Chapter 5  Lymphatic System

♦ Overview
- The lymphatic system consists of the following components (Figure 5.1, Derrickson):
  (i) lymphatic vessels, which contain a fluid called lymph, (ii) lymphatic organs, which include the lymph nodes, tonsils, spleen, and the thymus gland; and (iii) lymphocytes, which include B cells and T cells.

♦ Functions
- The lymphatic system has 2 major functions (Figure 5.2, Derrickson):
  1. It drains the tissues of excess interstitial fluid.
     - Recall that some H2O moves from the blood into the interstitium as cells undergo gas, nutrient, and waste exchange with the capillaries.
     - The H2O in the interstitial fluid can diffuse into body cells if needed.
     - If there is too much H2O in the interstitium, the excess interstitial fluid drains into a nearby lymphatic vessel (usually a lymphatic capillary).
     - Note that if this excess interstitial fluid were to remain in the interstitium, the tissues would swell (edema), which causes tissue damage.
     - Once inside of a lymphatic capillary, the interstitial fluid is called lymph.
     - Thus, lymph is any excess interstitial fluid found within the lymphatic vessels of the body.
     - The excess interstitial fluid will eventually make it back to the blood because lymphatic vessels ultimately merge with veins.
     - Any pathogens (viruses, bacteria, etc.) that happen to be in the interstitium trying to invade body cells will also be swept into the lymphatic capillaries as a component of lymph (just like a swimmer may be swept away from the shore by a tidal wave).
  2. It participates in immunity.
    □ immunity
      - resistance to disease
    - This function is achieved by the leukocytes (white blood cells) of the body.
    - Because of its role in immunity, the lymphatic system is also called the immune system.
Lymphatic Vessels
- Lymphatic Capillaries
  - The lymphatic system begins with the **lymphatic capillaries**, which are the smallest lymphatic vessels (Figure 22.2, Tortora).
  - Like a blood capillary, a lymphatic capillary consists of endothelial cells.
  - However, a lymphatic capillary differs from a blood capillary in 2 major ways:
    - A lymphatic capillary lacks a basement membrane.
    - The endothelial cells of a lymphatic capillary overlap.
  - This arrangement allows for unidirectional flow of fluid into the lymphatic capillary.
  - As excess interstitial fluid approaches a lymphatic capillary, the endothelial cells spread apart, forming large spaces between each other.
  - These spaces are larger than the pores in a regular blood capillary and allow small molecules (like H₂O) **and** large substances (such as proteins, viruses, bacterial cells, cancer cells, and debris) to move from the interstitium into the lumen of the lymphatic capillary.
  - Thus, a lymphatic capillary is **far more permeable than a blood capillary**.
  - If the lymph tries to move out of the lymphatic capillary back into the interstitium, the endothelial cells come back together and overlap with one another, which closes off the spaces and essentially traps the lymph within the lymphatic vessel.

-Larger Lymphatic Vessels
- Lymphatic capillaries converge to form larger lymphatic vessels; a larger lymphatic vessel resembles a vein in structure, but has a thinner wall and more valves.

Pathway of Lymph Flow Through the Lymphatic Vessels (Figure 22.3, Tortora)

Excess interstitial fluid (and any dissolved pathogens and debris) flows from the interstitium into the lymphatic capillaries, forming lymph.

The lymph then moves into larger lymphatic vessels. As these larger lymphatic vessels course through the body, they give rise to lymph nodes, where lymph is filtered of any pathogens and debris.

Lymph eventually flows into the largest lymphatic vessels: the **right lymphatic duct** and the **thoracic (left lymphatic) duct**.

Finally, lymph moves from the right lymphatic duct and the thoracic (left lymphatic) duct into the right and left subclavian veins, respectively.
Lymphatic Organs

The lymphatic organs include the lymph nodes, the tonsils, spleen, and the thymus gland (Figure 5.1, Derrickson).

