Pathophysiology

CHAPTERWISE NOTES

Blood Related Disorders

PHARMA

PHARMACOLOGY

Blood Related Disorders

➤ Alterations in Hematologic Function and Oxygen Transport:

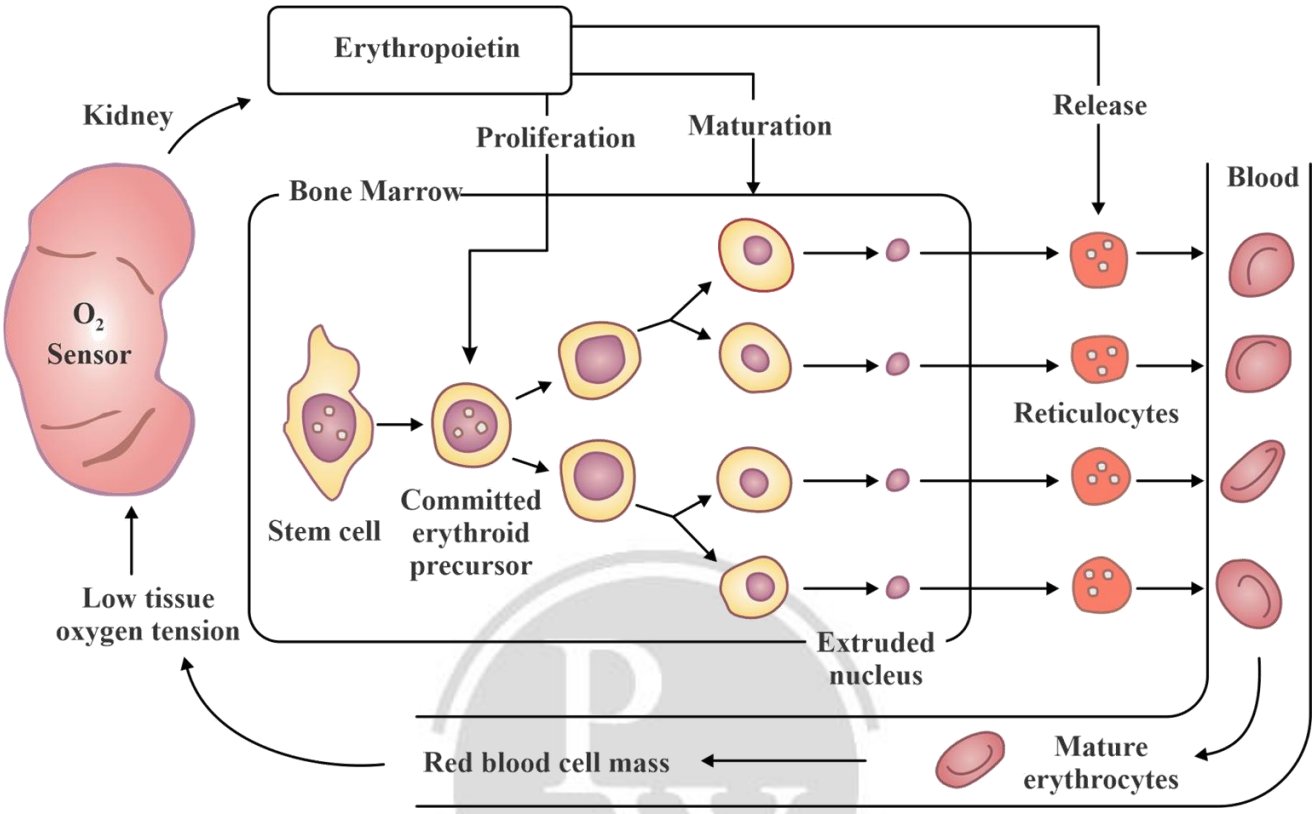
- ✶ Blood is essential for oxygen, nutrients, and ion transport, serving as a buffer between cells and the environment.
- ✶ **Hematopoiesis**, the process of blood cell formation, is regulated by factors like erythropoietin, which responds to hypoxia by promoting RBC production in the bone marrow.
- ✶ The mature RBC's biconcave shape and hemoglobin structure facilitate oxygen transport efficiently.

