Department of Anesthesia Techniques
Title of the lecture:- Introduction to Hematology
Dr. Wala Noori Majeed Bairem
Dr. Amasee Falah Al-Shammari
Lecture one\ 2ND course

Hematology

I. Introduction to Hematology:

Hematology: is the branch of medicine concerned with the study, diagnosis, treatment, and prevention of diseases related to blood and blood-forming organs.

Blood is a dynamic tissue composed of:

- Plasma (liquid component)
- Cellular elements
- Red blood cells (RBCs)– carry oxygen via hemoglobin
- White blood cells (WBCs)– part of the immune system
- Platelets (thrombocytes)– critical for hemostasis

Hematopoiesis :The physiologic process of formation of blood cells is called as hematopoiesis.

Hematopoiesis formation sites:

- First quarter of gestation: It takes place in the yolk sac, outside the embryo.
- In the second quarter of gestation: The liver mainly takes part and to a lesser extent the spleen, start of the bone marrow and lymphoid organs to take part in hematopoiesis in mammals.
- At the time of birth nearly all blood cells are produced in the bone marrow (medullary hematopoiesis) and hematopoiesis immediately or gradually stops in the liver and spleen.
- In certain disease conditions, when there is great need for blood cells these two organs retain their ability for manufacturing blood cells (extra medullary hematopoiesis).

Hematologic disorders can arise from:

- Defects in production (e.g., aplastic anemia)

- Abnormal function (e.g., hemophilia)
- Excessive destruction (e.g., hemolytic anemias)
- Malignant transformation (e.g., leukemias, lymphomas)

Bone marrow: is soft, gelatinous tissue that fills the medullary cavities, the centers of bones.

There are two types of bone marrow:

- *Red marrow* composed of hematopoietic tissue (active marrow).
- *Yellow marrow* composed of fat cells (inactive marrow).

Both types of bone marrow are enriched with blood vessels and capillaries. Bone marrow makes more than 200 billion new blood cells every day.

Active sites of hematopoiesis are: pelvis, vertebra, skull, ribs, sternum, and proximal ends of long bones.

Note: All the blood cells circulating in the peripheral blood are derived from the primitive mesenchymal cells called as pluripotent hematopoietic stem cells (PHSCs); the term pluripotent refers to the ability to produce many cell types.

Regulation and control of hemopoiesis:

1. POIETINS:

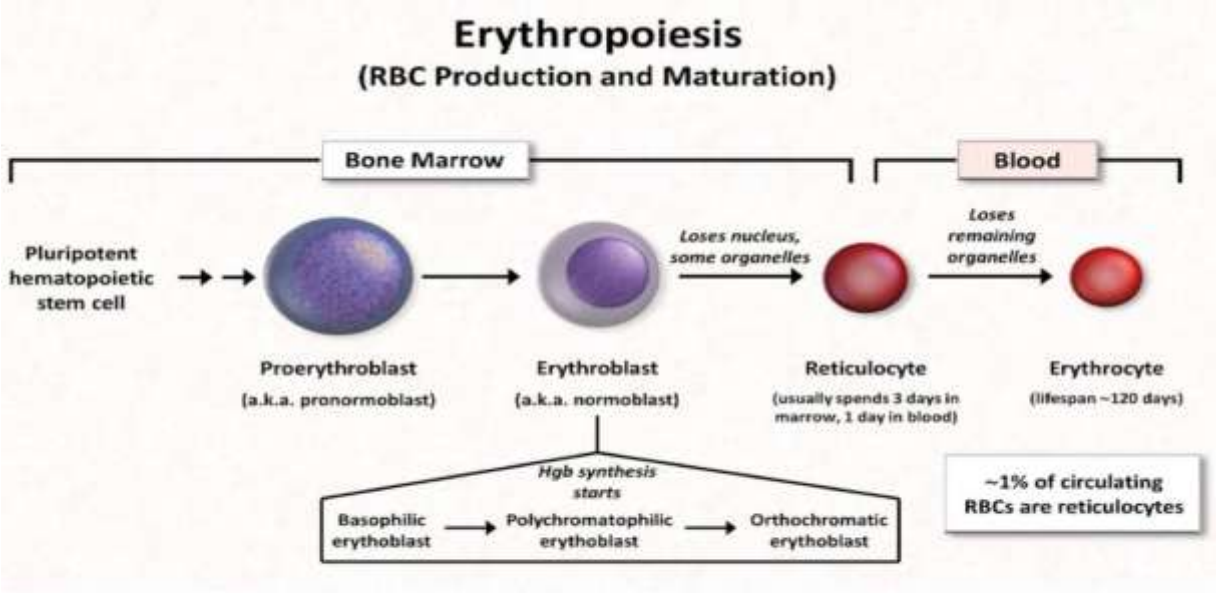
a) Erythropoietin (EPO); It is a hormone-like circulatory glycoprotein produced mainly in the kidney; lesser amount is produced in Kupffer cells in the liver. EPO stimulate erythropoiesis in response to hypoxia.

b) Thrombopoietin (TPO): It is synthesized in the kidney and in the liver; it stimulates platelets production on different levels in the bone marrow (BM).

