CHAPTER 35 LYMPH TRANSPORT AND IMMUNITY

Chapter Outline

35.1 Lymphatic System

A. Lymphatic System Characteristics
   1. The mammalian **lymphatic system** consists of lymphatic vessels and lymphoid organs.
   2. This system is closely associated with the cardiovascular system and has three main functions.
      a. Lymphatic vessels take up excess tissue fluid and return it to the bloodstream.
      b. Lacteals receive lipoproteins at the intestinal villi and the lymphatic vessels transport these fats to the bloodstream.
      c. Lymphatic system helps defend the body against disease.

B. Lymphatic Vessels
   1. Lymphatic vessels are extensive; most regions have lymphatic capillaries.
   2. The structure of the larger lymphatic vessels resembles veins, including the presence of valves.
   3. The movement of fluid is dependent upon skeletal muscle contraction; when the muscles contract, fluid is squeezed past a valve that closes, preventing it from flowing backwards.
   4. The lymphatic system is a one-way system that begins with **lymphatic capillaries**.
      a. They take up fluid that has diffused out of the blood capillaries and has not been reabsorbed.
      b. If excess tissue fluid is produced or not absorbed, it will accumulates and result in edema.
      c. **Edema** is the swelling caused by buildup of fluid from excessive production or inadequate drainage.
   5. Once tissue fluid enters the lymphatic capillaries, it is called **lymph**.
   6. Lymphatic capillaries join as **lymphatic vessels** that merge before entering one of two ducts.
      a. The **thoracic duct** is larger than the right lymphatic duct.
         1) It serves the lower extremities, abdomen, left arm, left side of the head and neck, and the left thoracic region.
         2) It then delivers lymph to the left subclavian vein of cardiovascular system.
      b. The **right lymphatic duct** is smaller.
         1) It serves the right arm, the right side of the head and neck, and the right thoracic region.
         2) It then delivers lymph to the right subclavian vein of the cardiovascular system.

C. Lymphoid Organs
   1. The lymphoid organs are: lymph nodes, spleen, thymus gland, and the red bone marrow.
   2. **Lymph nodes** are small (about 1–25 mm) ovoid or round masses of lymphoid tissue located along lymphatic vessels.
   3. A lymph node has two regions: the outer cortex and the inner medulla.
   4. The cortex contains nodules where lymphocytes congregate to fight off pathogens.
   5. Macrophages are concentrated in the medulla and cleanse the lymph.
   6. Lymph nodes cluster in certain regions of the body (inguinal nodes in the groin and axillary nodes in the armpits).
   7. The tonsils are located in a ring around the pharynx.
      a. The larger pharyngeal tonsils are the adenoids are on posterior wall above the border of soft palate.
      b. The larger palatine tonsils are on either side of the posterior oral cavity; they are most apt to be the first to be infected.
   8. The **spleen** is located in the upper left abdominal cavity just below the diaphragm.
      a. The spleen is similar to a lymph node but it is much larger, about the size of a fist.
      b. Instead of cleansing the lymph, the spleen cleanses the blood.
      c. A capsule divides the spleen into lobules which contain sinuses filled with blood.
      d. A spleen nodule contains the following:
         1) **red pulp** contains red blood cells, lymphocytes, and macrophages; it helps to purify blood that passes through by removing microorganisms and worn-out or damaged red blood cells.

2) **white pulp** contains mostly lymphocytes.

e. If the spleen ruptures due to injury, it can be removed; its functions are assumed by other organs.
f. However, a person without a spleen is more susceptible to infections and may require antibiotic therapy.

8. The **thymus gland** is located along the trachea behind the sternum in the upper thoracic cavity.
   a. The thymus gland is larger in children than in adults and may disappear completely in old age.
   b. It is divided into lobules by connective tissue; lobules are the site of T lymphocyte maturation.
   c. The interior (medulla) of each lobule consists mostly of epithelial cells which produce thymic hormones (e.g., **thymosin**), that aid maturation of T lymphocytes.
9. The **red bone marrow** is the origin for all blood cells including all leukocytes that function in immunity.
   a. **Stem cells** are continually-producing cells that differentiate into various blood cells.
   b. Most bones of a child have red bone marrow but in adults, red bone marrow is only in skull, sternum, ribs, clavicle, pelvic bones and vertebral column.
   c. Red bone marrow consists of reticular fibers produced by reticular cells packed around thin-walled sinuses.
   d. Differentiated blood cells enter the bloodstream at these bone sinuses.

