The Lymphatic System

Chapter 22

The Lymphatic System has 4 main components

- Lymph: a fluid similar to plasma, but without the plasma proteins.
- Lymphatic vessels (lymphatics): the network that carries lymph from peripheral tissues to the venous system.
- Lymphoid tissues and lymphoid organs: found throughout the body.
- Lymphocytes which include phagocytes and other immune system cells.

Functions of the Lymphatic System

- The main function of the lymphatic system is to produce, maintain and distribute lymphocytes.
- Lymphocytes are produced and stored in lymphoid tissues (such as the tonsils), and lymphoid organs (such as the spleen and thymus), and are also produced in red bone marrow.
- Lymphocytes circulate in the blood, enter the interstitial fluid through capillaries, and return to the blood stream through lymphatic vessels.
- The circulation of fluids from blood plasma to lymph and back to the venous system also transports other immune system cells (such as macrophages and microphages) as well as hormones, nutrients and waste products.

Lymphatic Vessels

- The vessels that carry lymph are called lymphatic vessels.
- The lymphatic system begins with the smallest vessels called lymphatic capillaries or terminal lymphatics.
- Lymphatic capillaries differ from blood capillaries in 4 ways:
  - They start as pockets rather than tubes.
  - They have larger diameters.
  - They have thinner walls.
  - In section, they are flat or irregular.
• The endothelial cells of lymphatic capillaries are not tightly bound together, but they overlap.
• The overlap acts as a one-way valve that allows fluids, solutes and larger materials such as viruses, bacteria and debris to enter the vessel, but prevents them from returning to the intercellular space.
• Special lymphatic capillaries (lacteals) in the small intestine transport lipids from the digestive tract.

• From the lymphatic capillaries, the lymphatic system is divided into the superficial lymphatics and deep lymphatics.
• The superficial lymphatics are located in the skin, mucus membranes, and serous membranes lining body cavities.
• The deep lymphatics are larger vessels that accompany deep arteries and veins.
• The superficial lymphatics and deep lymphatics join to form the large lymphatic trunks that empty into 2 major collecting vessels: the thoracic duct and the right lymphatic duct.

• The thoracic duct and the right lymphatic duct empty into the left and right subclavian veins respectively
• Blockage of lymph drainage from a limb produces lymphedema, which causes severe swelling and interferes with the proper functioning of the immune system.
Lymphocytes

• Lymphocytes make up 20-30% of circulating leukocytes; but most lymphocytes are stored, not circulating.
• There are 3 classes of circulating lymphocytes:
  – T cells (thymus-dependent)
  – B cells (bone-marrow derived)
  – NK cells (natural killer cells)

T Cells

• T cells make up 80% of circulating lymphocytes. There are 3 main types of T cells:
  – Cytotoxic T cells, which attack cells infected by viruses and produce cell-mediated immunity
  – Helper T cells which stimulate the function of T cells and B cells
  – Suppressor T cells which inhibit the function of T cells and B cells
• Helper and suppressor T cells are regulatory T cells, because they control the sensitivity of the immune response. Other types of T cells include inflammatory T cells and suppressor/inducer T cells.

B Cells

• B cells make up 10-15% of the circulating lymphocytes.
• B cells differentiate into plasma cells, which produce and secrete antibodies (immunoglobulin proteins).
• Immunoglobulin proteins bind to targets called antigens, which are the identifying parts of any pathogen or foreign compound.
• The binding of a specific antibody to its specific antigen starts a chain of events called antibody-mediated immunity which destroys the target compound or organism.

NK Cells

• NK cells or large granular lymphocytes make up 5-10% of circulating lymphocytes.
• NK cells are responsible for immunological surveillance; attacking foreign cells, virus-infected cells, and cancer cells.

Lymphoid Tissues

• Lymphoid tissues are connective tissues dominated by lymphocytes.
• A lymphoid nodule is areolar tissue with densely packed lymphocytes.
• Each nodule has germinal center which contains dividing lymphocytes.
• Lymphoid nodules are found in lymph nodes, the spleen, the respiratory tract (tonsils), and along digestive and urinary tracts.
• The appendix also contains a mass of fused lymphoid nodules.
Lymphoid Organs

- The lymphoid organs include the lymph nodes, the thymus and the spleen.
- A fibrous connective-tissue capsule separates lymphoid organs from surrounding tissues.

Lymph Nodes

- Lymph nodes range from 1 mm to 25 mm in diameter.
- Bundles of collagen fibers, called trabeculae, extend from the capsule into the interior of the lymph node.
- Blood vessels and nerves reach the lymph node at the hilus.
- Afferent lymphatic vessels carry lymph from peripheral tissues to the lymph node.
- Efferent lymphatics leave the lymph node at the hilus and carry lymph to the venous circulation.

Lymph Nodes

- Lymph nodes are filters that purify the lymph before it is returned to the venous circulation. Debris, pathogens, and 99% of the antigens are removed.
- The extracted antigens are “presented” to lymphocytes, or attached to dendritic cells to stimulate lymphocyte activity.
- Antigen presentation is the first step in the immune response.
- Lymphoid tissues and lymph nodes are distributed to monitor peripheral infections and deal with them before they reach the vital organs of the trunk.