2. Colony Stimulating Factors (CSFs): They are glycoproteins act directly on haemopoietic sub–populations in the BM, produced from adventitial cells, T lymphocytes, macrophages and stromal cells, e.g., stem cell factor (SCF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF) etc.

3. Interleukins: It is a family of proteins produced by different cells (cytokines) like fibroblasts, macrophages, activated T lymphocytes, endothelial cells... etc. they control some aspects of hematopoiesis & immune response.

Erythropoiesis: the process of red blood cell (RBC) production is a tightly regulated, dynamic system essential for oxygen delivery. It occurs primarily in the bone marrow and is influenced by a variety of hormonal, nutritional, environmental, and pathological factors. Disruptions in any of these can lead to anemia or polycythemia.



Key Regulator: Erythropoietin (EPO):

- **Source:** Primarily peritubular interstitial cells in the kidney (some from liver, especially in fetal life).
- **Stimulus:** Tissue hypoxia (detected via oxygen-sensing prolyl hydroxylase–HIF pathway).
- **Action:**

✓ Binds EPO receptors on erythroid progenitors (CFU-E, proerythroblasts).

✓ Promotes survival, proliferation, and differentiation → increases RBC production in 2–5 days.

Clinical note: In chronic kidney disease (CKD), EPO deficiency is a major cause of anemia of chronic disease.

Hormonal &Cytokine Influences

1. Thyroid hormones: Enhance EPO sensitivity and basal metabolic rate → mild anemia in hypothyroidism.
2. Androgens: Stimulate EPO production → higher hematocrit in males; used therapeutically (e.g., danazol in aplastic anemia).
3. Glucocorticoids: May increase RBC survival (mild erythrocytosis).
4. Inflammatory cytokines (e.g., IL-6, TNF-α):
   - ✓ Suppress erythropoiesis in anemia of chronic inflammation.
   - ✓ Increase hepcidin → iron sequestration in macrophages.

Nutritional Factors:

Adequate substrates are essential for hemoglobin synthesis and RBC maturation:

Nutrient	Role in Erythropoiesis	DeficiencyManifestation
Iron	Corecomponentofheme	Microcytic hypochromic Anemia
Vitamin B12	DNA synthesis (via folate metabolism)	Macrocytic anemia, neurologic symptoms
Folate (B9)	DNA/RNA synthesis in rapidly dividing erythroblasts	Macrocytic anemia (no neurologic signs)
Copper	Cofactor for ceruloplasmin (iron oxidation/transport)	Anemia (often with neutropenia)
Vitamin B6 (Pyridoxine)	Cofactor in heme synthesis	Sideroblastic anemia
Vitamin E	Protects RBC membrane from oxidative damage	Hemolysis (especially in premature infants)

Oxygen Availability & Environmental Factors:

1. High altitude: Chronic hypoxia → ↑ EPO → secondary polycythemia.
2. Smoking: Carbon monoxide binds hemoglobin → functional hypoxia → mild polycythemia.
3. Chronic lung/heart disease: Tissue hypoxia → compensatory erythrocytosis.

Erythrocyte lifespan

- The average erythrocyte lifespan: ~120 days in healthy adults.
- In certain disease situations the survival time of the erythrocytes is shortened, particularly some nutritional deficiencies (iron, vitamin B12, folic acid.

Why Do Erythrocytes Die After ~120 Days?

As RBCs age, they undergo progressive changes:

1. Membrane changes: Loss of membrane phospholipid asymmetry and surface area → decreased deformability.
2. Oxidative damage: Accumulation of reactive oxygen species damages hemoglobin and cytoskeletal proteins.
3. Metabolic exhaustion: Depletion of ATP and NADPH impairs ion pumps and antioxidant defenses.
4. Recognition by macrophages: Aged RBCs display "eat-me" signals like exposed phosphatidylserine and altered surface proteins.

These changes make older RBCs less flexible—critical because they must navigate narrow splenic sinusoids (3 μm) despite being ~7–8 μm in diameter.

Site of Erythrocyte Clearance:

Primary site: Spleen (also liver and bone marrow to a lesser extent).

Mechanism:

1. Macrophages in the red pulp of the spleen phagocytose senescent or damaged RBCs.
2. Hemoglobin is broken down into:

- ✓ Heme → converted to biliverdin → bilirubin (unconjugated).
- ✓ Globin →recycled into amino acids.
- ✓ Iron → bound to transferrin and reused for erythropoiesis or stored as ferritin.

Factors That Shorten or Prolong RBC Lifespan:

Shortened Life span	Prolonged Life span
Hemolytic anemias (sickle cell, G6PD deficiency, hereditary spherocytosis)	**Hypersplenism absent (e.g.,post-splenectomy– RBCs may live longer)**
Mechanical trauma (e.g., prosthetic heart valves)	**Certain storage conditions (not physiologic)**
Infections (e.g., malaria)	**___**
Autoimmune hemolytic anemia	**___**

Clinical Application

1. Anemia evaluation: Differentiating between decreased production vs. increased destruction hinges on understanding RBC turnover.
2. Neonatal jaundice: Fetal RBCs have a shorter lifespan (~70–90 days) → increased bilirubin load.
3. Chronic kidney disease: Reduced EPO → fewer new RBCs → relative excess of older cells.
4. HbA1c interpretation: Reflects average glycemia over ~2–3 months__ the typical RBC lifespan. In conditions with shortened RBC survival (e.g., hemolysis), HbA1c may be falsely low.