35.2 Nonspecific Defenses

A. **Immunity** is the ability to defend against infectious agents, foreign cells, and abnormal cancer cells.
   1. Immunity includes both nonspecific and specific defenses.
   2. The four nonspecific defenses include barrier to entry, inflammatory reaction, natural killer cells, and protective proteins.

B. Barriers to Entry
   1. Skin and the mucous membranes lining the respiratory, digestive, and urinary tracts are mechanical barriers.
   2. Oil gland secretions inhibit the growth of bacteria on the skin.
   3. Ciliated cells lining the upper respiratory tract sweep mucous and particles up into the throat to be swallowed.
   4. The stomach has a low pH (1.2–3.0) that inhibits the growth of many bacteria.
   5. The normal harmless bacteria that reside in the intestine or vagina prevent pathogens from colonizing.

C. Inflammatory Reaction
   1. If tissue is damaged, a series of events occurs known as the **inflammatory reaction**.
   2. The inflamed area has four symptoms: redness, pain, swelling, and heat.
   3. **Mast cells** occur in tissues and resemble basophils.
   4. When tissue damage occurs, tissue cells and mast cells release chemical mediators, such as histamine and kinins.
      a. Kinins and histamine cause vasodilation and increased permeability of capillaries.
      b. Enlarged capillaries produce redness and a local increase in temperature.
      c. The swollen area and the kinins stimulate free nerve endings, causing pain.
   5. Neutrophils and monocytes migrate by amoeboid movement to the site of the injury; they escape from the blood by squeezing through the capillary wall.
   6. When monocytes enter tissues, they differentiate into **macrophages** that ingest huge amounts of pathogens.
   7. Connective and lymphoid tissues have resident macrophages that devour old blood cells and debris.
   8. Macrophages trigger an explosive increase in leukocytes by releasing colony-stimulating factors; this diffuses into blood and is transported to red bone marrow to stimulate the production of WBCs.
   9. Pus is the accumulation of dead neutrophils along with tissue, cells, bacteria and living WBCs.
   10. Aspirin, ibuprofen, and cortisone are anti-inflammatory agents that counter the chemical mediators of inflammation.

D. Natural Killer Cells
   1. Natural killer cells kill virus-infected cells and tumor cells by cell-to-cell contact; they lack any specificity or memory.
   2. The **complement system**, simply called complement, is a number of plasma proteins designated by the letter C and a subscript.
      a. One activated complement protein activates another protein in set series of domino reactions.
      b. Therefore a limited amount of protein can activate many other proteins.

c. It "complements" certain immune responses, which accounts for its name.
d. It amplifies an inflammatory reaction by attracting phagocytic cells to the site of infection.
e. Some complement binds to antibodies already on the surface of pathogens, thereby increasing the probability that pathogens will be phagocytized by a neutrophil or macrophage.
f. Some complement proteins form a **membrane attack complex** that produces holes in bacterial cell walls and plasma membranes; fluids and salts then enter to the point where the cell bursts.

3. **Interferon** is a protein produced by virus-infected animal cells.
   a. Interferon binds to the receptors of noninfected cells, producing substances interfering with viral replication.
   b. Interferon is specific to a species; therefore only human interferon can be used in humans.

35.3 Specific Defenses

A. If nonspecific defenses fail to prevent an infection, specific defenses activate against a specific antigen.
1. **Antigens** are foreign substances, protein or polysaccharide, that stimulate immune system to react.
2. Pathogens have antigens but antigens can also be components of foreign or cancer cells.
3. We do not ordinarily become immune to our own cells; the immune system can tell "self" from "nonself."
4. In this manner, the immune system aids rather than counters homeostasis.
5. Lymphocytes recognize antigens because they have antigen receptors; the protein shape allows them to combine like a lock and key.
6. During maturation, enough differentiation occurs that there is a lymphocyte for any possible antigen.

B. 1. Immunity usually lasts for some time; we do not ordinarily get the same illness a second time.
2. Specific immunity is primarily the result of the action of B lymphocytes and T lymphocytes.
3. B lymphocytes mature in the bone marrow; T lymphocytes mature in the thymus gland.
4. **B lymphocytes** (B cells) give rise to plasma cells that produce antibodies.
5. **Antibodies** are large globular proteins that combine with and neutralize antigens.
6. Antibodies are secreted into the blood, lymph, and other body fluids.
7. **T lymphocytes** either directly attack cells that bear nonself proteins or regulate the immune response.

