NR507 Edapts

Week 1

EDapt Module Questions

- **Hives (Urticaria)** - Type 1 Allergic Reaction – dermal/skin manifestation.
- **Allergic Contact Dermatitis** – Type 4 Allergic Reaction - an example of a Type IV hypersensitivity reaction mediated by T-cells. When the individual comes in contact with the antigen (e.g. poison ivy), an antigen complex is formed. On subsequent exposure to the antigen, sensitized T-cells activate the inflammatory process that causes the allergic contact dermatitis to appear.
- Type 2 (Cytotoxic/tissue-specific) hypersensitivity reactions are mediated by: IgG or IgM.
- Which of the following are considered the "first responders" of the innate immune system? **Neutrophils** appear first in any immune response.
- **Anaphylaxis** is a Type 1 Allergic Reaction - Type 1 hypersensitivity reactions are mediated by IgE and mast cells. An individual who is highly sensitized to the antigen may experience anaphylaxis.
- Damage occurs with ABO incompatibility because: Complement damages RBC membrane causing cell lysis. Damage from ABO incompatibility occurs because of the effects of complement on the RBC membrane that results in RBC lysis.
- The diagnosis for an individual who presents to the office with sudden swollen lips and eyes, shortness of breath and throat tightness after a bee sting is: anaphylaxis. The symptoms are consistent with the life-threating condition, anaphylaxis after being exposed. to a bee sting.
- Which of the following assessment findings would be expected in a patient who presents with urticaria? Eosinophilia. Eosinophils are present in the allergic reaction.
- Type IV cytotoxic hypersensitivity reactions are mediated by: T-cells.
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Types of Hypersensitivity Reactions

Type	❖ Mechanism	❖ Example	❖ Pathology
I.	❖ IgE action on mast cells	❖ Hay fever	❖ Mast cell degranulation results in an inflammatory response
II.	❖ Tissue-specific destruction or impairment because of: ❖ Antibody binding followed by lysis via complement ❖ Antibody binding followed by macrophage phagocytosis ❖ Antibody binding followed by neutrophil destruction ❖ Antibody-dependent cell (NK)-mediated cytotoxicity, or ❖ Antireceptor antibodies	❖ 1-ABO incompatibility ❖ 5-Graves' disease	❖ 1-Complement damages RBC membrane and cells lyse ❖ 5-Autoantibodies specific for thyroid tissue impair receptor for TSH
III.	❖ Antigen-Antibody complex deposited in tissues	❖ Raynaud's phenomenon	❖ Complex deposited in small peripheral vessels in cool temperatures leading to vasoconstriction and

			blocked circulation
IV.	❖ Cytotoxic T cell-mediated	❖ Contact dermatitis (e.g., poison ivy)	❖ T cells attack tissue directly (no antibody)

Edapt Slides

Type I: Allergic Reaction

On initial encounter with an allergen, the individual will first produce IgE antibodies. Afte r the allergen is cleared, the remaining IgE molecules will be bound by mast cells, baso phils, and eosinophils that contain receptors for the IgE molecules. This process is refer red to as sensitization. On subsequent exposure to the allergen, the IgE molecules locat ed on the sensitized cells induces their immediate degranulation. This causes the releas e of inflammatory mediators such as histamine, leukotrienes, and prostaglandins that re sults in vasodilation, bronchial smooth muscle contraction, and mucus production. Type I hypersensitivity reactions can be local or systemic. Systemic reactions can result in an aphylaxis, a potentially life
threatening condition. Allergic asthma is an example of a Type I hypersensitivity reactio n. On exposure to certain allergens (typically inhaled), individuals with allergic asthma e xperience inflammation of the airways, characterized by tissue swelling and excessive mucus production. This narrowing of the airways makes it difficult to breathe.

Type II Hypersensitivity Reaction

A Type II hypersensitivity reaction is tissue-specific and usually occurs as a result of haptens that cause an IgG antibody or IgM antibody mediated response. The antibodies are specifically directed to the antigen located on the cell membrane. A hapten is a small molecule that can cause an immune response when it attaches to a protein.

