Hematologic A&P

Components of Blood

Components:
- blood plasma (46-63% of total blood volume): Composed mainly of water (91%). Also contains nutrients, electrolytes, dissolved gases, organic waste products, and signaling molecules, such as hormones. The components of blood plasma also affect the osmotic pressure (the result of a difference in solute concentration between two fluids)
- formed elements of blood (37-54% of the total blood volume): refers to the cells and cell fragments found suspended within the blood plasma - RBC, WBC, Platlets

PLASMA PROTEINS
- Albumins - group of transport proteins produced by the liver that carry steroid hormones and fatty acids. In addition, they produce the colloid osmotic pressure of blood (which tends to 'pull' water into the circulation from the interstitial fluid). Albumins also act as a blood buffer, helping to keep the pH of blood stable.
- Fibrinogens - family of **blood clotting** proteins produced by the liver.
- Globulins are proteins produced in the liver and by B cell lymphocytes. Alpha and beta globulins transport fat-soluble vitamins, lipids, and iron. Gamma globulins, particularly the immunoglobulins (also known as antibodies) contribute to the immunological response of the body.
- Enzymes are proteins that **catalyze** chemical reactions, increasing the rate at which the reactions take place. Blood plasma contains various enzymes, and transports them to their site of action.

OTHER SOLUTES | Electrolytes, Nutrients, dissolved gases, organic waste
SIGNALING MOLECULES | Hormones

Formation of Blood Cells

Hemopoiesis/hematopoiesis: process by which the formed elements of blood develop.
- embryo within the yolk sac. As the fetal development continues, the blood forming elements move into the liver and spleen since bones have not yet formed. As bones calcify and the medullary cavity of bones form, the blood forming cells move in to form red bone marrow.
- After birth - blood cell formation takes place in red bone marrow, where stem cells undergo cell division (proliferation) and differentiate into cells that ultimately give rise to the formed elements of blood.

Erythropoiesis: process by which **red blood cells (erythrocytes)** are produced.
- In adults, new red blood cells are produced in the bone marrow of the sternum, vertebrae, ribs, base of the skull, and the proximal ends of the long bones.

1. Stem Cell Stage - multipotent stem cells (hemocytoblasts)
2. Myeloid stem cells
3. Proerythroblast: the earliest distinguishable red blood cell precursor
4. Basophilic erythroblasts
5. Polychromatic erythroblasts
6. Orthochromatic erythroblasts (meaning of the same color)
7. Reticulocyte is an immature red blood cell
8. Erythrocytes: mature retic's

RBC

- the most abundant cells in the blood: transport oxygen from the lungs to the body's tissues and return carbon dioxide from the tissues to the lungs, which is critical for cellular metabolism and respiratory gas exchange.
- do not have a nucleus and are absent of most organelles, leaving space for large amounts of hemoglobin (Hb)
- Hemoglobin is a molecule consisting of a protein called globin, made up of four polypeptide chains, and an organic molecule, heme, with an iron at the center
- Carbon dioxide is transported in red blood cells as bicarbonate (HCO_3^-)

RED BLOOD CELL LIFE CYCLE | 120 Days
1. Circulating red blood cells become damaged > pass through the liver, spleen, and red bone marrow
2. phagocytized + broken down. hemoglobin is split into heme and globin for recycling later
3. hemoglobin breaks down further into amino acids
4. heme part of hemoglobin is split into iron (Fe^{3+}) and non-iron parts
5. Fe^{3+} immediately binds to a transporter protein called transferrin & non-iron part of heme converted into biliverdin > further converted bilirubin which is released into the bloodstream and travels to the liver.