C. B Cells and Antibody-Mediated Immunity
1. Each type of B cell carries its specific antibody as a membrane-bound receptor on its surface.
2. When a B cell in a lymph node of the spleen encounters an appropriate antigen, it is activated to divide.
3. The resulting cells are **plasma cells**, mature B cells that mass-produces antibodies in the lymph nodes and spleen.
4. The **clonal selection theory** states that the antigen selects the B cell to produce a clone of plasma cells.
5. A B cell will not clone until its antigen is present; it recognizes the antigen directly.
6. However, B cells are stimulated to clone by **helper T cell** secretions.
7. Some cloned B cells do not participate in antibody production but remain in the blood as memory B cells.
8. Once the threat of infection has passed, development of new plasma cells ceases; those present die.
9. Apoptosis is the process of programmed cell death; apoptosis is critical to maintaining tissue homeostasis.
10. Defense by B cells is called **antibody-mediated immunity**.
11. It is also called **humoral immunity** because antibodies are present in the blood and lymph; a humor is a body fluid.

D. Structure of IgG
1. The most common antibody (IgG) is a Y-shaped protein molecule with two arms.
2. Each arm has a "heavy" and "light" polypeptide chain.
   a. These chains have **constant regions** and **variable regions**.
   b. The **constant regions** have amino acid sequences that do not change; the constant regions are not identical among all antibodies.

c. The variable regions have portions of polypeptide chains whose amino acid sequence changes providing antigen specificity; it forms the antigen binding sites of antibodies—their shape is specific to antigen.

3. The antigen binds with a specific antibody at the antigen-binding site.
4. The **antigen-antibody complex** (or immune complex) marks the antigen for destruction by being engulfed by neutrophils or macrophages, or it may activate complement.
5. If complement attaches to antigens on the surface of pathogens, it renders them more easily phagocytized.

E. Other Types of Antibodies
1. There are five different classes of circulating antibodies or immunoglobulins (Igs).
2. IgG Antibodies
   a. These are the major type in blood; less is in the lymph and tissue fluid.
   b. IgG antibodies bind to pathogens and toxins.
3. IgM Antibodies
   a. These are pentamers; they contain five Y-shaped structures.
   b. IgM appears in blood soon after an infection begins and disappears before it is over.
   c. They are good activators of the complement system.
4. IgA Antibodies
   a. IgA contains two Y-shaped structures.
   b. They attack pathogens before they reach the blood.
   c. They are the main type of antibody in bodily secretions.
5. The role of IgD antibodies is to serve as receptors for antigens on immature B cells.
6. IgE antibodies are involved in immediate allergic reactions.

F. T Cells and Cell-Mediated Immunity
1. Like B cells, T cells have unique antigen receptors.
2. However, the receptors of cytotoxic and helper T cells cannot recognize antigen present in the tissues, lymph, or blood.
3. Instead, antigen must be presented to them by an **antigen-presenting cell** (**APC**).
4. When an **antigen-presenting cell** presents a viral or cancer cell antigen, the antigen is first linked to an **MHC protein**; together they are presented to a T cell.
5. Human MHC proteins are called HLA (human leukocyte-associated) antigens; they are self proteins.
6. Importance of **major histocompatibility complex** (**MHC**) **proteins** was recognized when it was discovered they contribute to the difficulty of transplanting tissues from one person to another.
7. When a donor and recipient are histocompatible, it is likely a transplant will be successful.
8. When a macrophage antigen is presented to a T cell, the T cell recognizes the antigen.
   a. Once a helper T cell recognizes the antigen, it undergoes clonal expansion and produces **cytokines** stimulating immune cells to remain active and perform its functions.
   b. Once a cytotoxic T cell is activated, it undergoes clonal expansion and destroys any cell that possesses antigen if the cell bears the correct HLA antigen presented earlier.
   c. As the infection disappears, the immune reaction wanes and few cytokines are produced.
   d. The few T cells that do not undergo apoptosis survive as memory cells.
9. Apoptosis occurs in the thymus if the T cell bears a receptor to recognize a self antigen; if apoptosis does not occur, T-cell cancers result (i.e., lymphomas and leukemias).

G. Types of T Cells
1. Cytotoxic T cells and helper T cells are responsible for cell-mediated immunity.
2. **Cytotoxic T Cells**
   a. They destroy antigen-bearing cells (e.g., virus-infected or cancer cells).
   b. They have storage vacuoles that contain perforin molecules.
   c. **Perforin molecules** perforate a plasma membrane; water and salts then enter causing the cell to burst.