Hematopoiesis

Aspect	Details
Definition	The process by which blood cells are formed.
Origin	All blood cells derive from a common **stem cell.**
Fetal Hematopoiesis	**Early:** in blood vessels- Mid: in fetal **liver and spleen**- Late: shifts to **bone marrow**
Adult Hematopoiesis	Occurs **lifelong** in **bone marrow**
Regulatory Factors	Growth factors, cytokines, **and erythropoietin (EPO)**

Erythropoietin

Feature	Details
Source	Produced by **kidney** in response to **hypoxia**
Type	**Glycoprotein hormone**
Function	Stimulates **proliferation, maturation, and release** of erythrocytes from stem cells in bone marrow

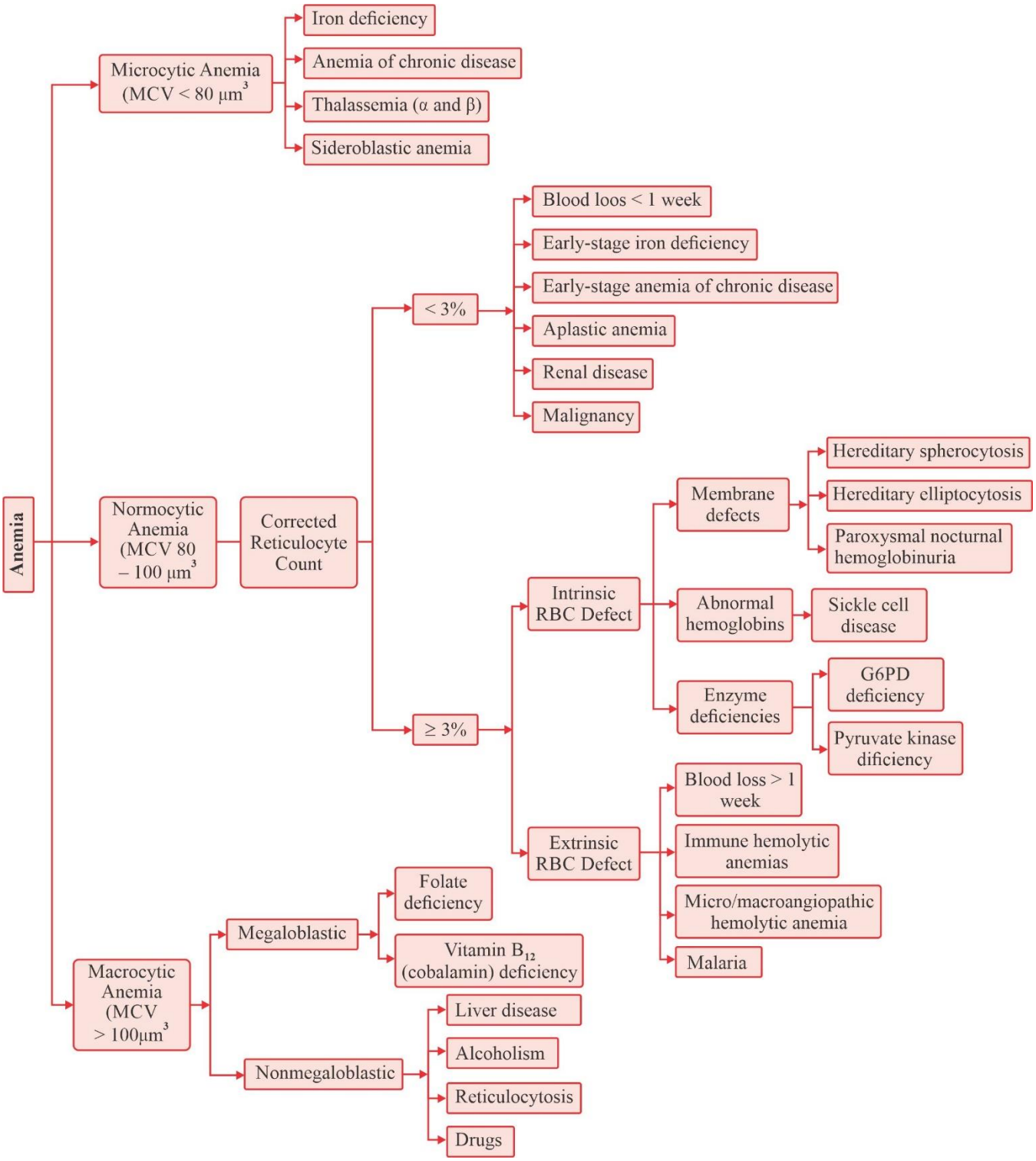


Anemia:

- Anemia is characterized by a reduced number of red blood cells (RBCs), decreased hemoglobin levels, or both, leading to impaired oxygen delivery to tissues.
- It often arises as a symptom of underlying diseases or abnormalities.

Manifestation:

- Fatigue
- Pallor
- Shortness of breath
- Dizziness
- Increased heart rate.
- Specific manifestations depend on the type and severity of anemia.


Anemia
Microcytic Anemia (MCV < 80 μm³)
Iron deficiency
Anemia of chronic disease
Thalassemia (α and β)
Sideroblastic anemia
Normocytic Anemia (MCV 80 – 100 μm³)
Corrected Reticulocyte Count
< 3%
Blood loos < 1 week
Early-stage iron deficiency
Early-stage anemia of chronic disease
Aplastic anemia
Renal disease
Malignancy
≥ 3%
Intrinsic RBC Defect
Membrane defects
Hereditary spherocytosis
Hereditary elliptocytosis
Paroxysmal nocturnal hemoglobinuria
Abnormal hemoglobins
Sickle cell disease
Enzyme deficiencies
G6PD deficiency
Pyruvate kinase dificiency
Extrinsic RBC Defect
Blood loss > 1 week
Immune hemolytic anemias
Micro/macroangiopathic hemolytic anemia
Malaria
Macrocytic Anemia (MCV > 100μm³)
Megaloblastic
Folate deficiency
Vitamin B12 (cobalamin) deficiency
Nonmegaloblastic
Liver disease
