Unit 11 Study Guide

This guide was developed to assist you in your studies and is not meant to be a complete guide for the unit exam:

1. Describe the composition, elements, and function of the hemopoietic system. (CLO 2)
    a. Describe how blood partitions following centrifugation.
        i. ~58% plasma settles on top
            1. plasma is composed of 92% water, 7% protein, and 1% gases
        ii. <1% white blood cells in the middle
        iii. 42% red blood cells lie at the bottom
    b. Describe the organic and inorganic elements of plasma.
        i. **Inorganic** - Ions
        ii. **Organic**- Amino acids, proteins, glucose, lipids, nitrogen waste, trace elements and vitamins
            1. Proteins:
                a. Albumins - involved in plasma colloid osmotic pressure, also carriers
                b. Globulins - clotting factors, enzymes, antibodies, carriers
                c. Fibrinogen - blood clotting
                d. Transferrin - iron transport
2. Describe the cellular elements of blood, including immature forms and subtypes, and describe the functions and distinguishing characteristics of each. (CLO 2)
    a. List the three types of blood cells and specific functions.
        i. Red blood cells (erythrocytes): transport O2 to tissues and remove CO2 waste.
            1. Erythroblast - has a nucleus
            2. Reticulocyte - stage where nucleus is expelled
            3. Erythrocyte - does NOT have a nucleus
        ii. White blood cells (leukocytes): regulate immune function
            1. Lymphocytes
            2. Eosinophil
            3. Basophil
            4. Monocyte
            5. Neutrophil
        iii. Platelets (thrombocytes): clotting
            1. Megakaryocyte - become platelets, go to the venous sinusoids and then split off into smaller platelets in the circulation
    b. List distinguishing characteristics and functions of white blood cell subtypes
        i. **Lymphocytes:** T cells and B cells specific immune responses

ii. **Monocytes:** Phagocytes, migrate to tissue and develop into macrophages, chronic inflammation
iii. **Neurophils:** Phagocytes, acute inflammation
iv. **Eosinophils:** allergies, produce toxic compounds against invading pathogens
v. **Basophils (mast cells):** release histamine during tissue injury

3. Differentiate blood's cellular elements starting from a pluripotent hematopoietic stem cell and including key cytokines involved in development. (CLO 2)

a. Describe blood cell production or hematopoiesis and its niche.
i. Hematopoiesis is blood cell formation
1. takes place in the bone marrow
2. we need for new blood cells to be produced over and over again to replenish the cells that die off
3. Every type of blood cells come from a single progenitor cell that we call the pluripotent hematopoietic STEM cell

b. Define pluripotent hematopoietic stem cell.
i. All blood cells from a single stem cell, referred to as the pluripotent hematopoietic stem cell
1. commits to specific fates/lineages, giving rise to distinct mature blood cells in circulation

c. Describe the different lineages of committed progenitor cells that give rise to mature cells in circulation.

TABLE 16.1 Cytokines Involved in Hematopoiesis

Name	Sites of Production	Influences Growth or Differentiation of
Erythropoietin (EPO)	Kidney cells primarily	Red blood cells
Thrombopoietin (TPO)	Liver primarily	Megakaryocytes
Colony-stimulating factors, interleukins, stem cell factor	Endothelium and fibroblasts of bone marrow, leukocytes	All types of blood cells; mobilizes hematopoietic stem cells

d. Describe red blood cell maturation in the bone marrow and RBC migration into the vasculature.
i. During Hematopoiesis, cells go through different developmental stages, migrate through bone marrow stroma and enter venous sinusoids as mature cells
1. Red blood cells lose their nuclei during development
ii. Mature cells enter circulation by squeezing between endothelial cells