3. **Helper T Cells** regulate immunity by improving the response of other immune cells.
    a. When exposed to an antigen, they enlarge and secrete cytokines.
    b. **Cytokines** stimulate the helper T cells to clone and other immune cells to perform their functions.
        1) Cytokines stimulate the macrophages to phagocytize.
        2) Cytokines stimulate B cells to become antibody-producing plasma cells.
    c. HIV, the cause of AIDS, infects primarily helper T cells and inactivates the immune response.
4. **Memory T cells** remain and can jump-start an immune reaction when the same antigen reenters body.

35.4 Immunity in Other Animals

A. Nonspecific Immunity in Invertebrates
    1. In 1882, the Russian Elie Metchnikoff observed phagocytes gathered around a thorn in a starfish.
    2. In 1979, the Swedish Hans G. Boman discovered antibacterial peptides in silkmoths.
    3. Sea stars have cells similar to macrophages that release interleukinlike chemicals.
B. Specific defense mechanisms only evolved among vertebrates.
    1. Gary W. Litman studied sharks that rely on both antibody diversity and inherited immunity to familiar pathogens.
    2. Cell-mediated immunity based on T cells probably predates the antibody-mediated immunity based on B cells.

35.5 Induced Immunity

A. Two Types of Induced Immunity
    1. Immunity is acquired naturally through infection or artificially by medical intervention.
        a. **Active immunity** is where an individual makes their own antibodies.
        b. **Passive immunity** is where an individual receives prepared antibodies.
B. Active Immunity
    1. Active immunity sometimes develops naturally after a person is infected.
    2. However, active immunity is often induced when a person is well so that future infection is prevented.
    3. **Immunization** uses vaccines to provide the antigen to which the immune system responds.
    4. To prepare vaccines, usually pathogens are treated so they are no longer virulent.
    5. Genetically engineered bacteria can also produce antigen proteins from pathogens; the protein is then used as a vaccine.
    6. After a vaccine is given, the immune response is measured by the antibody level in serum—the **antibody titer**.
        a. After the first exposure, a **primary response** occurs from no antibodies to a slow rise in titer.
        b. After a brief plateau, a gradual decline follows as antibodies bind to antigen or simply break down.
        c. After a second exposure, a **secondary response** occurs and antibody titer rises rapidly to a level much greater than before; this is a "booster."
        d. The high antibody titer is now expected to prevent any disease symptoms if the individual is infected.
        e. Active immunity depends on memory B and memory T cells responding to lower doses of antigen.
        f. Active immunity is usually long-lived although a booster may be required every so many years.
C. Passive Immunity
    1. Passive immunity occurs when an individual is given prepared antibodies to combat a disease.
    2. It is short-lived because antibodies are not made by individual's own B cells.
    3. Newborn infants are immune to some diseases because the mother's antibodies have crossed the placenta.
    4. Breast-feeding also promotes passive immunity—the antibodies are in the mother's milk.
    5. Passive immunity is also needed when a patient is in immediate danger from an infectious disease or toxin.
    6. A person may be given a gamma globulin injection (serum that contains antibodies against the agent) taken from an individual or animal who has recovered from it.
    7. If antibodies are made with immunized horses, some individuals become sick with **serum sickness**.
D. Cytokines and Immunity
    1. **Cytokines** are signaling molecules produced by either lymphocytes, monocytes or other cells.
    2. Cytokines stimulate white blood cell formation; they may work as adjunct therapy for cancer and AIDS.
    3. Interferon and interleukins are used to improve the ability of an individual's T cells to fight cancer.

4. Cancer cells with altered proteins on their cell surface should be attacked by cytotoxic T cells.
5. Cytokines may awaken the immune system and lead to the destruction of cancer.
    a. Researchers withdraw T cells from a patient and culture them in the presence of interleukin.
    b. The T cells are re-injected into the patient; doses of interleukin then maintain the killer activity of the T cells.
6. Interleukin antagonists may help prevent skin or organ rejection, autoimmune diseases, and allergies when used as adjuncts for vaccines.

E. Monoclonal Antibodies
1. Every plasma cell derived from the same B cell secretes antibodies against the same antigen; these are **monoclonal antibodies**.
2. Monoclonal antibodies can be produced in vitro.
    a. B lymphocytes are removed from the body (usually mice are used) and exposed to a particular antigen.
    b. Activated B lymphocytes are fused with myeloma cells (malignant plasma cells that divide indefinitely).
    c. Fused cells are called **hybridomas** because they result from two different cells (hybrid) and one is cancerous, therefore the suffix "-oma."
3. Monoclonal antibodies are used for quick, reliable diagnosis of various conditions such as pregnancy.
4. They identify infections, sort out different T cells, and distinguish between normal and cancer cells.
5. They can distinguish cancerous from normal cells and can be used to carry isotopes or toxic drugs to kill tumors.

