The Lymphatic System and Body Defenses

The Lymphatic System

- Consists of two semi-independent parts
  - Lymphatic vessels
  - Lymphoid tissues and organs
- Lymphatic system functions
  - Transports escaped fluids back to the blood
  - Plays essential roles in body defense and resistance to disease

Lymphatic Characteristics

- Lymph—excess tissue fluid carried by lymphatic vessels
- Properties of lymphatic vessels
  - One way system toward the heart
  - No pump
  - Lymph moves toward the heart
    - Milking action of skeletal muscle
    - Rhythmic contraction of smooth muscle in vessel walls

Relationship of Lymphatic Vessels to Blood Vessels

Lymphatic Vessels

- Lymph capillaries
  - Walls overlap to form flap-like minivalves
  - Fluid leaks into lymph capillaries
  - Capillaries are anchored to connective tissue by filaments
  - Higher pressure on the inside closes minivalves
  - Fluid is forced along the vessel

Lymphatic Vessels

- Lymphatic collecting vessels
  - Collect lymph from lymph capillaries
  - Carry lymph to and away from lymph nodes
  - Return fluid to circulatory veins near the heart
    - Right lymphatic duct
    - Thoracic duct

Lymphatic Vessels

Lymph

- Harmful materials that enter lymph vessels
  - Bacteria
  - Viruses
  - Cancer cells
  - Cell debris

Lymph Nodes

- Filter lymph before it is returned to the blood
- Defense cells within lymph nodes
  - Macrophages—engulf and destroy foreign substances
  - Lymphocytes—provide immune response to antigens

Lymph Nodes
Lymph Node Structure

- Most are kidney-shaped and less than 1 inch long
- Cortex
  - Outer part
  - Contains follicles—collections of lymphocytes
- Medulla
  - Inner part
  - Contains phagocytic macrophages

Flow of Lymph Through Nodes

- Lymph enters the convex side through afferent lymphatic vessels
- Lymph flows through a number of sinuses inside the node
- Lymph exits through efferent lymphatic vessels
- Fewer efferent than afferent vessels causes flow to be slowed

Other Lymphoid Organs

- Several other organs contribute to lymphatic function
  - Spleen
  - Thymus
  - Tonsils
  - Peyer’s patches

Spleen

- Located on the left side of the abdomen
- Filters blood
- Destroys worn out blood cells
- Forms blood cells in the fetus
- Acts as a blood reservoir

Thymus Gland

- Located low in the throat, overlying the heart
- Functions at peak levels only during childhood
- Produces hormones (like thymosin) to program lymphocytes

Tonsils

- Small masses of lymphoid tissue around the pharynx
- Trap and remove bacteria and other foreign materials
- Tonsillitis is caused by congestion with bacteria

Peyer's Patches

- Found in the wall of the small intestine
- Resemble tonsils in structure
- Capture and destroy bacteria in the intestine

Mucosa-Associated Lymphatic Tissue (MALT)

- Includes
  - Peyer’s patches
  - Tonsils
  - Other small accumulations of lymphoid tissue
- Acts as a sentinel to protect respiratory and digestive tracts

Body Defenses
The body is constantly in contact with bacteria, fungi, and viruses.

The body has two defense systems for foreign materials:
- Innate (nonspecific) defense system
- Adaptive (specific) defense system

Immunity—specific resistance to disease

**Immune System**
**Body Defenses**

- Innate defense system (nonspecific defense system)
  - Mechanisms protect against a variety of invaders
  - Responds immediately to protect body from foreign materials

- Adaptive defense system (specific defense system)
  - Specific defense is required for each type of invader

**Innate Body Defenses**

Innate body defenses are mechanical barriers to pathogens such as:

- Body surface coverings
  - Intact skin
  - Mucous membranes
- Specialized human cells
- Chemicals produced by the body

**Surface Membrane Barriers: First Line of Defense**

- Skin and mucous membranes
  - Physical barrier to foreign materials
  - Also provide protective secretions
    - pH of the skin is acidic to inhibit bacterial growth
    - Sebum is toxic to bacteria
    - Vaginal secretions are very acidic

**Cells and Chemicals: Second Line of Defense**

- Phagocytes
- Natural killer cells
- Inflammatory response
- Antimicrobial proteins
- Fever

**Cells and Chemicals: Second Line of Defense**

- Phagocytes
  - Cells such as neutrophils and macrophages
  - Engulf foreign material into a vacuole
  - Enzymes from lysosomes digest the material

**Phagocytes**
Internal Innate Defenses: Cells and Chemicals

- Natural killer (NK) cells
  - Can lyse (disintegrate or dissolve) and kill cancer cells
  - Can destroy virus-infected cells

Cells and Chemicals: Second Line of Defense

- Inflammatory response
  - Triggered when body tissues are injured
  - Four most common indicators of acute inflammation
    - Redness
    - Heat
    - Swelling
    - Pain
  - Results in a chain of events leading to protection and healing