Lymph Nodes

- Large lymph nodes at the groin and base of the neck are often called lymph glands.
- Lymph nodes associated with the gut, trachea, lungs and thoracic duct protect against pathogens within the digestive and respiratory systems.
- Lymph glands swell in response to inflammation.
- Chronic or excessive enlargement (lymphadenopathy) may indicate infections, endocrine disorders or cancer.
The Thymus

- The thymus, located in the mediastinum, deteriorates after puberty, diminishing the effectiveness of the early immune system.
- The thymus produces T cells and several hormones (thymosins) that promote the development of lymphocytes.

The Spleen

- The spleen contains a large collection of lymphoid tissues. The main functions of the spleen are:
  - the removal of abnormal blood cells and other blood components by phagocytosis
  - the storage of iron recycled from red blood cells
  - the initiation of immune responses by B cells and T cells in response to antigens in circulating blood

The Lymphatic System and Body Defenses

- The body’s defense mechanisms provide resistance to fight infection, illness and disease.
- There are 2 general categories of defenses:
  - Nonspecific defenses which work the same against any type of invading agent.
  - Specific defenses against specific pathogens.
- Specific resistance or immunity is developed after exposure to environmental hazards or pathogens.
- Specific defenses depend on the activities of lymphocytes.

Nonspecific Defenses

- The 7 types of nonspecific defenses are:
  - physical barriers
  - phagocytic cells
  - immunological surveillance
  - interferons
  - complement
  - inflammation
  - fever
Physical Barriers

- Physical barriers keep hazardous materials outside the body.
- Physical barriers include:
  - the outer layer of skin
  - hair
  - epithelial layers of internal passageways
  - secretions that flush away materials (sweat glands, mucus, urine)
  - secretions that kill or inhibit microorganisms (enzymes, antibodies and stomach acid)

Phagocytes

- Phagocytes attack and remove dangerous microorganisms.
- There are 2 classes of phagocytes:
  - microphages (neutrophils and eosinophils)
  - macrophages (large phagocytic cells derived from monocytes)
- Microphages leave the bloodstream and enter peripheral tissues to fight infections.
- Macrophages are distributed throughout the body, and respond to pathogens in several ways:
  - Engulf the pathogen and destroy it with lysosomal enzymes.
  - Bind to the pathogen so that other cells can destroy it.
  - Destroy the pathogen by releasing toxic chemicals into the interstitial fluid.

Immunological Surveillance

- The constant monitoring of normal tissues by natural killer cells (NK cells) is called immunological surveillance.
- NK cells identify cells that have components not found on normal cells (antigens), and attach to the abnormal cell.
- NK cells are not selective about their targets; they will attack any abnormal cells, anywhere in the body.
- The Golgi apparatus in the attached NK cell forms vesicles full of perforin, which migrate to the abnormal cell and perforate (lyse) it.
Immunological Surveillance
- NK cells attack cancer cells and cells infected with viruses.
- Cancer cells that have tumor specific antigens are identified as abnormal by NK cells. Some cancer cells avoid detection or resist NK cells (immunological escape).
- Cells that are infected with viruses present abnormal proteins on their outer membranes, which allow NK cells to identify and destroy them.

Interferons
- Interferons are proteins released by activated lymphocytes and macrophages which trigger the production of antiviral proteins in normal cells.
- Antiviral proteins do not kill viruses, but block their replication in the cell.
- There are 3 types of interferons:
  - alpha interferons, produced by leukocytes, stimulate NK cells
  - beta interferons, secreted by fibroblasts, slow inflammation
  - gamma interferons, secreted by T cells and NK cells, stimulate macrophage activity
- Interferons are cytokines: chemical messengers released by tissue cells to coordinate local activities, or that act as hormones to affect tissues throughout the body.

Complement
- Plasma contains 11 special complement (C) proteins that form the complement system (a system that complements the action of antibodies).
- Complements work together in cascades similar to those in the clotting system.
- Both pathways end with the conversion of an inactive complement protein (C3) to the active form (C3b).

Complement
- Complement activation has several effects:
  - Stimulation of inflammation
  - Attraction of phagocytes
  - Enhancement of phagocytosis:
  - Destruction of target cell membranes:
    - 5 complement proteins join to form a membrane attack complex (MAC)

Inflammation
- Inflammation (the inflammatory response) is a localized response that causes certain signs and symptoms:
  - swelling (tumor)
  - redness (rubor)
  - heat (calor)
  - and pain (dolor)
- Any stimulus that kills cells or injures tissue can trigger inflammation.
Inflammation

- The effects of inflammation include:
  - Temporary repair and barrier against pathogens.
  - Retards spread of pathogens into surrounding areas.
  - Mobilization of local and systemic defenses
  - Facilitation of repairs (regeneration)

Inflammation and tissue repair occur in several steps:

- When tissue is damaged, injured cells release prostaglandins, proteins and potassium ions that change the interstitial environment and stimulate mast cells.
- Mast cells release histamine, which increases capillary permeability, and heparin, which inhibits clotting.
- Increased blood flow raises the local temperature, causing the area to swell, redden and become painful.