35.6 Immunity Side Effects

A. Allergies
1. **Allergies** are hypersensitivities to substances such as pollen and other everyday substances.
2. A response to these antigens, called **allergens**, usually involves tissue damage.
3. Immediate and delayed allergic responses are two of four possible responses.
4. Immediate Allergic Response
    a. Immediate responses occur within seconds of contact with an allergen.
    b. Coldlike symptoms are common.
    c. IgE antibodies are attached to plasma membrane of mast cells in tissues and basophils in blood.
    d. When an **allergen** attaches to IgE antibodies on these mast cells, they release large amounts of histamine and other substances, which cause the cold symptoms or even anaphylactic shock.
    e. A severe systemic reaction is **anaphylactic shock**, a sudden drop in blood pressure.
5. Allergy shots sometimes prevent the onset of allergic symptoms.
    a. Injections of the allergen cause the body to build up high quantities of IgG antibodies.
    b. These combine with allergens received from the environment before they have a chance to reach IgE antibodies located on the plasma membrane of mast cells and basophils.
6. Delayed Allergic Response
    a. Delayed responses are initiated by sensitized memory T cells at the site of allergen in the body.
    b. The allergic response is regulated by the cytokines secreted by both T cells and macrophages.
    c. The tuberculin skin test is an example: positive test shows prior exposure to TB bacilli but requires some time to develop reddening of tissue.

B. Blood Typing
1. Four blood types are designated by antigens present on red blood cells.
2. Individuals have naturally-occurring antigens to blood type proteins not present on their blood cells.
3. RBCs with a particular antigen **agglutinate** when exposed to corresponding antibodies.
4. **Agglutination** is the clumping of red blood cells due to a reaction between antigens on the red blood cells.
5. To receive blood, the recipient's plasma must not have an antibody that causes donor cells to agglutinate.
    a. Recipients with type AB blood can receive any type blood; they are the universal recipient.
    b. Recipients with type O blood cannot receive A, B, or AB; but they are a universal donor.
    c. Recipients with type A blood cannot receive B or AB.
    d. Recipients with type B blood cannot receive A or AB.

C. Rh System
    1. Rh factor is an important antigen in human blood types.
    2. Rh positive (Rh^+) has the Rh factor on red blood cells; Rh negative (Rh^-) lacks the Rh antigen on RBCs
    3. Rh-negative individuals do not have antibodies to Rh factor but make them if exposed to Rh^+ blood.
    4. Rh factor is particularly important during pregnancy.
        a. **Hemolytic disease of the newborn** is possible if the mother is Rh negative and the father is Rh positive.
        b. Rh positive is a genetically dominant trait; an Rh negative mother and an Rh positive father pose a Rh conflict.
        c. The child's Rh positive RBCs can leak across the placenta into the mother's circulatory system when the placenta breaks down.
        d. The presence of the "foreign" Rh positive antigens causes the mother to produce anti-Rh antibodies.
        e. Anti-Rh antibodies pass across the placenta and destroy the RBCs of the Rh positive child.
        f. The Rh problem has been solved by giving Rh^- women an Rh immunoglobulin injection (called Rho-Gam) either midway through the first pregnancy or no later than 72 hours after giving birth to an Rh^+ child.
            1) The injection includes anti-Rh antibodies that attack a child's RBCs before they trigger the mother's immune system.
            2) The injection is not effective if the mother has already produced antibodies; timing is important.

D. Tissue Rejection
    1. Tissue rejection occurs because cytotoxic T cells cause disintegration of foreign tissue; this is a correct distinguishing between self and nonself.
    2. Selection of compatible organs and administration of immunosuppressive drugs prevent tissue rejection.
    3. Transplanted organs should have the same type of HLA antigens as in the recipient.
    4. Cyclosporine and tacrolimus both act by inhibiting the response of T cells to cytokines.

E. Autoimmune Diseases
    1. **Autoimmune diseases** result when cytotoxic T cells or antibodies mistakenly attack the body's own cells as if they bear foreign antigens.
    2. The cause is not known but autoimmune diseases sometimes appear following recovery from an infection.
    3. In myasthenia gravis, the neuromuscular junctions do not work properly and muscular weakness results.
    4. In multiple sclerosis (MS), the myelin sheath of nerve fibers is attacked.
    5. Persons with systemic lupus erythematosus present many symptoms before dying from kidney damage.
    6. Heart damage following rheumatic fever and type I diabetes are also autoimmune diseases.
    7. There are no cures for autoimmune diseases but they are controlled by drugs.