1. lymph nodes
   - small, bean-shaped masses that are located between lymphatic vessels
   - Locations
     - Single lymph nodes are found throughout the body.
     - Lymph nodes can also exist in groups; this is especially the case with the lymph nodes in the neck, armpit, and groin.
     - These lymph nodes are called cervical nodes, axillary nodes, and inguinal nodes, respectively.
   - Structure
     - Within a lymph node is reticular connective tissue, which consists of the following (Figure 22.6, Tortora):
       a. reticular fibers
          - thin collagen fibers that interact together to form a netlike association
       b. macrophages
       c. lymphocytes
          - both B cells and T cells
   - Function
     Lymph nodes filter the lymph of foreign substances (pathogens and debris, etc.).

     Lymphatic vessels bring lymph to lymph nodes.

     As lymph travels through each lymph node, any foreign substances in the lymph are trapped by the netlike reticular fibers, which then allows the macrophages and lymphocytes to destroy them (like a spider that traps and then kills a fly in its web).

2. tonsils
   - located in the pharynx (throat) and the oral cavity
   - 3 types (Figure 23.3b, Tortora):
     a. pharyngeal tonsil
        - unpaired
        - also called the adenoid
        - located in wall of the nasopharynx
     b. palatine tonsils
        - paired
        - located in the posterior end of the oral cavity
        - The palatine tonsils are most susceptible to infection and may have to be removed (tonsillectomy).
     c. lingual tonsils
        - paired
        - located at the base of the tongue
-Structure
- The tonsils consist of reticular connective tissue containing reticular fibers, macrophages, and lymphocytes.

-Function
- The tonsils trap and destroy any pathogens that enter the pharynx and oral cavity from inhaled air or from ingested food and beverages.
  - Close inspection of the external structure of the tonsils reveals that the tonsils contain invaginations (folds) that form valleys called crypts.
  - As pathogens in air, food, or liquid interact with the tonsils, the pathogens become trapped in the crypts.

By chance, the pathogens then move deeper into the reticular connective tissue within the tonsils, where the macrophages and lymphocytes destroy them.

3. spleen
- the largest lymphatic organ
- located on the left side of the body between the diaphragm and the stomach

-Structure
- The spleen consists of reticular connective tissue that is organized into regions called white pulp and red pulp (Figure 22.7, Tortora).
  - In addition, the spleen is heavily vascularized: the splenic artery provides blood to the spleen, while the splenic vein drains it.
  - Since the spleen is so heavily vascularized, trauma to the spleen can cause severe bleeding and even death.
  - If this happens, the spleen must be removed (splenectomy) to stop the bleeding.

-Functions
- The spleen is involved in 2 major functions:
  a. It filters the blood of pathogens.
     The splenic artery brings blood to the spleen.

From the splenic artery, blood eventually moves into the reticular connective tissue that forms the white pulp and the red pulp.

As blood moves through the white pulp and red pulp, lymphocytes and macrophages remove and destroy any pathogens that get caught in the reticular fibers.
The blood then moves from the white pulp and red pulp into the splenic vein, which takes the filtered blood away from the spleen.

–Hence, the filtering function of the spleen is similar to that of the lymph nodes; the only difference is that the spleen filters blood, while the lymph nodes filter lymph.

b. It destroys worn out blood cells.
-As blood is filtered in the spleen, the macrophages can remove and destroy any worn out blood cells via phagocytosis.

4. thymus gland
- bilobed gland that partially covers the superior portion of the heart (Figure 22.5, Tortora)
-The size of the thymus gland changes with age: it is largest during infancy and childhood and gradually gets smaller as we age.
-Structure
  -The thymus gland contains T lymphocytes (T cells).
-Function
  The thymus gland promotes the maturation of T cells.
  -Immature T cells are initially produced in the red bone marrow.

  Afterwards, these immature T cells are released into the blood and then migrate to the thymus gland.

  The thymus gland produces hormones called thymosins that mature the T cells.

  The mature T cells then migrate back into the blood. Some T cells patrol the blood for pathogens, while others move into lymphatic organs (like the lymph nodes) to fight pathogens there.