1. Erythropoietin, colony stimulating factor, and thrombopoietin are cytokines that regulate maturation of RBSs, WBCs and Thrombocytes

iii. Research has shown that there are chemical signals called cytokines that drive these cells to become one fate or another

e. List the major cytokines that regulate red blood cell, white blood cell and thrombocyte maturation.
   i. Erythropoietin->primarily produced in the kidneys-maturations of RBS
      1. Erythropoiesis-red cell production
   ii. Colony Stimulating Factor->produced by macrophages, endothelial cells, and lymphocytes in the marrow-granulocytes
      1. Leukopoiesis-WBC production
   iii. Thrombopoietin->primarily produced in the liver-influences the differentiation of megakaryocytes-production of platelets
      1. Thrombopoiesis-thrombocyte production
f. Describe function and characteristics of red blood cells
   i. Normal RBC's have a biconcave disk shape to accommodate hemoglobin, and a flexible cytoskeleton for traversing capillaries
   ii. Changes in the normal RBC shape or size indicate certain pathologies e.g. spherocytosis, microcytes, or sickled RBC's
      1. Sickle cell disease reduces the ability of hemoglobin to carry oxygen and can lead to anemia, swelling and bleeding in the joints
g. Describe hemoglobin
   i. Made in the bone marrow
   ii. Molecular structure and function:
      1. Four globin chains-centered around a heme group called a porphyrin ring
      2. Oxygen is accommodated in the porphyrin ring-one O2 molecule binds Fe
      3. Most common type is Hb A
      4. Variants of globin chain
         a. Hb A2 is a normal variant
         b. Hb S-Sickle cell-anemia
   iii. Iron (Fe): is a structural base for the porphyrin ring
      1. Without Fe-oxygen not carried in the blood
      2. Hemoglobin synthesis requires dietary iron as well as vitamin B12, vitamin B6, folic acid
      3. 65% of iron in body is in hemoglobin
         a. the rest-myoglobin in skeletal muscles and stored in the cytosol of most cells

4. Ferritin-cytosolic storage protein for Fe requires a signal to release Fe into bloodstream
    a. a small amounts in the plasma-Fe plasma carrier
5. Transferrin-is a plasma protein produced in the liver and functions to transport iron (Fe) through the blood to the liver, sleep and bone marrow

h. Describe bilirubin
    i. Bilibrubin is carried by plasma albumin to the liver, metabolized, and secreted in bile, leaves the body in feces, and a small amount in the urine
    ii. Liver disease prevents bilirubin metabolism and gives a jaundice appearance-> causing the skin and whites of the eyes to take on a yellow cast

i. Identify the causes of anemia based on red blood cell status.
    i. Reduction in oxygen carrying capacity of the blood
        1. Disorder of the erythrocytes- abnormal quantity/ quality
        2. Morphology of the RBC- peripheral (blood) smear
        3. Low hemoglobin- present in all anemia
            a. <14 g/dL (men)
            b. <12 g/dL (women)
        4. Low hematocrit
            a. <41% in adult males
            b. 37% in adult females
        5. Other CBC values

TABLE 16.2 Causes of Anemia

Accelerated Red Blood Cell Loss
Blood loss: cells are normal in size and hemoglobin content but low in number
Hemolytic anemias: cells rupture at an abnormally high rate
Hereditary
Membrane defects (example: hereditary spherocytosis)
Enzyme defects
Abnormal hemoglobin (example: sickle cell anemia)
Acquired
Parasitic infections (example: malaria)
Drugs
Autoimmune reactions
Decreased Red Blood Cell Production
Defective red blood cell or hemoglobin synthesis in the bone marrow
Aplastic anemia: can be caused by certain drugs or radiation
Inadequate dietary intake of essential nutrients
Iron deficiency (iron is required for heme production)
Folic acid deficiency (folic acid is required for DNA synthesis)
Vitamin B_{12} deficiency (B_{12} is required for DNA synthesis): may be due to lack of intrinsic factor for B_{12} absorption
Inadequate production of erythropoietin