Alcoholism
Reticulocytosis
Drugs

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Hematopoiesis

Type of Anemia	Cause	Key Manifestations	Risk Populations	Treatment / Notes
Hemolytic Anemia	Excess RBC destruction due to autoimmune diseases, drugs (e.g., quinine), toxins, infections, cancer	Fatigue, pallor, jaundice, splenomegaly, hemoglobin release into blood	Varies	Treat underlying cause, supportive care
Blood Loss Anemia	Acute trauma, chronic bleeding (ulcers, malignancies)	Shock (acute), iron deficiency (chronic), pallor, fatigue	Trauma patients, GI disease patients	Control bleeding, iron replacement
Iron-Deficiency Anemia	Poor intake, malabsorption, chronic bleeding	Microcytic hypochromic anemia, fatigue, pallor	Vegetarians, menstruating/pregnant women	Iron supplements, correct underlying cause
B_{12} / Folate Deficiency Anemia	Poor diet, malabsorption, pernicious anemia (lack of intrinsic factor)	Macrocytic anemia, neurologic issues (B_{12}), abnormal RBCs, short lifespan	Elderly, alcoholics, GI disorder patients	B_{12}/folate supplementation, treat GI issues
Sickle Cell Anemia	Genetic mutation (HbS) causing sickled RBCs (autosomal recessive)	Fatigue, pain crises, ischemia, organ damage, jaundice, splenomegaly, infection risk	Blacks (1 in 500 births in U.S.)	Avoid stressors, transfusions, immunizations, bone marrow transplant
Thalassemia (α or β)	Genetic defect in α or β hemoglobin chain production	Mild to severe anemia, growth delay, bone deformity, hepatosplenomegaly, iron overload	β: Mediterranean; α: Asians; both: Blacks	Transfusions, iron chelation, bone marrow transplant
Aplastic Anemia	Bone marrow failure (drugs, radiation, toxins, infection, congenital)	Pancytopenia: fatigue, pallor, infections, bleeding, lethargy	Chemo patients, radiation exposure, viral infection	Remove cause, transfusions, bone marrow transplant