-Note that B cells are produced and matured in the red bone marrow and, therefore, do not have to migrate to the thymus gland.
Immunity

- Immunity
  - resistance to disease
- 2 major types:
  1. nonspecific immunity
     - the ability to protect the body from any foreign substance in a general, nonspecific way
     - Recall that there are several types of white blood cells that are involved in nonspecific immunity (neutrophils, monocytes/macrophages, eosinophils, and basophils).
  2. specific immunity
     - the ability to protect the body from any foreign substance in a way that involves specificity and memory
     - Recall that specific immunity is achieved through the activities of B lymphocytes and T lymphocytes (also called B cells and T cells, respectively).

- Note that the difference between nonspecific immunity and specific immunity is based on specificity and memory.
  - specificity
    - Specific immunity targets a specific pathogen (example: \textit{E. coli} vs. the influenza virus).
      - The more specific the immune response is, the easier it is to kill the invading pathogen.
    - Nonspecific immunity is more general and, therefore, can target any type of pathogen (any type of bacterium or virus, etc.)
      - A major disadvantage to this generalized approach is that it is harder to kill a pathogen without being able to specifically target it.
  - memory
    - Specific immune responses involve memory, while there is no memory associated with nonspecific immunity.
    - A person often becomes ill upon the first exposure to a particular pathogen.
      - This is because it usually takes time for nonspecific immunity and for specific immunity to become effective.
    - Because specific immunity involves memory, the person does not get sick due to a subsequent exposure to the same pathogen because the specific immunity response acts quicker this time around.
    - Since there is no memory associated with nonspecific immunity, the nonspecific immunity response will still occur at the same slow pace as before and the person runs the risk of still becoming sick until the nonspecific immunity response can become effective.
Specific Immunity: A Closer Look

In order to describe specific immunity any further, one must first understand the concept of an antigen.

**antigen**

-Definition

An antigen is any substance that the body recognizes as being foreign (nonself) and is therefore immunogenic (promotes a specific immune response).

-Examples:

  Most antigens are foreign proteins:
  
  1. different components of pathogens
     - a. the capsid (protein coat) or glycoproteins of a virus
     - b. the proteins in the cell wall and flagellum of a bacterial cell
  2. pollen
     - During their reproductive cycles, many plants release pollen-- a multicellular male structure that gives rise to sperm.
     - The cell membranes of the cells in pollen contain proteins that are immunogenic in many people.
  3. certain foods
     - The proteins found in peanuts are immunogenic in many people.
  4. foreign human cells
     - Cells from other people contain proteins that are immunogenic.
       Examples:
       - a. the A or B antigens in the cell membranes of the blood cells of a person that has a blood type different than yours
       - b. the MHC antigens found in nucleated cells of the tissues and organs of other people
         - This concept will be discussed shortly.
       - c. strange proteins found in the cell membranes of cells that become cancerous in your body
         - As a normal cell turns into a cancer cell, it produces strange proteins that the body will recognize as foreign.

-Once antigens are introduced into the body, B cells and T cells will find them and destroy them.

-Note that most plastics are not immunogenic; consequently, they can be used to replace damaged heart valves or damaged areas of the hip or knee without fear of rejection from the body.
MHC Proteins: the Self-Antigens

-Our cells contain a variety of macromolecules.
- The majority of lipids, nucleic acids, carbohydrates, and proteins are the same from person to person and, consequently, are not immunogenic to other people.
- However, there is a group of proteins called the major histocompatibility complex (MHC) that is unique from individual to individual and, consequently, causes an immune response when introduced into another person (Figure 5.3, Derrickson).

Major histocompatibility complex
- a special group of proteins found in the plasma membrane of nucleated cells
- unique from individual to individual
  - Exception: identical twins
- serve as cellular “identity tags” or self-antigens
  - Self-antigens are proteins that belong in one person and nobody else.
  - The MHC complex is the basis of tissue rejections during tissue or organ transplantations.
    - However, the MHC antigens in the cells of one of your close relatives are very similar to your own MHC antigens; therefore, a close relative can donate an organ to you without there being a severe immunogenic response in your body.
- not found in RBCs
  - RBCs are non-nucleated cells; consequently, they lack MHC proteins.
  - Nevertheless, RBCs do contain their own self-antigens: the antigens of the ABO blood group and those of the Rh blood group.

Production of B cells and T cells

- B cells and T cells are produced in red bone marrow from hemocytoblasts via the process of hematopoiesis.

