require a vitamin K antagonist such as warfarin, not a DOAC.

PREGNANCY / MECHANICAL-VALVE DECISION

Pregnancy?	Avoid warfarin
Mechanical heart valve?	Use a vitamin K antagonist such as warfarin, not a DOAC.

MONITORING

- **UFH**: aPTT or anti-Xa, CBC, platelets and bleeding
- **warfarin**: INR, interacting medicines and diet consistency
- **LMWH and DOACs**: renal function, CBC and bleeding; routine INR does not measure their effect

Key tests

- aPTT
- INR
- CBC / platelets
- Renal function
- Clinical signs of bleeding

MAJOR SAFETY POINTS

- all anticoagulants increase bleeding risk; active major bleeding is a contraindication
- **heparin or LMWH**: previous HIT or severe thrombocytopenia is a major caution; stop heparin and assess if HIT is suspected
- **warfarin**: avoid in pregnancy; many drug and food interactions
- **DOACs**: dose or suitability depends on renal function; avoid in mechanical heart valves
- recent intracranial bleeding, major surgery or high-risk lesions require specialist risk-benefit assessment

URGENT WARNING

Black stools, vomiting blood, severe headache, sudden weakness or uncontrolled bleeding needs urgent assessment.

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