Immune System Notes

I. The immune system consists of innate and acquired immunity.
   A. An animal must defend itself against unwelcome intruders—the many potentially dangerous viruses, bacteria, and other pathogens it encounters in the air, in food, and in water.
   B. It must also deal with abnormal body cells, which, in some cases, may develop into cancer.
   C. **Innate immunity** (non-specific)
      1. Innate defenses are largely nonspecific, responding to a broad range of microbes.
      2. Innate immunity consists of external barriers formed by the skin and mucous membranes, plus a set of internal cellular and chemical defenses that defend against microbes that breach the external barriers.
      3. The internal defenses include macrophages and other phagocytic cells that ingest and destroy pathogens.
   D. **Acquired immunity** (specific)
      1. Acquired immunity develops only after exposure to microbes, abnormal body cells, or other foreign substances.
      2. Acquired defenses are highly specific and can distinguish one inducing agent from another.
      3. This recognition is achieved by white blood cells called **lymphocytes,** which produce two general types of immune responses.
         a. In the **humoral response**, cells derived from B-lymphocytes secrete defensive proteins called antibodies that bind to microbes and target them for elimination.
         b. In the cell-mediated response, cytotoxic lymphocytes directly destroy infected body cells, cancer cells, or foreign tissue.

II. Innate Immunity Provides Broad Defenses against Infection
   A. **Skin** and other first line defenses
      1. Intact skin is a barrier that cannot normally be penetrated by bacteria or viruses, although even minute abrasions may allow their passage.
         a. Skin cells are sloughed constantly, making it more difficult for microbes to colonize.
         b. The pH of oil and sweat is between 3 and 5 which discourages the growth of microbes.
         c. Microbial colonization is also inhibited by the washing action of saliva, tears, and mucous secretions that continually bathe the exposed epithelium.
            (1) Saliva and tears contain the enzyme **lysozyme,** which digests the cell walls of many bacteria, destroying them.
      2. Although the skin provides a physical barrier to pathogens, any areas of the body not protected by skin are susceptible to infection. These areas are covered by **mucus membrane**.
         a. The mucous membranes that line the digestive, respiratory, and genitourinary tracts bar the entry of potentially harmful microbes.
         b. Cells of these mucous membranes produce mucus, a thick fluid that traps microbes and other particles.
      3. Many microbes present in food or water, or those in swallowed mucus, are unable to survive in the highly acidic environment of the stomach.

B. Phagocytic cells devour foreign cells.
   1. One type of white blood cell (WBC) is the **phagocyte**, whose role is to engulf invaders by phagocytosis.
   2. Glycoproteins on cell membranes serve as cell labels so the phagocytes can differentiate between self and nonself.
   3. Cells damaged by invading microbes release chemical signals that attract some phagocytes from the blood.
      a. The phagocytes enter the infected tissue, engulfing and destroying microbes there.
   4. Some phagocytes, the **macrophages**, can stay for long periods in the spleen, lymph nodes, and other **lymphatic** tissues.
      a. Microbes that enter the blood become trapped in the spleen, while microbes in interstitial fluid flow into lymph and are trapped in lymph nodes where they are destroyed by macrophages.

C. A variety of proteins function in innate defense either by attacking microbes directly or by impeding their reproduction.
   1. The **complement system** is a group of about 30 different blood proteins.
      a. Certain molecules on the surface of microbes activates the complement system
         (1) Complement proteins generate a **membrane attack complex (MAC),** which forms a small hole in the membrane of an invading microbe, lysing it.
         (2) Some components of the complement system also attract macrophages which increases phagocytosis.
   2. The **interferons** defend against viral infection.
      a. These proteins are secreted by virus-infected body cells and induce uninfected neighboring cells to produce substances that inhibit viral reproduction.
      b. This limits cell-to-cell spread of viruses, helping to control viral infection.
      c. Because they are nonspecific, interferons produced in response to one virus may confer short-term resistance to unrelated viruses.
      d. One type of interferon activates phagocytes.

D. Damage to tissue by a physical injury or the entry of microbes leads to the release of chemical signals that trigger a localized **inflammatory response.**
   1. One of the chemical signals of the inflammatory response is **histamine,** a chemical stored in special cells in connective tissues.
   2. When injured, these cells release histamine.
      a. Histamine causes vasodilation near the injury, increasing blood flood. This causes the redness and heat associated with inflammation.
      b. Some fluid leaks out of the blood-filled vessels into neighboring tissue, causing swelling.
      c. The increased blood blood flow brings more phagocytes.
   3. Many types of cells can release chemicals when injured to attract phagocytes to the area.

4. Fever results from more widespread infection.
    a. Macrophages release chemicals which set the body's thermostat at a higher temperature, resulting in a fever.
    b. The fever may increase phagocytosis, speed tissue repair, and inhibit bacterial growth.

E. **Natural killer (NK) cells** do not attack microorganisms directly but destroy virus-infected body cells.
    1. They also attack abnormal body cells that could become cancerous.