Once they are produced, the B cells remain in the red bone marrow for a while to undergo maturation. T cells, however, do not mature in red bone marrow. Once they are produced, T cells migrate via the blood to the thymus gland to undergo maturation there with the help of thymosins (thymic hormones). During the maturation process, the B cells and the T cells become immunocompetent, which is the process by which B cells and T cells develop specific antigen-binding receptors in their plasma membranes.
Once the maturation process has been completed, the immunocompetent B cells and T cells leave the red bone marrow and thymus gland, respectively, and migrate into the blood and into the reticular connective tissue of lymphatic organs. These lymphocytes continuously travel between the blood and lymphatic organs as they patrol these areas for antigens.

-Immunocompetence and the Diversity of Antigen Receptors
-There are millions of different antigens in the environment that could potentially cause a person to become sick.
-Fortunately, the body already contains a specific B cell or T cell that can destroy each one of these antigens before you even encounter them!!!!!!
-Hence, there are millions of different types of B cells and millions of different types of T cells in the body; each of these cells contains a specific antigen-binding receptor in its plasma membrane (Figure 5.4, Derrickson).

-Clonal Selection
-Again, there are millions of different types of B cells and millions of different types of T cells in the body.
-However, there are only a few copies of each of these different types of B cells and T cells before the initial exposure to antigens.
-Such a small army consisting of only a few copies of each of these lymphocytes is not enough to fight a massive invasion of pathogens.
-As a solution to this problem, when a B cell or T cell binds to an antigen, it undergoes clonal selection.

clonal selection
- the process by which a B cell or T cell divides into a clone of cells that can bind to the same antigen
- results in the production of more B cells or T cells (often thousands of them) that can be used to destroy an antigen
- In addition, the cells of the clone become differentiated.
- Although the differentiated cells of the clone bind to the same antigen, they function differently in the specific immune response that is about to occur.
Formation of B Cell Clones (Figure 5.5, Derrickson)

An antigen invades the body.

The receptor on the appropriate B cell binds to the antigen.

The B cell is then activated by cytokines released from a helper T cell.

The B cell subsequently undergoes clonal selection, resulting in the production of many plasma cells and memory B cells. Both of these cell types bind to the same antigen as the original B cell.

(i) plasma cells
- secrete antibodies into the blood or other body fluids

antibody
- also called an immunoglobulin (Ig)
- a protein that binds to and subsequently destroys an antigen
- The antibodies secreted by the plasma cell are specific for the antigen that was recognized by the original B cell.
- Antibodies are found in many types of body fluids (blood, saliva, lymph, tears, mucus, breast milk, etc.)

(ii) memory B cells
- cells that remember the antigen that caused the original B cell to undergo clonal selection
- Should the same antigen invade the body again, the memory B cells immediately produce more plasma cells and more memory B cells that possess the same antigen specificity.
- Consequently, there is a rapid production of antibodies produced by the plasma cells, which results in the quick destruction of the pathogen.
- This response is so fast that the person typically does not exhibit any signs of being ill.
- Memory B cells stay around in the body for decades.
Formation of T cell clones (Figure 5.6, Derrickson)

An antigen invades the body.

The receptor on the appropriate T cell binds to the antigen.

The T cell is then activated by cytokines released from a helper T cell.

The T cell subsequently undergoes clonal selection, resulting in the production of many cytotoxic T cells, helper T cells, suppressor T cells, and memory T cells. All of these cell types bind to the same antigen as the original T cell.

(i) cytotoxic T cells
- also called killer T cells
- Cytotoxic T cells function by poking holes in the cell membrane of their target antigens, which results in cell lysis and cell death.

(ii) helper T cells
- activate both B cells and T cells, resulting in clonal selection
  - Consequently, a specific immune response cannot be achieved without the helper T cells.
- Helper T cells activate B cells and T cells via the secretion of chemicals called cytokines (example: interleukin).

(iii) suppressor T cells
- reduce the activity of B cells and T cells once the pathogen has been destroyed
- Hence, these cells only become active once the battle is over and victory has been declared.