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Thalassemia

Aspect	Details
Definition	Genetic disorder with absent or defective hemoglobin α or β chain production
Types	**α-thalassemia**: Defective α-globin chains (common in Asians and Blacks) **β-thalassemia**: Defective β-globin chains (common in Mediterranean and Blacks)
Genetic Forms	**Heterozygous (trait)**: Mild or no symptoms **Homozygous (disease)**: Severe anemia requiring frequent transfusions
Symptoms (Homozygous)	Severe anemia, Growth retardation, Hepatosplenomegaly, Bone deformities, Congestive heart failure, Iron overload
Symptoms (Heterozygous)	Mild or no anemia, symptoms appear under stress or exercise
Pathophysiology	Impaired oxygen transport → Hypoxia ↑ Erythropoiesis → Bone changes Hemolysis → RBC destruction
Iron Overload Causes	Increased GI iron absorption - Frequent transfusions
Complications	Liver and heart injury from iron, Risk of transfusion-transmitted infections (Hepatitis, HIV)
Treatment	Avoid physiological stress, Prompt infection control and immunizations, Frequent transfusions, Bone marrow transplant (curative but risky)

Polycythemia

Type	Cause	Key Manifestations	Risk Groups	Treatment
Relative Polycythemia	Loss of plasma volume (dehydration, stress)	↑ RBC concentration (not actual RBC number), increased blood viscosity	Anyone with fluid loss or dehydration	Rehydration, restore fluid volume
Primary Polycythemia	Excessive bone marrow stem cell proliferation (Polycythemia vera – neoplastic)	↑ RBCs, ↑ blood volume & viscosity, thrombus risk, ischemia, hepatosplenomegaly	Men aged 40–60	Phlebotomy (blood removal), chemotherapy, radiation to suppress marrow
Secondary Polycythemia	Excess erythropoietin production in response to hypoxia	Similar to primary polycythemia; increased RBCs as a compensatory mechanism	High-altitude dwellers, chronic smokers, COPD patients	Treat underlying hypoxia; oxygen therapy if needed

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Plasma Volume Expanders

Feature	Description
Definition	Intravenous (IV) fluids containing large molecules that increase or maintain circulating blood volume (plasma volume) by drawing fluid into vessels via oncotic pressure.
Mechanism	Contain large molecules that cannot easily cross capillaries, creating oncotic pressure that draws water from the interstitial space into the bloodstream.
Primary Use Cases	- Hemorrhage (bleeding) - Shock (e.g., hypovolemic, septic) - Severe burns - During surgery to manage fluid balance
Main Categories	**1. Natural Colloids:** Derived from human blood. **2. Synthetic Colloids:** Artificially manufactured.
Types & Examples	**Natural**: Albumin, Fresh Frozen Plasma (FFP) **Synthetic**: Dextrans, Gelatins, Hydroxyethyl Starches (HES)
Key Considerations & Risks	Fluid Overload (pulmonary edema) Coagulopathy (clotting issues) Renal Impairment (especially with HES) Allergic Reactions Generally, more expensive than crystalloids
Current Guideline Trend	Often used after or in conjunction with crystalloids; HES use is restricted due to safety concerns (renal injury, mortality).