Macrophages are the primary effector cells of Type II responses. Typical examples of

Type II reactions are drug allergies, as well as allergies against infectious agents. The Type II response begins with the antibody binding to the antigen and may cause the following.

- The cell to be destroyed by the antibody
- Cell destruction through phagocytosis by macrophages
- Damage to the cell by neutrophils triggering phagocytosis
- Natural killer cells to release toxic substances that destroy the target cell
- Malfunction of the cell without destruction

Examples of type II reactions include drug allergies, hemolytic anemia, blood transfusion mismatch with resulting transfusion reaction and Rh hemolytic disease.

Type III Immune-Complex Reaction

The Type III hypersensitivity reaction is also an antigen-antibody response. The major difference between Type II and Type III responses is that in a Type II response, the antibody binds to the antigen on the cell surface, but in Type III responses, the antibody binds to the antigen in the blood or body fluids and then circulates to the tissue. Type III reactions are not organ specific and use neutrophils as the primary effector cell. In type III hypersensitivity reactions immune-complex deposition (ICD) causes autoimmune diseases, which is often a complication. As the disease progresses a more accumulation of immune-complexes occurs, and when the body becomes overloaded the complexes are deposited in the tissues and cause inflammation as the mononuclear phagocytes, erythrocytes, and complement system fail to remove immune complexes from the blood. One of the classic Type III reactions is serum sickness.

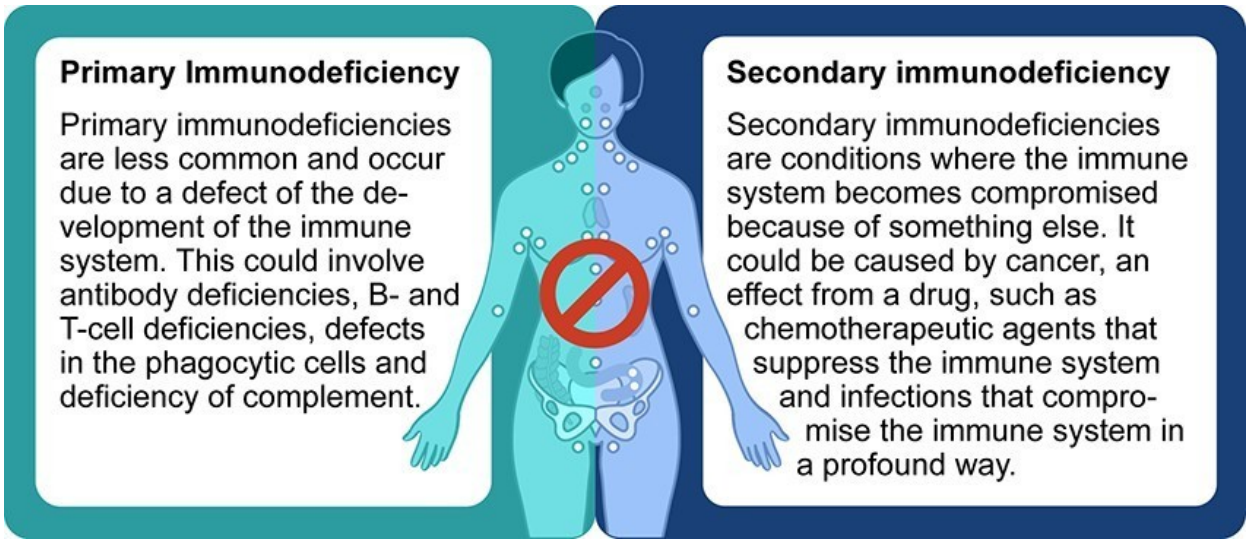
Type IV Cell-Mediated, Delayed Reaction

The type IV hypersensitivity reactions are known as cell-mediated responses and use lymphocytes and macrophages as primary mediators. Unlike the first three types of responses, which are humoral immune functions, a Type IV response is mediated by T-lymphocytes and does not use antibodies. A typical reaction from a Type IV cell-mediated response would be a localized contact dermatitis. When the individual comes in contact with the antigen, T-cells are activated and move to the area of the antigen.