Blood Group

Blood is classified according to the presence of different genetically determined *glycoprotein (antigens: agglutinogens)* and glycolipid antigens on the outer surface of red blood
- Transfusion Reactions: agglutination: red blood cells to clump together, forming a large, cross-linked complex. The active plasma proteins cause the red blood cells to rupture and leak hemoglobin into the blood plasma, known as hemolysis, ultimately resulting in kidney damage

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WBC

Granulocytes / granular leukocytes

- large nuclei and specialized enzyme-filled **granules** within their cytoplasm
- Neutrophils are most abundant, accounting for up to 50-70% of white blood cells. Function: Due to their abundance and mobility, neutrophils are often the first cells at the site of an inflammation.
- Eosinophils: 2-4% of white blood cells. Function: histamine
- Basophils: less than 1% of white blood cells. Function: contain heparin, histamine, and serotonin

Agranulocytes / agranular leukocytes

- large nuclei and small cytoplasmic granules not visible under a light microscope.
- Lymphocytes constitute about 20-30% of the white blood cell population.
  - Three types:
    - T lymphocytes (T cells):cell-mediated immunity, attacking virus infected cells, fungi, cancer cells, and some bacteria.
    - B lymphocytes (B cells): antibody-mediated immune response, producing antibodies against antigens to destroy bacteria.
    - and natural killer cells (NK cells): attack tumor cells and virus infected cells.
- Monocytes account for about 2-8 % of white blood cells. Function: Engulf and remove cellular debris and microbes by phagocytosis.

Hemostatis

- vital physiological response that prevents localized hemorrhage, or mass blood loss, after tissue injury
  1. VASCULAR SPASM
     - triggered by neural reflexes and locally acting chemicals released from activated platelets. immediately slowing blood loss
  2. PLATELET PLUG FORMATION
     - A. Platelet adhesion - Platelets stick to the exposed collagen and connective tissue of a damaged blood vessel
     - B. Platelet release reaction - Once the platelets start to clump, they become activated, interact with neighboring platelets, and release chemicals, such as ADP, thromboxane A2, and serotonin
     - C. Platelet aggregation
  3. COAGULATION (BLOOD CLOTTING)
     - A. Instrisic
       - Exposed Collagen, Active Factor XII, [Active Factor X, inactive Factor V] = Prothombinase
     - B. Extrinic
       - Tissue Trauma, Tissue Factor, inactive Factor X, inactive Factor V

CONTROL OF BLOOD CLOTTING

- VITAMIN K
- PROSTACYCLIN - opposes the actions of thromboxane A2, inhibiting platelet adhesion
- ANTICOAGULANTS - antithrombin, which inhibits clotting factors XII, X, and II, heparin, which inhibits thrombin, and activated protein C, which inactivates other major clotting factors and stimulates plasminogen activators
- THROMBOSIS -may form within a blood vessel due to damaged lining endothelial cells caused by trauma, infection, or atherosclerosis, or due to the accumulation of clotting factors in slow flowing blood.
- EMBOLISM - once a thromus breaks away from vessel wall
- ANTITHROMBIN - Inhibit clotting factors XII, X, & II
- HEPARIN - inhibits thrombin

TEST	*IRON DEFICIENCY ANEMIA*	*THALASSEMIA*	*ANEMIA OF CHRONIC DISEASE*	*SIDEROBLASTIC ANEMIA*
Serum ferritin level	Decreased	Increased	Normal to increased	Normal to increased
Red blood cell distribution width	Increased	Normal to increased	Normal	Increased
Serum iron level	Decreased	Normal to increased	Normal to decreased	Normal to increased
Total iron-binding capacity	Increased	Normal	Slightly decreased	Normal
Transferrin saturation	Decreased	Normal to increased	Normal to slightly decreased	Normal to increased

Anemia

- Anemia is a reduction in the oxygen-carrying capacity of blood due to a lack of circulating RBC or a decrease in the quality or quantity of hemoglobin.
- When arterial oxygen levels are low, the kidneys increase production and excretion of erythropoietin to stimulate the bone marrow to increase RBC production.
- Red blood cells are produced within the bone marrow through the process of erythropoiesis
- RBC Distrubition Width (RDW) - Earliest lab markers in developing Micro/Macro-cytic anema

Clinical Manifestations

- weakness, fatigue, pallor, muscle pain, increased respiratory rate, exertional dyspnea, dizziness, and fainting, dizziness/ lightheadedness, tachycardia, irritability, muscle weakness, headache, slowed thought process, decreased attention span, systolic heart murmur, dark urine, splenomegaly, hepatomegaly, icteric sclera, jaundice, low blood pressure (late sign of shock), cool skin, decreased peripheral pulses, circulatory collapse and pain (found in sickle cell anemia), frontal bossing (found in beta-thalassemia)

