Pathology summary

Anemia of Low Production

General Causes:
Nutritional deficiency, chronic inflammation, and bone marrow failure. This type affects a significant portion of the population in both developed and developing countries.

Iron Deficiency Anemia (IDA):
Most common anemia. Iron stored in ferritin and hemosiderin in bone marrow, liver, and spleen.
Symptoms: Pica, glossitis, spooning of nails, and cognitive impairment.
Lab Findings: Low serum ferritin and iron increased total iron binding capacity, low reticulocyte hemoglobin content, and mean reticulocyte volume.
Causes: Chronic blood loss, dietary issues, decreased absorption, increased demands, and hypotransferritinemia.
RBCs appear hypochromic and microcytic.

Anemia of Chronic Disease:
Associated with chronic infections, cancer, and immune diseases.
High IL-6 leads to increased hepcidin, blocking iron transfer.
Presents with low serum iron but increased bone marrow iron stores and serum ferritin.

Megaloblastic Anemia:
Caused by vitamin B12 or folate deficiency. Impairs DNA replication, leading to ineffective erythropoiesis.
Symptoms: Glossitis, mild jaundice, pancytopenia, and neurological issues (in B12 deficiency).
Causes include decreased intake, increased demands, and malabsorption.
Aplastic Anemia:

Damage to bone marrow stem cells, leading to pancytopenia.
Causes: Idiopathic, drugs, viruses, and inherited defects.
Symptoms: Infections, bleeding, and anemia.
Lab Findings: Normochromic or macrocytic anemia decreased hematopoietic cells in bone marrow.

Myelophthisic Anemia:
Bone marrow infiltration by cancer or diseases like TB.
Presents with immature blood cells in peripheral blood.

Anemia of Renal Disease:
Due to decreased erythropoietin production.
Symptoms include decreased RBC production and abnormal platelet function.

Anemia of Liver Disease:
Multiple factors, including decreased synthesis of clotting factors and transferrin.
Acanthocytes may appear.
Anemia of Hypothyroidism:

Thyroid hormones stimulate erythropoiesis.
Anemia is usually normocytic but can be macrocytic.
Myelodysplastic Syndrome:

Acquired bone marrow disorder, mainly in older adults.
Results in defective blood cell maturation and refractory anemia.
Anemia Due to Blood Loss

Acute Blood Loss:
Causes hypovolemic shock if severe. Erythropoietin stimulates bone marrow after initial fluid shift.
Anemia is normochromic normocytic with reticulocytosis.

Chronic Blood Loss:
Often due to gastrointestinal issues or excessive menstruation.
Leads to iron deficiency, resulting in hypochromic microcytic anemia with low reticulocytes.
Hemolytic Anemia

General:
Increased RBC destruction due to extrinsic factors (infection, antibodies) or intrinsic RBC abnormalities (hereditary membrane defects, enzyme issues).
Symptoms include jaundice and splenomegaly.

Polycythemia Overview

Definition:
Increase in total RBC mass above the normal range.
Includes erythrocytosis (increased number of RBCs).
Types:

1. Relative Polycythemia:
Caused by decreased plasma volume.
Triggers: water deprivation, severe diarrhea, diuretics.

2. Absolute Polycythemia:
True increase in RBC mass due to increased bone marrow production.
Can be primary or secondary.
Primary Polycythemia (Polycythemia Vera):

Autonomous high bone marrow production.

Low erythropoietin levels, splenomegaly present.
Caused by a mutation in the JAK2 tyrosine kinase in bone marrow stem cells.
Leads to excessive proliferation of erythroid, myeloid cells, and megakaryocytes.

Symptoms: Plethora, cyanosis, headache, dizziness, pruritus (aquagenic), peptic ulcers, secondary gout.

Complications: Thrombosis, bleeding, spent phase (fibrotic bone marrow), potential transformation to acute myeloid leukemia.

Lab Findings: High hemoglobin, high hematocrit, leukocytosis, thrombocytosis, JAK2 mutation, hypercellular bone marrow with panmyelosis.

Secondary Polycythemia:
Due to systemic hypoxia leading to high erythropoietin and increased erythropoiesis.
Causes: High altitude, cyanotic heart disease, chronic pulmonary diseases, sleep apnea, renal or liver cancer, smoking, alcohol use, blood doping.
No splenomegaly present.