The antigen is taken up, processed, and presented to macrophages, leading to epidermal reactions characterized by erythema, cellular infiltration and vesicles.

Immunodeficiency

- An example of a primary immunodeficiency is: Chronic granulomatous disease (CGD) is an example of a primary immunodeficiency
- Systemic Lupus Erythematosus (SLE) is an example of an autoimmune disease.
- Malnutrition is the predominant cause of secondary immune deficiencies worldwide.
- A primary immunodeficiency is the result of a single gene defect. It is not usually inherited; 60% appear within the first two years of life.
- Pneumocystis carinii is an example of a secondary immune disease due the having HIV. HIV has compromised the patient increasing susceptibility to invasion by opportunistic organisms
- Cancer is a type of secondary immunodeficiency.
- A primary immunodeficiency is due to a defect of the development of the immune system.
- Chronic Granulomatous Disease is a primary immunodeficiency that results from severe X-linked or autosomal defects in the respiratory system.



A common secondary immunodeficiency in the U.S. is Human Immunodeficiency Virus (HIV). HIV is an RNA virus that invades the body through any cell in the body by direct contact of an individual's blood or body secretions. The virus has a strong affinity for cells of the immune system, especially the CD4+ T-cells. Once the virus invades, it replicates to cause extensive damage to the immune system. Without a normally functioning immune system, the individual becomes susceptible to opportunistic infections, cancer, neurological diseases, wasting and death.

In summary, patients may become immunocompromised from primary and secondary sources. Primary immunodeficiencies are genetically determined, which means that there is a genetic defect that results in the loss of essential cells of the immune system. Secondary immunodeficiency is caused by something external to the immune system. For example, when an individual takes a chemotherapeutic agent to treat cancer, this can result in immunodeficiency.

- Primary Immunodeficiency
    - Chronic granulomatous Disease of Childhood
    - DiGeorge Syndrome
    - Job Syndrome
    - Common Variable Immunodeficiency
    - Familial Mediterranean fever
- Secondary Immunodeficiency
    - Human Immunodeficiency Virus
    - Pneumocystis Carinii
    - Pneumonia
    - Sinus infection
    - Lung cancer

Autoimmunity

- Psychological stress is one of the factors that can depress a person's normal immune function.
- A rash confined to the checks is common in SLE.
- 90% of patients diagnosed with SLE will have a positive ANA.
- Sjorgren's Syndrome is associated with autoantibodies and auto-reactive T-cells against apoptotic cells
- **Systemic Lupus Erythematosus - Tissue inflammation, vasculitis, rash, tissue inflammation – Immune System Changes - Autoantibodies and auto- active T-cells against DNA and nucleoprotein antigens**
- **Rheumatoid Arthritis - Joint inflammation, stiffness and pain; loss of range of motion - Autoantibodies and auto-reactive T-cells and B-cells against joint-associated antigens**
- **Multiple Sclerosis - Formation of sclerotic plaque in the brain; leads to muscle weakness and ataxia - Autoantibodies and auto-reactive T-cells against brain antigens**
- **Sjogren's Syndrome - Inflammation in salivary and lacrimal glands - Autoantibodies and auto-reactive T-cells against apoptotic cells**
- Autoantibodies and T-cells, and in some cases, B-cells can be involved in autoimmune diseases.
- The presence of a low number of autoantibodies does not automatically indicate the development of a full autoimmune disease.
- Presenting clinical manifestations of an autoimmune disease will depend on the area of the body affected.

Autoimmunity is an alteration in the ability of the body to tolerate its own self-antigens. Under normal functioning, the immune system does not attack the individual's own antigens. Especially with aging and even healthy individuals across the life span, individuals may produce small quantities of antibodies (autoantibodies) against their

own antigens. The presence of a low number of autoantibodies does not automatically indicate the development of a full autoimmune disease. But autoimmune diseases may occur when the immune system overreacts again self-antigens to the extent that tissue damage occurs. The damage is caused by the autoantibodies and T-cells. Autoimmune diseases include: Rheumatoid Arthritis, Systemic Lupus Erythematosus, Multiple Sclerosis, and Sjogren's Syndrome. Presenting clinical manifestations will depend on the area of the body affected. Regardless of the affected body area, autoantibodies and T-cells, and in some cases, B-cells, react in the associated body system to produce the characteristic signs and symptoms.