4. List the components of a complete blood count. (CLO 2)
    a. Define CBC and its utility.
        i. CBC: provides a panal of values including cell counts. hemoglobin, centration, cell size that get compared to normal standard ranges typically found in males and females.
        ii. abnormal CBC values may indicate the potential for disease including, anemia, coagulation disorder, infection, autoimmune disorder, allergies.
    b. Compare gender differences in hematocrit, hemoglobin content and RBC counts.
        i. Hematocrit (%): Percent of total blood of total blood volume occupied by pack RBCs, provides an indication of the relative thickness of the blood.
            1. Males - 40-54%
            2. Females - 37-47%
        ii. Hemoglobin (g Hb/dL): reflects the oxygen-carrying capacity of RBCs
            1. Males - 14-17
            2. Females - 12-16
        iii. Red Cell Count (cells/uL): a machine counts erythrocytes as they stream through a beam of light
            1. Males - 4.5-6.5 x 10^6
            2. Females - 3.9-5.6 x 10^3
    c. Describe conditions associated with high and low hematocrit.
        i. **<u>High Hematocrit:</u>**
            1. Polycythemia vera - stem cell dysfunction, the bone marrow makes too many red blood cells
            2. Relative polycythemia vera - decreased plasma volume
        ii. **<u>Low Hematocrit:</u>**
            1. Anemia - a condition in which there is not enough healthy red blood cells to carry adequate oxygen to the tissues
            2. Increased plasma volume
    d. Distinguish between total and differential WBC counts.
        i. **<u>Total White Count (cells/uL):</u>** a total white cell count includes all types of leukocytes but does not distinguish between them
        ii. **<u>Differential White Cell Count:</u>** presents estimates of the relative proportions of the five types of leukocytes in a thin blood smear stained with biological dyes
    e. Describe conditions associated with high and low WBC counts.
        i. **<u>Leukocytosis</u>** - High WBC total count: pathogenic microorganism, autoimmune
            1. High differential WBC count - diagnostic value
        ii. **<u>Leukopenia</u>** - Low WBC count: cancer, chemotherapy, or malnutrition
    f. Describe conditions associated with high neutrophil and high eosinophil counts.

i. High neutrophil counts are associated with acute infection
ii. High eosinophil net counts can be sign of allergy

5. Apply knowledge of the hemopoietic system physiology to discuss the pathogenesis and clinical manifestations of blood disorders. (CLO 2 & 5)

a. Define hemostasis and the major steps behind hemostasis.
   i. Hemostasis is the physiological process that stops bleeding at the site of an injury, while maintaining blood flow in the circulation
   ii. The three major steps of hemostasis include:
      1. Vasoconstriction
      2. Platelet plug formation
      3. Coagulation

b. Describe the formation of a platelet plug and the paracrine molecules involved in platelet activation
   i. Vasoconstriction and Platelet Plug Formation
      1. Platelets adheres to exposed collagen in damaged vessels via integrins
      2. Activated platelets release the paracrine molecules to reinforce vasoconstriction and attract more platelets
         a. Serotonin
         b. Platelet-activating factor (PAF)
         c. Adenosine Diphosphate (ADP)
         d. Thromboxane A2 (membrane phospholipid conversion)
      3. Platelet aggregation is restricted to the area of damage
         a. Prostacyclin and nitric oxide made by intact endothelium-inhibits platelet adhesion and aggregation

c. Define the coagulation cascade and list the two pathways involved in coagulation
   i. Two coagulation cascade pathways involve the sequential activation of plasma proteins and convert a plug into a clot
      1. The intrinsic pathways requires contact between exposed collagen, platelets and clotting factor XII
      2. The extrinsic pathway relies on Thromboplastin (Tissue Factor III) released from injured vascular cells and clotting factor VII

d. Link thrombin activation to the polymerization of fibrin during clot formation.
   i. The two pathways converge in the activation of Thrombin and subsequent formation of fibrin polymers that make up the clot
      1. Ca2+ -> important in the conversion of an inactive precursors to an active enzyme

e. Define fibrinolysis and link plasmin activation during fibrinolysis.