(iv) memory T cells
- cells that remember the antigen that caused the original T cell to undergo clonal selection
- Should the same antigen invade the body again, the memory T cells immediately produce more cytotoxic T cells, helper T cells, suppressor T cells, and memory T cells possess the same antigen specificity.
  - Consequently, the pathogen is quickly killed by the huge numbers of cytotoxic T cells.
  - This response is so rapid that the person typically does not exhibit any signs of being ill.
- Like memory B cells, memory T cells also stay around in the body for decades.
-Acquired Immunity
  -There are four ways to acquire specific immunity:

1. **active natural immunity**
   - specific immunity (i.e. proliferation of B cells/antibodies or T cells) that a person develops due to natural exposure to an antigen (i.e. by chance)
   - The person will typically develop signs of illness since there has not been a previous encounter with the antigen.

2. **active artificial immunity**
   - specific immunity that a person develops due to deliberate exposure to an antigen by a process called vaccination
   - In this process, a person receives a vaccine, which consists of an attenuated (weakened) pathogen.
   - Since the pathogen is attenuated, it does not cause harm to the body but it is still immunogenic and will result in the production of either B cells/antibodies or T cells.
   - Years after the vaccine has been administered, the person may need a booster shot to stimulate the number of memory cells in that person’s body just in case some of the previous memory cells that developed after the first vaccination have dwindled in number.

3. **passive natural immunity**
   - specific immunity that develops when antibodies are passed from mother to fetus through the placenta or from mother to infant via breast milk
   - Neither a fetus nor an infant has a well-developed immune system and, therefore, both are susceptible to frequent pathogenic invasions.
   - Passive natural immunity assures that the fetus and the infant are not totally helpless.
   - These antibodies do not last forever; they are eventually broken down and the infant will have to rely on his or her own developing immune system to provide protection.

4. **passive artificial immunity**
   - specific immunity that a person develops by receiving serum
   - often involves the following steps:
     Vaccinate an animal (like a horse or rabbit)

     The animal’s immune system will respond to the vaccination by making antibodies in its blood.
Remove the blood from the animal and then extract the serum, which contains the antibodies.

Inject the antibodies into the person that needs immunity to provide **immediate protection**.

-Passive artificial immunity is the preferred type of acquired immunity when there is an epidemic and, consequently, there is not enough time for a person to develop his or her own specific immune response.

♦ Clinical Applications and Disorders

- Look up the following clinical applications and disorders in Tortora:

1. metastasis through lymphatic vessels  
   p. 818
2. ruptured spleen  
   p. 818
3. tonsillitis  
   p. 819
4. abscesses and ulcers  
   p. 824
5. graft rejection and tissue typing  
   p. 834
6. monoclonal antibodies  
   p. 836
7. cancer immunology  
   p. 840
8. AIDS  
   p. 841, 843-844
9. allergens, type I (anaphylactic) reactions, and anaphylactic shock  
   p. 844
10. autoimmune diseases  
   p. 844-845

11. infectious mononucleosis  
   p. 845

12. lymphomas  
   p. 845

13. systemic lupus erythematosus  
   p. 845-846

14. allograft  
   p. 846

15. autograft  
   p. 846

16. lymphedema  
   p. 846

17. splenomegaly  
   p. 846

18. xenograft  
   p. 846
Figure 5.1
Components of the Lymphatic System
Figure 5.2
Lymphatic System Function
Figure 5.3
MHC Proteins
Figure 5.4
Diversity of B Cells and T Cells

B cell 1
Antigen L
Antigen receptor

B cell 2
Antigen R
Antigen receptor

T cell 1
Antigen M
Antigen receptor

T cell 2
Antigen C
Antigen receptor
Figure 5.5
B Cell Clonal Selection

- Antigen
- Antigen receptor
- B cell
- Activation of B cell by helper T cell
- Clonal selection
- Plasma cell (many copies)
- Antibody
- Memory B cell (many copies)
Figure 5.6
T Cell Clonal Selection

- Antigen
- Antigen receptor
- T cell
- Activation of T cell by helper T cell
- Clonal selection
- Cytotoxic T cell (many copies)
- Helper T cell (many copies)
- Suppressor T cell (many copies)
- Memory T cell (many copies)