Symptoms and Effects:
Symptoms: Headache, dizziness, blurred vision, tissue ischemia due to slow circulation and hyperviscosity.
High hemoglobin concentration: >16.5 g/dL in men, >16 g/dL in women.
High hematocrit: >49% in men, >48% in women.
In polycythemia vera:
additional symptoms include aquagenic pruritus, secondary gout, peptic ulcers, spent phase, and blast crisis (transforming PCV to AML)
Additional lab findings JAK2 mutation, low EPO, panmyelosis, leukocytes, and thrombocytosis are common

Hemolytic Anemias Overview

Pathophysiology:
RBC lifespan is less than 120 days.
Hypoxia triggers erythropoietin release, causing erythroid hyperplasia.
Hemoglobin is released from damaged RBCs.
Serum haptoglobin decreases in hemolysis.
Classification:

Extravascular Hemolysis:
Occurs in the spleen.
RBCs with abnormal shapes or antibodies are removed by macrophages.
Symptoms: jaundice, pigmented gallstones, splenomegaly.

Intravascular Hemolysis:
Occurs inside the bloodstream.

Symptoms: hemoglobinemia, hemoglobinuria, hemosiderinuria, iron deficiency.
G6PD Deficiency
Inheritance: X-linked.
Mechanism: Deficiency leads to reduced glutathione, making cells vulnerable to oxidants.
Triggers: Infections, certain drugs, fava beans.
Symptoms: Hemolysis, Heinz bodies, bite cells.
Immune Hemolytic Anemia

Warm Type:
High-affinity auto-antibodies (IgG).
Occurs at body temperature.
RBCs are destroyed in the spleen.
Associated with lupus, drugs, and idiopathic cases.

Cold Type:
Low-affinity auto-antibodies (IgM).
Occurs in cooler areas of the body.
Can cause Raynaud phenomenon.
Linked to infections and B-cell lymphoma.
Hereditary Spherocytosis
Inheritance: Autosomal dominant or recessive.
Mutation: Affects RBC membrane proteins like ankyrin.
Characteristics: Spherocytes are nondeformable, leading to extravascular hemolysis.
Symptoms: Vary from asymptomatic to severe.
Paroxysmal Nocturnal Hemoglobinuria
Cause: Mutation in PIGA gene affecting cell membrane proteins.
Mechanism: Leads to spontaneous lysis of blood cells, especially during sleep.
Complications: Thrombosis is common.
Traumatic Hemolysis
Causes: Physical force or turbulence (e.g., prosthetic valves, physical activities).
Characteristic: Schistocytes in blood from RBC fragmentation.
Each type of hemolytic anemia has distinct causes and symptoms, with varying degrees of severity and treatment approaches.

Memorization Tips
Symptoms: Focus on unique symptoms (e.g., Heinz bodies for G6PD).
Associations: Link with diseases or conditions (e.g., lupus with warm type).
Mnemonic for Order: "Good Immune Systems Help Protect" (G6PD, Immune, Spherocytosis, Hemoglobinuria, Physical).

Hemoglobinopathies Overview
Definition:
- Inherited disorders affecting the production of α or β globin chains.
- Autosomal recessive inheritance.
- Common in the Middle East, Africa, and Southeast Asia.

Thalassemia

α-Thalassemia:

Caused by deletions in α-globin genes on chromosome 16.
Silent carrier (1 or 2 deletions), Hemoglobin H disease (3 deletions), and hydrops fetalis (4 deletions).
Hemoglobin H and Barts have high oxygen affinity.

β-Thalassemia:

Caused by point mutations in β-globin gene on chromosome 11.
β0 (no production) and β+ (reduced production).
Thalassemia minor (mild anemia), intermedia, and major (Cooley anemia).
Symptoms: Hypochromic microcytic anemia, target cells, basophilic stippling, poikilocytosis.
Thalassemia major causes growth retardation, skeletal abnormalities, and requires regular transfusions.
Diagnosed by hemoglobin electrophoresis (increased HgA2 and HgF).

Sickle Cell Anemia

Overview:

Most common familial hemolytic anemia.
Autosomal co-dominance; prevalent in Africa and the Middle East.
Caused by a glutamic acid to valine substitution in β-globin.

Pathogenesis:

Deoxygenated HgS polymerizes, causing sickle-shaped RBCs.
Repeated sickling damages cell membranes, leading to hemolysis.
Sickle cells can cause vaso-occlusive crises and organ infarctions.

Clinical Features:

Chronic hemolytic anemia, starting after 6 months of age.
Crises triggered by infection, dehydration, and acidosis.
Complications: Hand-foot syndrome, acute chest syndrome, stroke, autosplenectomy.
Sickle cell carriers are typically asymptomatic.

Laboratory Findings:

Blood smear shows sickle and target cells.
Hemoglobin electrophoresis confirms diagnosis.

By/ Ghazi Alshammari