Week 2

Hematological Disorders

Anemias

Normocytic – same size – MCV 80-99 dL
Normochromic – normal red color

- Which of the following is not a clinical characteristic of anemia? Bradycardia is not characteristic of anemia. Tachycardia is present due to hypoxemia.
- Which of the following normocytic anemias is characterized by hyperchromic RBCs? Hereditary spherocytosis is a normocytic anemia characterized by hyperchromic RBCs.
- Which of the following indices measures the average size of red blood cells? The MCV is the index that measures the average size of RBCs.
- Which of the following is characterized as a microcytic, hypochromic anemia? Iron deficiency anemia is a microcytic, hypochromic anemia.
- Which of the following would normocytic-normochromic indicate? Normocytic-normochromic indicates a cell that is normal in size and normal in hemoglobin level.
- Identification of the type of anemia involves an examination of size of the RBC only. **FALSE** Determining both the size and color of the RBCs is an important step in identifying the type and source of the anemia.

- Which of the following is a type of macrocytic anemia? Vitamin B-12 deficiency is an example of a macrocytic anemia
- Which of the following symptoms reflects decreased tissue oxygenation as an effect of anemia? Weakness, fatigue, dyspnea, pallor
- The most common type of anemia is: Iron deficiency anemia. IDA is the most common type of anemia worldwide.
- Which of the following would indicate that the patient's iron stores are depleted? A low ferritin level indicates that the patient's iron stores are depleted.
- Which of the following anemias can be categorized as microcytic-hypochromic? Iron deficiency anemia, sideroblastic anemia, and thalassemia anemia
- The treatment of iron deficiency anemia includes: Iron supplementation is indicated for the treatment of IDA.
- Which of the following are iron-rich foods? Spinach, lima beans, meat
- A transferrin deficiency will most likely result in: IDA. Transferrin saturation checks how many places on transferrin that can hold iron. Normal values are 20% to 50%. In severe cases of iron-deficiency anemia, this number may fall below 10%.
- When iron stores are depleted, the cell's mitochondria are still able to utilize iron effectively due to compensatory mechanisms. **FALSE.** When iron stores are depleted, the cell's mitochondria are unable to utilize iron effectively.
- Although less common, transferrin deficiencies and mitochondrial defects can lead to iron deficiency anemia. **TRUE**

Macrocytic Anemias

- Folic acid is essential to the body because it: Plays a major role in the maturing of RBCs. Folate (folic acid) is an essential vitamin for RNA and DNA synthesis within the maturing erythrocyte.
- One of the common precipitating factors of folate deficiency is alcohol abuse. **TRUE**
- A non-megaloblastic anemia would be caused by: liver disease. Liver disease causes a non-megaloblastic anemia.

- ❖ Loss of vibratory sense in a patient with Vitamin B-12 deficiency is due to which of the following pathophysiological changes: posterior and lateral column spinal cord changes due to nerve demyelination. The posterior and lateral columns of the spinal cord are affected, causing a loss of position and vibration sense, ataxia, and spasticity.
- ❖ Which of the following lab values is normal or elevated for the patient with folate deficiency? Reticulocyte count is normal or elevated in a patient with folate deficiency.
- ❖ Which lab is normal in the early stages of pernicious anemia? MCHC is normal in patients with pernicious anemia.
- ❖ In a patient with pernicious anemia, which of the following lab values can be normal or low? Folate. Patients with pernicious anemia can have a normal or low folate level.
- ❖ Which of the following will be elevated in a patient with pernicious anemia? MCV is elevated in pernicious anemia.