III. Acquired Immunity Provides Specific Defenses against Infection

A. As microbes attempt to evade the innate immune system, they often encounter lymphocytes, the key cells of acquired immunity.

B. Any foreign molecule that is recognized by and elicits a response from lymphocytes is called an **antigen (ag).**
    1. Most antigens are large molecules such as proteins or polysaccharides.
    2. Most are molecules that protrude from the surface of pathogens or transplanted cells.

C. The immune system relies on two main types of lymphocytes: **B lymphocytes (B cells)** and **T lymphocytes (T cells).**
    1. Produced in the bone marrow, B cells mature in bone marrow while T cells mature in the thymus.
    2. Both types of lymphocytes circulate throughout the blood and lymph and are concentrated in the spleen, lymph nodes, and other lymphatic tissue.
    3. B and T cells recognize antigens by means of antigen-specific receptors embedded in their plasma membranes.
    4. Because each lymphocytes recognizes and responds to a specific antigen, they are said to be specific for that antigen.

D. The immune system can mount either a humoral or a cell-mediated response.
    1. **Humoral immunity** involves B cell activation and clonal selection and results in the production of antibodies that circulate in the blood plasma and lymph.
        a. Circulating antibodies defend mainly against free bacteria, toxins, and viruses in the body fluids.
    2. In **cell-mediated immunity,** activation and clonal selection of cytotoxic T lymphocytes allows these cells to directly destroy certain target cells, including "nonself" cancer and transplant cells.
    3. The humoral and cell-mediated immune responses are linked by cell-signaling interactions, especially via **helper T cells.**

IV. In the humoral response, B cells make antibodies against extracellular pathogens.

A. When antigen first binds to receptors on the surface of a B cell, the cell takes in a few of the foreign molecules

B. The B cell then presents antigen fragments to a helper B cell.

C. Many antigens (primarily proteins), called **T-dependent antigens,** can trigger a humoral immune response by B cells only with the participation of a helper T cell that has encountered the same antigen.

D. Other antigens, such as polysaccharides and proteins with many identical polypeptides, function as **T-independent antigens.**
   1. These large antigens bind simultaneously to a number of membrane antibodies on the B cell surface.
   2. This stimulates the B cell to generate antibody-secreting plasma cells without the help of cytokines.
   3. Any given humoral response stimulates a variety of different B cells, with each giving rise to thousands of clones.
      a. Each clone is estimated to secrete about 2,000 antibody molecules per second over the cell's 4- to 5-day life span.
      b. The antibody is specific to the shape of the antigen which triggered it.
   4. The antibodies can aid the disposal of antigens in several ways.
      a. Antibodies bind to proteins on the surface of a virus, blocking the virus's ability to infect a host cell.
      b. Antibodies enhance macrophage attachment to and phagocytosis of the microbes.
      c. Antibodies can cause **agglutination** of bacteria or viruses, making them easier targets for phagocytes.
      d. In **precipitation,** many small, soluble antigens can be linked together to form larger, insoluble complexes.
      e. Antibodies bound to antigens can trigger the complement system.

V. In the cell-mediated response, cytotoxic T cells destroy targeted cells.
   A. Antigen-activated cytotoxic T lymphocytes kill cancer cells and cells infected by viruses and other intracellular pathogens.
   B. Unlike B cells, T cells cannot recognize free ag, pieces of nonself proteins must be displayed on the cell surface, where they can be recognized by cytotoxic T cells.
      1. When a macrophage devours a microbe, it displays ag on it's membrane.
      2. When a helper T cell recognizes an antigen complex on an antigen-presenting cell, the helper T cell proliferates and differentiates into clones of activated helper T cells and memory helper T cells.Helper T (T_H) cells recognize ag on macrophage, becomes activated and divides rapidly producing clones
      3. The clones secrete interleukin and other chemicals which activate (or helps) other T and B cells.
      4. Cytotoxic T cells destroy infected cells.
         a. The death of the infected cell not only deprives the pathogen of a place to reproduce, but also exposes it to circulating antibodies of the humoral system.
         b. Because tumor cells carry distinctive molecules not found on normal cells, they are identified as foreign by the immune system.
         c. Cytotoxic T cells are also responsible for the rejection of tissue grafts and organ transplants.
            (1) To minimize rejection, attempts are made to match the tissues of the donor and recipient as closely as possible.
            (2) In addition to tissue matching, medication is used to suppress the immune response to the transplant.
      5. Suppressor T (T_S) cells turn off immune response but not well understood
      6. Memory T cells are long-lived and respond faster to second exposure

VI. The immune system has memory

A. The selective proliferation and differentiation of lymphocytes that occur the first time the body is exposed to an antigen is the **primary immune response.**

1. About 10 to 17 days are required from the initial exposure for the maximum immune response.
2. During this period, selected B cells produce antibodies and cytotoxic T cells kill infected cells.
3. While this response is developing, the affected individual may become ill, but symptoms of the illness diminish and disappear as antibodies and active T cells clear the antigen from the body.