Process of Erythropoiesis:

- Decreased arterial oxygen levels results in tissue hypoxia. > Tissue hypoxia stimulates the kidneys to increase production and excretion of erythropoietin. > Erythropoietin binds to erythropoietin receptors in the bone marrow, resulting in increased production of red blood cells. > An increase in red blood cells often corrects tissue hypoxia. > Improved tissue hypoxia signals the kidneys to reduce production and excretion of erythropoietin to a normal level.

Causes

- acute or chronic blood loss
- Impaired erythrocyte production
  - inherited genetic defects: thalassemia syndrome
  - nutritional deficiencies: B12 and folate deficiencies, iron deficiencies, renal failure, acute leukemia, or endocrine disorders)
- Increased erythrocyte destruction
  - inherited genetic defects: spherocytosis, enzyme deficiencies like pyruvate kinase deficiency, or hemoglobin abnormalities like thalassemia syndrome or sickle cell disease
  - acquired genetic defects: newborn (Rh disease), transfusion reactions, and autoimmune disorders; infection such as malaria; or cardiac traumatic hemolysis caused by defective cardiac valves

Diagnosis:

- Increased RBC distribution width (RDW) is one of the earliest lab markers in developing microcytic or macrocytic anemia

Normocytic Amemia

- MCV (normal range of 80 to 100 fL).
- **Causes:** acute blood loss, hemolytic amenia, Endocrine disorders, chronic hemoglobinpathies, hereditary spherocytosis, and paroxysmal nocturnal hemoglobinuria
- Color: neither pale nor dark
- **Risk Factors:**
  - Chronic inflammatory conditions - RA, CKD (EPO production), & inflammatory bowel disease
  - Infections
  - Cancer
  - Autoimmune diseases - RA, SLE, Vascultities, Sarcoidosis
  - Congestive HF - can impact erythropoiesis and iron metabolism
  - Age
  - Nutritional Status

Mechanism: Chronic inflammation affects the bone marrow, leading to impaired production of red blood cells despite adequate iron availability

Manifestations: fatigue, shortness of breath, pale skin, dizziness, or cognitive impairment

DX & RX:

- An elevated c-reactive protein (CRP) and elevated erythrocyte sedimentation rate (ESR) indicate inflammation and can support the diagnosis of anemia of chronic disease
- Transfusions for critically ill clients can worsen the outcomes and increase morbidity and mortality
- reticulocyte count is essential > determine bone marrow's response

Hemolytic Anemia

premature destruction of red blood cells, leading to the release of hemoglobin. The symptoms of fatigue, jaundice, and dark-colored urine are classic manifestations of hemolysis > in the bloodstream or within the spleen

- **Risk Factors:**
  - Congenital Inherited
    - G6PD deficiency, Thlassemia, Sickle Cell
  - Acquired
    - Transfusion Reactions, Hemolytic Dz (Newborn), Hemodialysis , Radiation, Bacterial/ Viral Infection (E-Coli) , Presence of prosthetic Heart Valve
  - Autoimmune / Medication (Allergic Reaction)

DX & RX:

- Labs = a low hemoglobin and hematocrit, an elevated reticulocyte count, increased bilirubin, or a positive Coombs test
- folic acid supp., immunosuppressive therapy, chelation therapy, splenectomy, or bone marrow transplantation

Aplastic Anemia

Etiology

Bone marrow damage or failure

Pathophysiology

Impairment or failure of bone marrow that leads to stem cell loss which decreases numbers of erythorocytes, leukocytes and platelets.

Signs and Symptoms

Pallor, weakness, dyspnea, leukopenia, thrombocytopenia

Causes

- chemical/radoation exposure (cancer)
- virus induced (hepatotis, Epstein-Barr)
- Tumor (Multiple Myeloma)
- Medications (PCN, Sulfa, Diuretics)