Lecture Outline: The Lymphatic System and Immunity

I. **The Lymphatic System and Immunity**

A. **Immune System vs. Lymphatic System**

1. The "immune system" describes a system of structures and processes that provide immunity, but it is **not an official organ system** itself and is not one of the 11 organ systems.
2. It involves structures spread across several different organ systems, including the lymphatic system and the digestive system.

B. **Role of the Lymphatic System**

1. It picks up fluid called **lymph** that continuously leaks out of the circulatory system at capillary beds.
2. Without the lymphatic vessels to pick up this leaked fluid, **edema** (swelling due to fluid buildup) would occur and could be dangerous.
3. Its major functions are to **return lost fluid to the bloodstream** and to **protect the body (immunity)**.

C. **Lymphatic Vessels**

1. **Lymph:** Fluid that originates from blood plasma that leaks out of blood capillaries, becoming extracellular fluid, and then is picked up by lymphatic vessels.
2. **Blinded Vessels:** Lymphatic vessels are not a closed loop; they have "blind ends" representing their starting points.
3. **Drainage Pathway:** Lymph travels through increasingly larger

lymphatic vessels, eventually forming large lymphatic ducts that dump directly into major veins (subclavian veins) in the shoulders, returning the fluid to the bloodstream. Lymph does not circulate like blood.

4. **Structure of Lymphatic Capillaries:**
    a. Their epithelial cells **overlap like shingles**, forming flap valves that allow fluid to enter but prevent it from flowing back out.
    b. **Connective tissue filaments** anchor these blind-ended capillaries to surrounding tissues, keeping them in place.
5. **Drainage Asymmetry:**
    a. Approximately **one-quarter of the body** (the upper right region) drains its lymph into the **right subclavian vein** via a lymphatic duct.
    b. The remaining **three-quarters of the body** drains into the **left thoracic duct** (the largest lymphatic vessel), which empties into the **left subclavian vein**.

II. **Lymph Nodes**

A. **Location and Number:** There are hundreds (approximately 400-500) of lymph nodes distributed throughout the body, often clustered in regions like the armpit (axillary nodes) and groin (inguinal nodes).

B. **Function:** Their primary role is immunity. Lymph must flow directly through them, allowing specialized cells inside to survey (surveil) the lymph for invading microorganisms and other harmful substances, which are then dealt with and killed.

C. **Structure:**

1. **Afferent and Efferent Vessels:** Lymph enters a lymph node through several smaller **afferent lymphatic vessels** and

leaves through fewer, larger **efferent lymphatic vessels**.

2. **Capsule and Follicles:** Each lymph node is enclosed by a fibrous connective tissue capsule. Inside, the node is subdivided into chambers or centers called **follicles**, which contain various white blood cells. The superficial interior is called the cortex, and the deeper part is the medulla.
3. **Hilum:** An indentation on the lymph node's surface, similar to that of a kidney, where the efferent vessels are located.

III. **Other Lymphatic Structures**

A. **Tonsils:** There are three major pairs of tonsils located in the pharyngeal (throat) region. They contain lymphatic tissue rich in protective white blood cells, positioned to defend against pathogens entering through the mouth.

B. **Thymus:**

1. Located in the mediastinum, between the lungs.
2. It is **most active and largest during youth**, gradually shrinking with age.
3. Its primary job is the **maturation of T lymphocytes** (T-cells), which originate in the bone marrow but travel to the thymus to develop into active, protective forms.

C. **Spleen:**

1. Located in the extreme upper left abdomen, next to the stomach.
2. Its major function is to **filter out old, dead, or non-functional red blood cells** (erythrocytes) from the blood.
3. Red blood cells are anucleated and wear out quickly from being squeezed through capillaries, requiring constant replacement and removal by the spleen. The spleen breaks them down, and raw materials are recycled.

D. **Peyer's Patches:** These are lymphatic tissues (lymphoid tissue) scattered throughout the small intestine. They protect against pathogens that might enter the body where nutrients are absorbed from food.

E. **Appendix:**

1. Located on the cecum (a pouch-like part of the large intestine).
2. Contains lymphoid tissue and contributes to immune function, similar to tonsils and Peyer's patches.
3. Often described as a **vestigial organ** as it is not essential for human survival.

IV. **Body Defenses: Innate (Non-specific) and Adaptive (Specific) Immunity**

A. **Innate Defenses (First and Second Lines of Defense):** These are inborn defense mechanisms that operate continuously and in the same non-specific way, regardless of the pathogen.

1. **First Line of Defense: External Barriers** – The initial defenses at the body's exterior.

a. **Skin (Epidermis):**

(1) A strong **mechanical barrier** that many harmful substances cannot penetrate.

(2) Produces **acidic secretions (acid mantle)** and **sebum** (body oil containing bactericidal chemicals) that inhibit bacterial growth on its surface.