Normocystic Anemias

- ❖ In hemolytic anemia, the destruction of lysis of RBCs is due to: In hemolytic anemia, there is a premature destruction/lysis of RBCs due to enzymes or toxins produced by the infectious agent, chemical release mediated by own immune system, or because of certain chemicals/drugs.
- ❖ Aplastic anemia can be caused by: Hepatitis is a physical agent known to cause aplastic anemia.
- ❖ Acute blood loss of anemia is usually associated with acute GI bleeding and labor and delivery complications. **TRUE.** Acute blood loss anemia is usually associated with acute GI bleeding, severe trauma, surgical or labor and delivery complication.
- ❖ Which of the following is a cause of hemolytic anemia? Transfusion reaction, drugs, infection
- ❖ The Reticulocyte count is low in aplastic anemia.

- The MCV is normal in hemolytic anemia.
- The reticulocyte count is high in post-hemorrhagic anemia.
- The MCHC will be normal in which of the following anemias? MCHC is normal in all three types of anemia listed.

Lab Value	Aplastic Anemia	Post-Hemorrhagic Anemia	Hemolytic Anemia
MCV	Normal	Normal	Normal
MCHC	Normal	Normal	Normal
Reticulocyte Count	Low	High	High

Hemoglobinopathies

- Which of the following statements are correct regarding thalassemia? Thalassemia may have many possible genetic mutations.

- The patient with sickle cell anemia is at high risk for stroke. **TRUE.** The abnormal RBCs in Sickle cell anemia can occlude cerebral, splenic and glomerular blood vessels and create a high risk for stroke.

- Cells that contain abnormal types of hemoglobin are more susceptible to infection by the parasite that causes malaria. **FALSE.** Cells that contain abnormal types of hemoglobin are more resistant to infection by the parasite that causes malaria.

- There are four genes involved in encoding synthesis of the alpha protein chains for Hb and are located on chromosome number 16. **TRUE**

- The pathophysiology of sickle cell anemia involves a single amino-acid change on the beta-chain. **TRUE**

- Review the list of statements concerning Sickle Cell Anemia and Thalassemia. Identify the appropriate anemia for each.

Sickle Cell Anemia	**Thalassemia**
Involves a single amino acid change on the beta-chain Increased red blood cell (RBC) hemoglobin S concentration, RBC dehydration, acidosis, and hypoxemia Characterized by acute painful episodes	May have many possible genetic mutations Ineffective erythropoiesis Occurs primarily in persons from southeast Asia and China

- Sickle cell anemia and thalassemia are more prevalent in which of the following geographic areas? Africa. Genetic mutations for sickle cell anemia and thalassemia are prevalent in those with African descents.

- Cells that contain abnormal types of hemoglobin are more susceptible to infection by the parasite that causes malaria. **FALSE.** Cells that contain abnormal types of hemoglobin are more resistant to infection by the parasite that causes malaria.

