HLS

Patho "mid" — Lec. 1

* ↓Red cell mass → ↓oxygen carrying capacity of blood → anemia → hypoxia
  ↳ ↑erythropoietin → compensatory erythroid hyperplasia in BM.
- Stem cell disease → macrocytic anemia.
- Hb conc. decreases with age.

*Reticulocyte count in (high) → hemolytic anemia
(low) → aregenerative anemia.

*Anemia → ↓BP → compensatory mechanisms: tachycardia / tachypnea / ↑red cell 2,3-diphosphoglycerate (binds to Hb → stabilizes the "T" state → oxygen liberation).

* Chronic hemolytic anemia → jaundice (Hb → bilirubin → hyperalbumiemia) / pigmented gallbladder stones (dark in color while cholestrol stones are translucent) / red urine.

*Chronic anemia (Thalassemia & sickle cell anemia) → extramedullary hematopoiesis → splenomegaly, hepatomegaly, growth retardation (due to hypoxia), bone deformities, secondary hemochromatosis (damage to endocrine glands & heart "becomes thick & blue due to the deposition of the iron").

*Anemia of chronic blood loss (the rate of RBC loss exceeds regeneration): appears hypochromic & microcytic, low reticulocytes.
- occurs in gastrointestinal diseases & in excessive menstruation.
- results in iron deficiency

* Anemia of acute blood loss (↓ intravascular volume):
- If loss is > 20% of blood volume → hypovolemic shock & death
- If loss is < 20% → fluid shifting from interstitial to intravascular space → dilutional anemia & worse hypoxia (stays 2-3 days)
→ appears normochromic normocytic with reticulocytosis.
- In internal hemorrhage: iron is restored from extravasated RBCs & used again in erythropoiesis.
- In external & GIT hemorrhage: iron is lost

Anemia of decreased production

* General causes:-

A) Nutritional deficiency : Iron deficiency anemia : IDA :

- Most common . - IDA is a chronic anemia .
- Liver → hepcidin → degradation of ferroportin (is used to transport iron) → inhibits iron absorption .
- High serum iron & inflammation → ↑ hepcidin
- Iron deficiency → low hepcidin
- Thalassemia major or primary hemaochromatosis → very low hepcidin
- RBCs appear: hypochromic, microcytic, poikelocytosis , target cell appearance " ⊙ " , low reticulocytes, thrombocytosis (↓ iron → ↑ megakaryocytes)
- Symptoms : pica (eating abnormal things) / glossitis & stomatitis / spooning of fingernails / restless leg syndrome / hair loss / blue sclera / cognitive impairment .

B) Anemia of chronic inflammation/disease :

↳ inhibits synthesis of erythropoietin .
↳ ↑ IL-6 → ↑ hepcidin

IDA	Anemia of chronic inflammation
hypochromic microcytic	Normal morphology then hypochromic microcytic
↓ reticulocytes	↓ reticulocytes
Serum ferritin ↓	Serum ferritin ↑
Total iron binding capacity "TIBC" ↑	TIBC ↓
Transferrin saturation ↓	Transferrin saturation is Normal to low
Transferrin receptor ↑	Transferrin receptor : Normal
Serum transferrin ↑	Serum transferrin ↓
Bone marrow aspirate ↓ (most accurate, invasive procedure, is stained used Perl's Prussian blue stain)	Bone marrow iron stores ↑

* Megaloblastic anemia: deficiency in vitamin B12 or folate → ↓thymidine → DNA replecation impairment → ↓hematopoietic cells.
- Viable nucleated RBCs take a longer time to mature → megaloblastoid (large in size, immature nucleus)

* Causes of folate deficiency: ↓dietary intake, ↑increased demand, intestinal disease, methotrexate (inhibits dihydrofolate reductase), beans & legume & alcohol & phenytoin "anti-epiliptic"
↳ inhibit absorption of folate.

* Causes of vitamin B12 deficiency: ① dietary deficiency, ② defective absorption → Pernicious anemia "autoimmune gastritis": autoreactive T-lymphocytes → parietal cell injury ↑autoantibodies → ↑damages → ↓intrinsic factor ↳ block binding of vitamin B12 to intrinsic factors ③ Gastrectomy → ↓intrinsic factors ④ Small bowel disease (malabsorption) ⑤ metformin (used for diabetes): inhibits absorption

* Functions of vitamin B12: recycling of tetrahydrofolate, synthesis of myelin sheath & neurotransmitters (dopamine & serotonin), metabolism of homocysteine.
- Degree of neuronal damage does not correlat with degree of anemia.

* Morphology of megaloblastic anemia: macroovalocyte, neutrophil nucleus is highly segmented.
* Symptoms: glossitis, mild jaundice, pancytopenia, in vitamin B12 deficiency: peripheral neuropathy, Neuropsychatic symptoms, degeneration of spinal cord → parasthesia & loss of proprioception (balance).