(3) **Keratin**, a major protein in the skin, makes it resistant to harmful chemicals.

e. **Mucous Membranes:** Linings of body openings (e.g., vagina, mouth, throat, alimentary canal). They produce **mucus**, a sticky substance that traps microorganisms and

debris, preventing them from entering the body, and also acts as a lubricant.

f. **Hairs:** Such as those in the nostrils, act as filters to trap large particles in inhaled air.

g. **Cilia:** Hair-like projections on cells lining the trachea move rhythmically to sweep mucus-trapped particles upward into the pharynx, where they are swallowed.

h. **Gastric Juice (Stomach):** The stomach's extremely low pH (high acidity) makes it highly inhospitable, destroying most pathogens swallowed into it.

i. **Acid Mantle (Vagina):** The acidic environment inhibits bacterial growth, similar to the skin.

j. **Lacrimal Secretions (Tears):** Lubricate the eyes and contain **lysozyme**, an enzyme that destroys invading microorganisms.

2. **Second Line of Defense: Internal Defenses** – Mechanisms that activate if pathogens breach the first line.

a. **Phagocytic Cells (Phagocytes):** Specialized cells that survey the body, recognize foreign or abnormal substances (like bacteria), and engulf them via **phagocytosis** to dismantle and render them harmless.

b. **Natural Killer (NK) Cells:** Cells of the body that recognize and kill the body's own cells that have become problematic, such as those infected by viruses or cancerous cells, preventing them from reproducing.

c. **Antimicrobial Proteins:** Proteins produced by normal body cells that prevent unicellular organisms from establishing themselves.

(1) **Complement:** A collection of plasma proteins that can lyse (split open) invading microorganism cells.

(2) **Interferons:** Signal molecules released by virus-infected cells to alert neighboring cells and trigger protective responses.

f. **Inflammatory Response (Inflammation):** A complex set of local occurrences in response to tissue damage or infection, characterized by redness, heat, pain, and swelling.

g. **Fever:** An elevated body temperature in response to substances called **pyrogens**. Fever helps protect the body by speeding up beneficial chemical reactions and making it harder for certain pathogens to survive or reproduce. Medicines to reduce fever are called **antipyretics**.

B. **Adaptive Defenses (Third Line of Defense):** These defense mechanisms are specific and acquired throughout a person's lifetime, adapting based on exposure to different pathogens or dangerous particles.

1. **Lymphocytes:** The major cell types responsible for these specific or adaptive defense mechanisms (e.g., T lymphocytes and B lymphocytes).
2. **Antibodies:** Y-shaped proteins produced by lymphocytes that have a specific shape at one end to recognize and bind to foreign material, known as **antigens**. This is a specific defense mechanism.
3. **Macrophages (Antigen Presenting Cells):** Specialized white blood cells that engulf foreign material (antigens), break them into pieces, and then display those pieces on their own surface. This allows other immune cells (like lymphocytes) to recognize the antigens.

V. **Mechanisms of Defense**

A. **Inflammatory Response Process:**

1. **Injurious Agent:** Damage (e.g., a cut) or infection occurs, damaging cells, including those lining blood vessels.
2. **Chemical Signals:** Damaged cells and proteins in the blood release chemical signals (e.g., kinins, histamine) into the affected area.
3. **Vasodilation:** These signals cause blood vessels in the injured area to **dilate (increase in diameter)**, bringing more blood and protective components to the site.
4. **Increased Capillary Leakiness:** Blood capillaries in the affected area become significantly more leaky, allowing fluid and immune cells to exit the bloodstream and accumulate in the surrounding tissue.
5. **Cardinal Signs of Inflammation:**
    a. **Redness:** Caused by the increased blood flow to the area.
    b. **Heat:** Also caused by the increased blood flow, delivering heat from the body's core and speeding up metabolic reactions.
    c. **Swelling (Edema):** Results from the accumulation of fluid that has leaked out of the capillaries into the tissue.
    d. **Pain:** Caused by pressure from the swelling on free nerve endings, which serves to signal the body to rest and allow healing of the injured part.
6. **Recruitment of White Blood Cells:** Chemical signals released during inflammation attract specific white blood cells, such as neutrophils and monocytes, from the bloodstream to the affected area.
7. **Diapedesis:** White blood cells actively squeeze between the cells lining the capillaries to leave the bloodstream and enter the injured tissue.

8. **Hemostasis:** The inflammatory response is often accompanied by **hemostasis**, the stoppage of bleeding, which involves complex chemical clotting processes.

B. **Phagocytosis:** The process by which phagocytes engulf and destroy foreign or harmful particles.
    1. **Engulfment (Phagosome formation):** The phagocyte extends its plasma membrane around the foreign body (antigen or pathogen), sealing it off within a vesicle called a **phagosome**.
    2. **Fusion with Lysosome (Phagolysosome):** The phagosome then fuses with a **lysosome**, another vesicle inside the cell that contains hydrolytic enzymes. This combined vesicle is called a phagolysosome.
    3. **Digestion and Exocytosis:** The lysosomal enzymes break down the foreign material into harmless raw materials. These materials can then be expelled from the cell (exocytosis) or recycled for the body's own use.