Inflammation and tissue repair occur in several steps:

- A blood clot forms around the damaged area, isolating it.
- Complements break down bacteria and attract phagocytes.
- Activated neutrophils attack debris and bacteria.
- Phagocytes and foreign proteins activate the body’s specific defense system.
- Macrophages clean up pathogens and cell debris.
- Fibroblasts form scar tissue

Fever

- Fever is a maintained body temperature above 37.2°C (99°F).
- The hypothalamus, which maintains normal body temperature, is affected by circulating pyrogens (pathogens, toxins, antibody complexes).
- The pyrogen released by active macrophages is a cytokine called endogenous pyrogen or interleukin-1 (IL-1).
- High body temperature increases body metabolism (accelerating defenses) and inhibits some viruses and bacteria.

Specific Defenses: An Overview of the Immune Response

- Specific resistance (immunity) responds to specific antigens with the coordinated action of T cells and B cells.
- T cells are responsible for cell-mediated immunity, which defends against abnormal cells and pathogens inside cells.
- B cells provide antibody-mediated immunity, which defends against antigens and pathogens in body fluids.
Forms of Immunity

- Immunity can be either innate (present at birth) or acquired (after birth).
- Acquired immunity can be either active (antibodies develop after exposure to an antigen) or passive (antibodies are transferred from another source).
- Active immunity can be either naturally acquired (through environmental exposure to pathogens) or induced (through vaccines containing pathogens).
- Passive immunity can also be either naturally acquired (from the mother) or induced (by an injection of antibodies).

Properties of Immunity

- All types of immunity have 4 general properties:
  - specificity
  - versatility
  - memory
  - tolerance

- Specificity means that each T cell or B cell responds only to an antigen with a specific molecular structure, ignoring all others.
- Versatility means the body produces a small number of many types of lymphocytes with different capabilities, so the immune system has the tools to fight many types of antigens.
- When an antigen activates a particular lymphocyte, that lymphocyte clones itself to produce a population of cells that can fight that specific antigen.

- Memory means that some activated lymphocytes (memory cells) stay in the circulation and provide immunity.
- If exposed to the same antigen at a later date, the immune system recognizes it and responds immediately.
- Tolerance means the immune system will ignore antigens it recognizes as “normal.”

The Immune Response
Immune Disorders

- Disorders of the immune system include
  - autoimmune disorders
  - immunodeficiency disease
  - allergies.

Autoimmune Disorders

- Autoimmune disorders result when the system that recognizes and ignores normal or self-antigens malfunctions.
- As a result activated B cells make antibodies against body cells and tissues (autoantibodies). Some common examples are: thyroiditis, rheumatoid arthritis, and insulin-dependent diabetes mellitus.
- Many autoimmune disorders are caused by a similarity between proteins in invading viruses and amino acid sequences in normal tissues.
- The antibody produced against the virus also attacks the similar body tissue.

Immunodeficiency Disease

- Immunodeficiency diseases can result from:
  - problems with embryological development of lymphoid tissues that can result in severe combined immunodeficiency disease (SCID)
  - viral infections such as HIV which can result in AIDS
  - immunosuppressive drugs or radiation treatments that can lead to complete immunological failure

Allergies

- Allergies are inappropriate or excessive immune responses to antigens.
- Antigens that trigger allergic reactions are called allergens.
- There are 4 categories of allergic reactions:
  - Type I: immediate hypersensitivity
  - Type II: cytotoxic reactions
  - Type III: immune complex disorders
  - Type IV: delayed hypersensitivity
Immediate Hypersensitivity

- The most commonly recognized type of allergy is Type I, immediate hypersensitivity, which includes allergic rhinitis (environmental allergies).
- Immediate hypersensitivity is a rapid and severe response to the presence of an antigen.
- Sensitization leads to the production of large quantities of IgE antibodies that are distributed throughout the body.
- A second exposure leads to a massive inflammation of all affected tissues.

Immediate Hypersensitivity

- The severity of the reaction depends on individual sensitivity and the locations involved.
- Allergen exposure at the body surface may restrict the allergic response.
- Reaction to allergens in the blood stream may result in fatal anaphylaxis.
- Anaphylaxis affects cells throughout the body.
- Changes in capillary permeability produce swelling (hives) on the skin, smooth muscles of the respiratory system contract, making breathing difficult, and peripheral vasodilatation can lead to circulatory collapse (anaphylactic shock).
- Mild symptoms of immediate hypersensitivity can be reduced by antihistamine drugs that block the action of histamine.

Stress and the Immune Response

- Glucocorticoids produced during the immune response help control the extent of the immune response.
- But long-term secretion of glucocorticoids due to chronic stress can inhibit the immune response and lower resistance to disease by:
  - Depression of the inflammatory response
  - Reduction in the abundance and activity of phagocytes in peripheral tissues
  - Inhibition of interleukin secretion