B. A second exposure to the same antigen at some later time elicits the **secondary immune response.**

1. This response is faster (only 2 to 7 days), of greater magnitude, and more prolonged.
2. The immune system's ability to generate secondary immune responses is called **immunological memory***,* and is based on long-lived T and B memory cells.
    a. These memory cells proliferate and differentiate rapidly when they later contact the same antigen.

VII. Immunity can be acquired naturally or artificially.

A. Immunity that results by recovering from an infection is called **active immunity** because it depends on the response of the infected person's own immune system.

1. Active immunity can be acquired naturally or artificially, by **immunization,** also known as **vaccination.**
    a. Vaccines include inactivated bacterial toxins, killed microbes, parts of microbes, viable but weakened microbes, and even genes encoding microbial proteins.
    b. These agents can act as antigens, stimulating an immune response and, more important, producing immunological memory.
2. A vaccinated person who encounters the actual pathogen will have the same quick secondary response based on memory cells as a person who has encountered the pathogen previously
3. Some infectious agents are not easily managed by vaccination because they change slightly over time.

B. Antibodies can be transferred from one individual to another, providing **passive immunity.**

1. This occurs naturally when antibodies of a pregnant woman cross the placenta to her fetus.
2. In addition, other antibodies are passed from mother to nursing infant in breast milk.
3. Passive immunity persists as long as these antibodies last, a few weeks to a few months.
4. Passive immunity can be transferred artificially by injecting antibodies from an animal that is already immune to a disease into another animal.

VIII. The immune system's capacity to distinguish self from nonself limits blood transfusion and tissue transplantation.
- A. In addition to attacking pathogens, the immune system will also attack cells from other individuals.
- B. One source of potential problems with blood transfusions is an immune reaction from individuals with incompatible blood types.
  1. Because blood group antigens are polysaccharides, they induce T-independent responses, which elicit no memory cells.
- C. However, another blood group antigen, the **Rh factor,** can cause mother-fetus problems because the antibodies produced for it are able to cross the placenta.
  1. This situation arises when a mother that is Rh-negative (lacks the Rh factor) has a fetus that is Rh-positive, having inherited the factor from the father.
  2. If small amounts of fetal blood cross the placenta late in pregnancy or during delivery, the mother mounts a humoral response against the Rh factor.
  3. The danger occurs in subsequent Rh-positive pregnancies, when the mother's Rh-specific memory B cells produce IgG antibodies that can cross the placenta and destroy the red blood cells of the fetus.
  4. To prevent this, the mother is injected with anti-Rh antibodies after delivering her first Rh-positive baby.
     a. She is, in effect, passively immunized (artificially) to eliminate the Rh antigen before her own immune system responds and generates immunological memory against the Rh factor, endangering her future Rh-positive babies.

IX. Immune disorders can lead to disease.
- A. Allergies are exaggerated responses to certain environmental antigens, called **allergens.**
  1. When B cells release certain antibodies in response to some antigens (*e.g.*, pollen), the antibodies attach to histamine-releasing cells
  2. This triggers the cell to release histamines.
     a. High levels of histamines cause dilation and increased permeability of small blood vessels.
     b. These inflammatory events lead to typical allergy symptoms: sneezing, runny nose, tearing eyes, and smooth muscle contractions that can result in breathing difficulty.
- B. Sometimes, an acute allergic response can result in **anaphylactic shock,** a life-threatening reaction to injected or ingested allergens.
  1. Anaphylactic shock results when there is widespread release of histamine which triggers abrupt dilation of peripheral blood vessels, causing a dramatic drop in blood pressure.
  2. Triggers of anaphylactic shock in susceptible individuals include bee venom, penicillin, or foods such as peanuts or fish.
  3. Epinephrine counteracts this allergic response.
- C. **Autoimmune diseases** are caused when the immune system loses tolerance for self and reacts against certain molecules of the body**.**
  1. In **lupus** (systemic lupus erythematosus) the immune system generates antibodies against molecules such as DNA and the proteins associated wth it.
     a. Symptoms include skin rashes, fever, arthritis, and kidney dysfunction.

D. In **rheumatoid arthritis**, the immune system destroys the cartilage and bone of joints, causing damage and painful inflammation.

E. Insulin-dependent diabetes mellitus, results when the insulin-producing cells of the pancreas are the targets of cytotoxic T cells.

F. **Multiple sclerosis** (MS) is the most common chronic neurological disease in developed countries.
   1. In MS, T cells attack and destroy the myelin sheath of neurons in the central nervous system.

G. **AIDS** is an immunodeficiency disease caused by a virus.
   1. In 1983, a retrovirus, now called **human immunodeficiency virus (HIV),** was identified as the causative agent of AIDS.
   2. HIV recognizes and infects T_H cells.
   3. Once inside the cell, the HIV RNA is reverse-transcribed, and the product DNA is integrated into the host cell's genome where it either remains dormant or begins the production of new virus particles.
   4. Some cells are killed by the effort of producing more viruses while others are destroyed by the immune system itself.