i. Coagulation relies on both platelets and specific clotting factors (enzymes) synthesized in the liver and calcium
ii. Fibrin fibers weave through the platelet plug and trap red blood cells in a msuh
iii. Activated XIII converts fibrin into a cross-linked polymer that stabilize the clot
    1. Plasminogen is part of the clot
iv. Clot breakdown (fibrinolysis) is mediated by the enzyme plasmin during vessel wall repair
    1. Tissue plasminogen activator (tPA) activates plasminogen

f. List endogenous anticoagulants and endogenous fibrinolytic factors.
    i. Endogenous Anticoagulants
        1. Heparin-block factors 9-12
        2. Antithrombin III-block factors 9-12
        3. Protein C-block factors 5-8
        4. Prostacyclin-inhibit platelet aggregation
    ii. Endogenous Fibrinolysis Factors
        1. Plasminogen (Plasmin)
        2. Tissue plasminogen activator (tPA)

g. Describe the etiology, pathophysiology, risk factors, complications and treatments of deep vein thrombosis.
    i. Etiology:
        1. Post op, undergoing surgery, patients who are immoble, chronic illness, and bed bound
    ii. Pathophysiology:
        1. Endothelial injury - collagen is exposed to blood and triggers thrombosis
        2. Alterations to blood flow - venous stasis (risk factors)
        3. Hypercoagulation - disruption of antithrombotic and prothrombotic factors
    iii. Risk Factors:
        1. Prolonged bed rest, marked immobility, dehydration, malignancy, history DVT, varicose veins, trama
    iv. complications:
        1. Pulmonary embolism (life threatening)
            a. When a thrombus dislodges it becomes an embolism
            b. Embolism travels to the heart via the inferior vena cava → heart will then pump the embolus to the pulmonary circulation, the embolus can lodge into the pulmonary arteries
        2. Side effects of the medications for DVT

a. can cause acute GI bleeding because the medications are anticoagulants

v. Treatments:

1. Blood thinners, monitored physical activity, DVT prevention exercises

h. Describe the etiology, pathophysiology, risk factors, complications and treatments of hemophilia.

i. Etiology:

1. impaired coagulation cascade, insufficient concentration or decreased activity of any coagulation factor, more common in men, women are carriers

ii. Pathophysiology:

1. Hemophilia A (classic hemophilia) - factor VIII sex-linked recessive trait, male>female

a. 80% of all cases of hemophilia involves factor VIII

2. Hemophilia B (christmas disease) - factor IX sex-linked recessive trait, male>femal

a. affects about 15% of all people with hemophilia, involves factor IX

3. Hemophilia C (Rosenthal syndrome) - autosomal inherited, affect males and females equally and factor XI deficiency

iii. Risk Factors:

1. Inherited deficiencies (factor VIII)

2. Acquired - liver failure, vitamin K deficiency, autoimmunity against a clotting factor, disseminated intravascular coagulation (consumes coagulation factors)

iv. Complications:

1. Bleeding into the brain, which can cause a stroke or increased intracranial pressure

v. Clinical Manifestations:

1. Slow, persistent bleeding from circumcision, immunizations, and other minor cuts, scratches

2. Excessive bruising

3. Persistent hemorrhage (hours to days after injury) following a minor injury
4. Severe hemorrhaging from the gums after dental extraction
5. Bleeding after brushing teeth
6. Severe nosebleeds
7. Gastric hemorrhage
8. Recurrent bleeding into subcutaneous tissue and muscles and around peripheral nerves and joints

vi. Treatments:

1. no cure or prenatal treatment
2. primary goals during bleeding episodes
    a. stop the bleeding as quickly as possible
    b. infuse missing factors until the bleeding stops or takes prophylactically
    c. may be recommended prior to PT or OT