II. Major Clinical Manifestations in Hematology:

Hematologic diseases often present through systemic or specific signs related to dysfunction in one or more blood components.

A. Manifestations of Anemia (RBC Disorders)

- ✓ Fatigue, pallor, dyspnea on exertion
- ✓ Tachycardia, palpitations
- ✓ Pica (in iron deficiency)
- ✓ Jaundice and dark urine (in hemolysis)
- ✓ Neurologic symptoms (e.g., paresthesia in B12 deficiency)

B. Manifestations of Leukocyte Disorders

- ✓ Leukopenia/neutropenia: recurrent or severe infections (bacterial/fungal).
- ✓ Leukocytosis: may be reactive (infection, stress) or malignant (leukemia).
- ✓ Lymphadenopathy, splenomegaly, night sweats, weight loss (B symptoms – suggestive of lymphoma).

C. Manifestations of Platelet/Coagulation Disorders:

Bleeding tendency:

- ✓ Petechiae, purpura, ecchymoses (platelet disorders).
- ✓ Hemarthrosis, deep tissue hematomas (coagulation factor deficiencies like hemophilia).
- ✓ Thrombosis: unexplained DVT/PE, stroke in young patients (e.g. antiphospholipid syndrome, Factor V Leiden).

D. Systemic Symptoms

- ✓ Fever, weight loss, fatigue (common in malignancies).
- ✓ Bone pain (e.g., in leukemia or marrow infiltration).

III. Key Investigations in Hematology

A systematic approach to diagnosis combines clinical suspicion with targeted lab testing.

1. Complete Blood Count (CBC) with differential:

- Hemoglobin (Hb), hematocrit (Hct) → assess anemia/polycythemia.

- MCV→ classify anemia (microcytic, normocytic, macrocytic).
- WBC count and differential → detect infection, leukemia, or marrow failure.
- Platelet count → evaluate thrombocytopenia/thrombocytosis.

2. Peripheral Blood Smear- Essential for morphology:

- Schistocytes → microangiopathic hemolytic anemia (e.g., Thrombotic Thrombocytopenic Purpura).
- Target cells → thalassemia, liver disease.
- Blast cells → acute leukemia.
- Howell-Jolly bodies → asplenia or hyposplenism.

3. Reticulocyte Count:

- Reticulocyte: Immature, a nucleate RBCs recently released from the bone marrow.
- The reticulocyte count is a simple but powerful test that reflects the bone marrow's ability to produce and release red blood cells (RBCs) in response to anemia or blood loss.

Measures bone marrow response:

- ↑ in hemolysis or blood loss.
- ↓ in marrow failure or nutritional deficiency

4. Iron Studies, B12, Folate Levels:

- For anemia workup:

- Low ferritin → iron deficiency.
- High MCV + lowB12→pernicious anemia.

5. Coagulation Tests:

Coagulation tests assess the integrity of the hemostatic system, which involves platelets, coagulation factors, blood vessels, and natural anticoagulants/fibrinolytics. These tests help diagnose bleeding disorders, monitor anticoagulant therapy, and evaluate thrombotic risk.

- PT/INR → extrinsic pathway (e.g., warfarin effect, liver disease).
- aPTT → intrinsic pathway (e.g., hemophilia A/B).
- Fibrinogen, D-dimer → DIC, thrombosis

6. Bone Marrow Aspiration &Biopsy:

Bone marrow examination: comprising aspiration and core biopsy is a cornerstone diagnostic procedure in hematology, oncology, and infectious disease. It provides critical information about cellularity, architecture, and cellular morphology of the hematopoietic system. Indicated for unexplained cytopenia's, suspected leukemia, lymphoma infiltration, or myelodysplastic syndromes.

7. Hemoglobin Electrophoresis:

Hemoglobin electrophoresis is a key laboratory test used to identify and quantify different types of hemoglobin (Hb) in the blood. It plays a central role in diagnosing hemoglobinopathies inherited disorders (e.g., sickle cell disease, thalassemia) caused by structural or quantitative abnormalities in globin chains.

8. Flow Cytometry & Cytogenetics:

Flow cytometry and cytogenetics are indispensable tools for diagnosing, classifying, and risk-stratifying hematologic malignancies especially leukemias, lymphomas, and myelodysplastic syndromes.

Why both?

- ✓ Flow cytometry tells us what the cells are (immunophenotype).
- ✓ Cytogenetics tells us what's wrong with their DNA (chromosomal abnormalities).

9. Direct Antiglobulin Test (Coombs Test):

The Direct Antiglobulin Test (DAT), commonly known as the Direct Coombs Test, is a pivotal laboratory assay used to detect antibodies or complement proteins attached to the surface of red blood cells (RBCs) in vivo. It is a cornerstone in diagnosing immune-mediated hemolytic anemias.