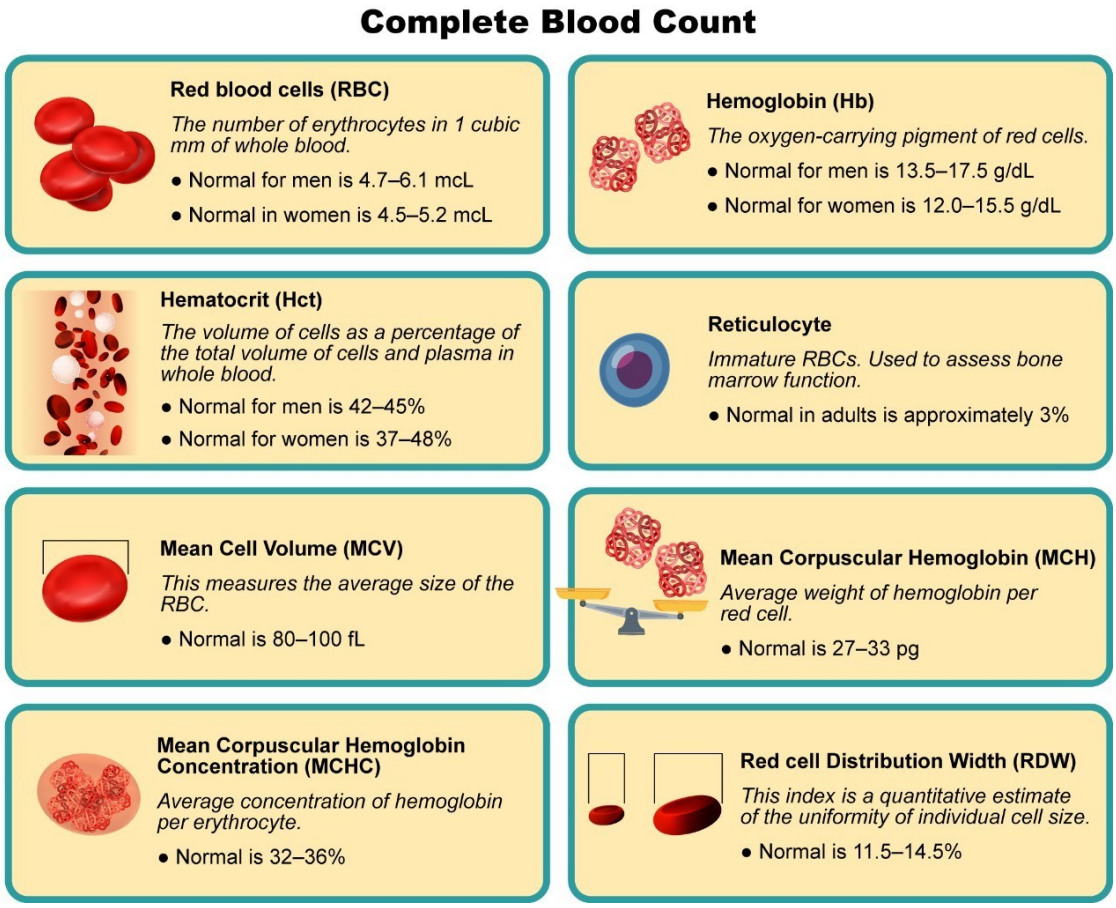
- Thalassemia is similar to sickle cell anemia in that the individual with thalassemia: Inherits an abnormal Hb gene from both parents. The thalassemia(s) are a group of related inherited autosomal recessive genetic disorders. Similar to sickle cell anemia, the affected individual must inherit an abnormal Hb gene from both parents.

- Sickle-cell anemia is an: Sickle-cell anemia is an autosomal recessive genetic disorder due to a defect of globin synthesis or structure.

- The patient with thalassemia is at high risk for stroke. **FALSE.** Stroke risk is high in patients with sickle cell anemia rather than thalassemia.

Anemia is a hematological disorder characterized by a reduction in the total number of circulating red blood cells (RBCs) and/or a decrease in hemoglobin (Hb) amount or function. Anemia stems from the Greek meaning of “without blood” and refers to the condition whereby the capacity of blood to transport oxygen to the tissues is reduced. Anemia can be caused by 1) impaired RBC production, 2) excessive blood loss, 3) increased RBC destruction OR any combination of the three.

In order to recognize and differentiate the type of anemia that is present, it is important to understand the components that make up the complete blood count (CBC). For the purposes of this content, we will discuss only the components that relate to red blood cells and their production.



[(32) Anaemia (anemia) - classification (microcytic, normocytic and macrocytic) and pathophysiology - YouTube]

Anemia Classification

Anemias can be classified into 3 categories based on the average size of the RBCs (MCV):

- Microcytic anemia (MCV<80 fL) describes RBCs that are small.
- Macrocytic anemia (MCV>100 fL) describes RBCs that are large.
- Normocytic anemia (MCV 80-99 fL) describes RBCs that are normal in size.

Microcytic (MCV<80 fL)	Normocytic (MCV 80-99 fL)	Macrocytic (MCV>100 fL)
Iron deficiency	Anemia of inflammation and chronic disease	B12 deficiency (pernicious anemia)