Flowchart of Inflammatory Events

Cells and Chemicals: Second Line of Defense

- Functions of the inflammatory response
  - Prevents spread of damaging agents
  - Disposes of cell debris and pathogens through phagocytosis
  - Sets the stage for repair

Cells and Chemicals: Second Line of Defense

- Phagocytosis
  - Neutrophils move by diapedesis to clean up damaged tissue and/or pathogens
  - Monocytes become macrophages and complete disposal of cell debris

Cells and Chemicals: Second Line of Defense

- Antimicrobial proteins
  - Attack microorganisms
  - Hinder reproduction of microorganisms

- Most important
  - Complement proteins
  - Interferon

Cells and Chemicals: Second Line of Defense

- Complement proteins
  - A group of at least 20 plasma proteins
  - Activated when they encounter and attach to cells (complement fixation)
  - Damage foreign cell surfaces
  - Release vasodilators and chemotaxis chemicals, cause opsonization

Cells and Chemicals: Second Line of Defense

- Interferon
  - Proteins secreted by virus-infected cells
  - Bind to healthy cell surfaces to interfere with the ability of viruses to multiply
- Fever
  - Abnormally high body temperature
  - Hypothalamus heat regulation can be reset by pyrogens (secreted by white blood cells)
  - High temperatures inhibit the release of iron and zinc from the liver and spleen needed by bacteria
  - Fever also increases the speed of tissue repair

Summary of Nonspecific Body Defenses

Adaptive Defense System: Third Line of Defense
- Immune response is the immune system’s response to a threat
- Immunology is the study of immunity
- Antibodies are proteins that protect from pathogens

Adaptive Defense System: Third Line of Defense
- Three aspects of adaptive defense
  - Antigen specific—recognizes and acts against particular foreign substances
  - Systemic—not restricted to the initial infection site
  - Memory—recognizes and mounts a stronger attack on previously encountered pathogens

Adaptive Defense System: Third Line of Defense
- Types of Immunity
  - Humoral immunity = antibody-mediated immunity
    - Provided by antibodies present in body fluids
  - Cellular immunity = cell-mediated immunity
    - Targets virus-infected cells, cancer cells, and cells of foreign grafts

Adaptive Defense System: Third Line of Defense
- Antigens (nonself)
  - Any substance capable of exciting the immune system and provoking an immune response
  - Examples of common antigens
    - Foreign proteins (strongest)
    - Nucleic acids
    - Large carbohydrates
    - Some lipids
    - Pollen grains
    - Microorganisms

Adaptive Defense System: Third Line of Defense
- Self-antigens
  - Human cells have many surface proteins
  - Our immune cells do not attack our own proteins
  - Our cells in another person’s body can trigger an immune response because they are foreign
    - Restricts donors for transplants

Adaptive Defense System: Third Line of Defense
Allergies
- Many small molecules (called haptens or incomplete antigens) are not antigenic, but link up with our own proteins
- The immune system may recognize and respond to a protein-hapten combination
- The immune response is harmful rather than protective because it attacks our own cells

Adaptive Defense System: Third Line of Defense
- Cells of the adaptive defense system
  - Lymphocytes respond to specific antigens
    - B lymphocytes (B cells)
    - T lymphocytes (T cells)
  - Macrophages help lymphocytes

Immunocompetent—cell becomes capable of responding to a specific antigen by binding to it
- Cells of the adaptive defense system
  - Lymphocytes
    - Originate from hemocytoblasts in the red bone marrow
    - B lymphocytes become immunocompetent in the bone marrow
      (remember B for Bone marrow)
    - T lymphocytes become immunocompetent in the thymus
      (remember T for Thymus)

Lymphocyte Differentiation and Activation
- Cells of the adaptive defense system (continued)
  - Macrophages
    - Arise from monocytes
    - Become widely distributed in lymphoid organs
    - Secrete cytokines (proteins important in the immune response)
    - Tend to remain fixed in the lymphoid organs

Functions of Cells and Molecules Involved in Immunity

Humoral (Antibody-Mediated) Immune Response
- B lymphocytes with specific receptors bind to a specific antigen
- The binding event activates the lymphocyte to undergo clonal selection
- A large number of clones are produced (primary humoral response)

Humoral Immune Response
- Most B cells become plasma cells
  - Produce antibodies to destroy antigens
  - Activity lasts for 4 or 5 days
- Some B cells become long-lived memory cells (secondary humoral response)

Humoral Immune Response
- Secondary humoral responses
  - Memory cells are long-lived
A second exposure causes a rapid response
The secondary response is stronger and longer lasting

Active Immunity
- Occurs when B cells encounter antigens and produce antibodies
- Active immunity can be
  - Naturally acquired during bacterial and viral infections
  - Artificially acquired from vaccines