C. **Antibody Function:** Antibodies, which are Y-shaped proteins, recognize and bind to specific antigens, leading to various protective effects.
    1. **Structure of Antibodies:**
        a. **Y-shape with binding tips:** Antibodies have a distinctive Y-shape with two identical binding sites at the tips of the "Y" arms, each precisely shaped to bind to a specific antigen.
        b. **Constant and Variable Regions:** Each antibody has a "constant" region (C) with the same amino acid sequence across all antibodies, and a "variable" region (V) at the binding tips, which gives each antibody its unique shape and antigen specificity.

2. **Mechanisms of Action (when bound to antigen):** Once an antibody binds to its specific antigen, it triggers various protective responses:
    a. **Neutralization:** Antibodies bind to and cover the antigen, making it unable to interact with body cells and cause damage.
    b. **Agglutination:** Antibodies can clump together foreign cells (e.g., incompatible red blood cells during a transfusion) by binding to multiple cells simultaneously.
    c. **Precipitation:** Antibodies can cause soluble antigens to precipitate (fall out) of solution, making them less harmful.
    d. **Complement Activation (Membrane Attack Complex - MAC):** Antibody-antigen binding can activate the complement system, leading to the formation of a **Membrane Attack Complex (MAC)**, which creates holes in the membrane of invading cells, causing them to lyse (explode).
    e. **Enhancement of Phagocytosis and Inflammation:** Antibody-antigen complexes are easily recognized and engulfed by phagocytic cells. Complement activation also enhances the inflammatory response.

VI. **Lymphocyte Development and Immunity Types**

A. **Origin of Blood Cells:** All formed elements of blood, including red blood cells, white blood cells (like lymphocytes), and platelets, are created from **hemopoietic stem cells in the red bone marrow**.

B. **Lymphocyte Types:** The two main types of lymphocytes involved in adaptive immunity are T lymphocytes and B lymphocytes.
    1. **T Lymphocytes (T-cells):** Originate in the bone marrow but

travel to and **mature in the thymus** (hence "T"), where they are exposed to the specific things they will recognize. Once mature (immunocompetent), they reside in lymph nodes.

2. **B Lymphocytes (B-cells):** Originate in the bone marrow and travel **directly to the lymph nodes** without going through the thymus.

C. **Immunocompetence and Antigen Activation:**

1. **Immunocompetent:** Describes a lymphocyte that has matured into its active form.
2. **Naive Lymphocyte:** An immunocompetent lymphocyte that has not yet been exposed to the specific antigen it is destined to recognize.
3. **Antigens:** Foreign particles or substances that antibodies recognize as non-self.
4. **Antigen-activated:** Refers to a lymphocyte that has recognized and bound to its specific antigen.

D. **Antibody Diversity:** The body produces millions of different kinds of antibodies, each with a unique variable region designed to recognize a specific antigen. This diversity is achieved by the ability of antibody genes to be scrambled and rearranged. Antibodies are produced randomly and continuously.

E. **Vaccines:** Work by introducing inactivated or partial pathogens (antigens) into the bloodstream. These antigens do not cause disease but are recognized by existing antibodies, triggering the body to produce a large "army" of specific antibodies and memory cells, providing future immunity against the actual pathogen.

F. **Primary vs. Secondary Immune Response:**

1. **Clonal Selection:** When a B cell (with specific antibodies on its surface) recognizes and binds to its corresponding antigen,

it is signaled to produce many identical copies of itself, forming a "clone" of B cells.

2. **Plasma Cells:** Some cells from the clone develop into **plasma cells**, which are specialized B cells that actively secrete large amounts of specific antibodies into the blood plasma.
3. **Memory B Cells:** Other cells from the clone develop into **memory B cells**. These cells retain the specific antibodies on their surface and persist in the body for many years or even a lifetime. They provide a rapid and strong **secondary immune response** if the same antigen is encountered again, preventing disease symptoms.

G. **Humoral Immunity:** Refers to immunity involving body fluids (humors), primarily mediated by antibodies circulating in the blood plasma.

1. **Active Humoral Immunity:** The body actively produces its own antibodies in response to antigen exposure.
    a. **Naturally Acquired:** Achieved through natural exposure to a pathogen (e.g., getting sick with a cold virus).
    b. **Artificially Acquired:** Achieved intentionally through exposure to antigens that do not cause disease (e.g., through vaccination).
2. **Passive Humoral Immunity:** Antibodies are acquired from an external source; the body does not produce its own antibodies.
    a. **Naturally Acquired:** Antibodies are passed from a mother to her fetus across the placenta, or to an infant through breast milk.
    b. **Artificially Acquired:** Antibodies produced by one person (or animal) are injected into another person to provide

temporary immunity (e.g., antitoxins).

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