Passive Immunity
- Occurs when antibodies are obtained from someone else
  - Conferred naturally from a mother to her fetus (naturally acquired)
  - Conferred artificially from immune serum or gamma globulin (artificially acquired)
- Immunological memory does not occur
- Protection provided by “borrowed antibodies”

Monoclonal antibodies
- Antibodies prepared for clinical testing or diagnostic services
- Produced from descendents of a single cell line
- Examples of uses for monoclonal antibodies
  - Diagnosis of pregnancy
  - Treatment after exposure to hepatitis and rabies

Types of Acquired Immunity
Antibodies (Immunoglobulins or Igs)
- Soluble proteins secreted by B cells (plasma cells)
- Carried in blood plasma
- Capable of binding specifically to an antigen

Antibody Structure
- Antibody classes
  - Antibodies of each class have slightly different roles
  - Five major immunoglobulin classes (MADGE)
    - IgM—can fix complement
    - IgA—found mainly in mucus
    - IgD—important in activation of B cell
    - IgG—can cross the placental barrier and fix complement
    - IgE—involved in allergies
Antibody function
- Antibodies inactivate antigens in a number of ways
  - Complement fixation
  - Neutralization
  - Agglutination
  - Precipitation

Antibody Function

Cellular (Cell-Mediated) Immune Response
- Antigens must be presented by macrophages to an immunocompetent T cell (antigen presentation)
- T cells must recognize nonself and self (double recognition)
- After antigen binding, clones form as with B cells, but different classes of cells are produced

Cellular (Cell-Mediated) Immune Response
- T cell clones
  - Cytotoxic (killer) T cells
    - Specialize in killing infected cells
    - Insert a toxic chemical (perforin)
  - Helper T cells
    - Recruit other cells to fight the invaders
    - Interact directly with B cells

Cellular (Cell-Mediated) Immune Response (continued)
- Regulatory T cells
  - Release chemicals to suppress the activity of T and B cells
  - Stop the immune response to prevent uncontrolled activity

A few members of each clone are memory cells

Functions of Cells and Molecules Involved in Immunity

Summary of Adaptive Immune Response

Organ Transplants and Rejection

Major types of grafts
- Autografts—tissue transplanted from one site to another on the same person
- Isografts—tissue grafts from an identical person (identical twin)
- Allografts—tissue taken from an unrelated person
- Xenografts—tissue taken from a different animal species

Organ Transplants and Rejection
- Autografts and isografts are ideal donors
- Xenografts are never successful
- Allografts are more successful with a closer tissue match

Disorders of Immunity: Allergies (Hypersensitivity)
- Abnormal, vigorous immune responses
- Types of allergies
  - Immediate hypersensitivity
    - Triggered by release of histamine from IgE binding to mast cells
Reactions begin within seconds of contact with allergen
Anaphylactic shock—dangerous, systemic response

Disorders of Immunity: Allergies (Hypersensitivity)
- Types of allergies (continued)
  - Delayed hypersensitivity
    - Triggered by the release of lymphokines from activated helper T cells
    - Symptoms usually appear 1–3 days after contact with antigen

Allergy Mechanisms
Disorders of Immunity: Immunodeficiencies
- Production or function of immune cells or complement is abnormal
- May be congenital or acquired
- Includes AIDS (Acquired Immune Deficiency Syndrome)

Disorders of Immunity: Autoimmune Diseases
- The immune system does not distinguish between self and nonself
- The body produces antibodies and sensitized T lymphocytes that attack its own tissues

Disorders of Immunity: Autoimmune Diseases
- Examples of autoimmune diseases
  - Multiple sclerosis—white matter of brain and spinal cord are destroyed
  - Myasthenia gravis—impairs communication between nerves and skeletal muscles
  - Type I diabetes mellitus—destroys pancreatic beta cells that produce insulin

Disorders of Immunity: Autoimmune Diseases
- Examples of autoimmune diseases
  - Rheumatoid arthritis—destroys joints
  - Systemic lupus erythematosus (SLE)
    - Affects kidney, heart, lung and skin
  - Glomerulonephritis—impairment of renal function

Self Tolerance Breakdown
- Inefficient lymphocyte programming
- Appearance of self-proteins in the circulation that have not been exposed to the immune system
  - Eggs
  - Sperm
  - Eye lens
  - Proteins in the thyroid gland

Self Tolerance Breakdown
- Cross-reaction of antibodies produced against foreign antigens with self-antigens
  - Rheumatic fever

Developmental Aspects of the Lymphatic System and Body Defenses
- Except for thymus and spleen, the lymphoid organs are poorly developed before birth
- A newborn has no functioning lymphocytes at birth, only passive immunity from the mother
- If lymphatics are removed or lost, severe edema results, but vessels grow back in time