Chapter 07
Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.
The Lymphatic and Immune Systems
Points to ponder

- What are the parts of the lymphatic system and what are their functions?
- What are the first and second lines of defense in nonspecific immunity?
- What is cell-mediated and antibody-mediated immunity in the third line of defense?
- What are the different types of B cells in these processes?
- What is active and passive immunity? Be able to describe how they are different and examples of each.
- Understand allergic reactions, tissue rejection, and immune system disorders as problems that the immune system faces.
Functions of the lymphatic system

• Lymphatic capillaries absorb excess tissue fluid and return it to the bloodstream.

• Lymphatic capillaries (lacteals) in the small intestine absorb fats associated with proteins.

• The lymphatic system works in the production, maintenance, and distribution of lymphocytes in the body.

• It helps in defense against pathogens.
What are the components of the lymphatic system?

- **Tonsil**: patches of lymphatic tissue; help to prevent entrance of pathogens by way of the nose and mouth.
- **Red bone marrow**: site for the origin of all types of blood cells.
- **Thymus**: lymphatic tissue where T lymphocytes mature and learn to tell "self" from "nonself".
- **Spleen**: cleanses the blood of cellular debris and bacteria, while resident lymphocytes respond to the presence of antigens.
- **Inguinal lymph nodes**: located in the groin region; cleanse lymph and alert the immune system to pathogens.
- **Thoracic duct**: empties lymph into the left subclavian vein.
- **Axillary lymph nodes**: located in the underarm region.
- **Right lymphatic duct**: empties lymph into the right subclavian vein.

*Figure 7.1 Functions of the lymphatic system components.*
Lymphatic vessels

• One-way valve system that carries fluid called lymph

• Made of capillaries, vessels, and ducts

• Function to return tissue fluid (which includes water, solutes, and cell products) to the bloodstream

• Larger vessels are similar in structure to veins and even have valves
Classifying lymphatic organs

- **Primary**
  - Red bone marrow
  - Thymus

Figure 7.2 Tissue samples from primary lymphatic organs.
Classifying lymphatic organs

- **Secondary**
  - Lymph nodes
  - Spleen

*Figure 7.2* Tissue samples from secondary lymphatic organs.
Primary lymphatic organs

• **Red bone marrow**
  – It is the site of blood cell production.
  – More bones in children have red marrow and it decreases as we age.
  – Some white blood cells mature here.

• **Thymus**
  – It is a bilobed gland found in the thoracic cavity superior to the heart.
  – It is largest in children and shrinks as we age.
  – Immature T lymphocytes move from the marrow to the thymus where they mature and 95% will stay.
Secondary lymphatic organs

• **Lymph nodes**
  – Small, oval-shaped structures found along the lymphatic vessels
  – Filled with B cells, T cells, and macrophages
  – Common in the neck, armpit, and groin regions

• **Spleen**
  – In the upper left region of the abdominal cavity
  – Filled with white pulp containing lymphocytes, and red pulp which is involved with filtering the blood
What do the nonspecific defenses include?

- **First line of defense**
  - Barriers to entry: physical and chemical

- **Second line of defense**
  - Phagocytic white blood cells
  - Inflammatory response
  - Protective proteins: complement and interferons
What are the innate immune defenses?

Figure 7.3 Overview of innate immune defenses.
The first line of defense

- Physical barriers
  - The skin is an effective physical barrier.
  - Tears, saliva, and urine physically flush out microbes.
  - Mucous membranes line the respiratory, digestive, reproductive, and urinary tracts.
  - Resident bacteria/normal flora that inhabit the body use available nutrients and space thus preventing pathogens from taking up residence.
The first line of defense

• Chemical barriers
  – Secretions of the oil glands
  – **Lysozyme** found in saliva, tears, and sweat
  – Acidic pH of the stomach and vagina
The second line of defense: Phagocytic white blood cells

- Includes neutrophils and macrophages
- Both leave circulation and move into tissue
- Are important in the inflammatory response
The second line of defense: Inflammatory response

- Four hallmark symptoms are redness, heat, swelling, and pain.

- **Histamine**, released by mast cells, causes the capillaries to dilate and become more permeable to phagocytic white blood cells.

- Increased blood flow to an area increases warmth, inhibiting some pathogens.
Increased blood flow also brings more white blood cells to an injured area, with neutrophils being the first scouts to kill pathogens.

This response can be short-lived, but if the neutrophils cannot control the damage, cytokines (chemicals) will call in more white blood cells including macrophages.
Summary of the inflammatory response

1. Injured tissue cells and mast cells release histamine, which causes capillaries to dilate and increases blood flow.

2. Macrophages phagocytize pathogens and release cytokines, which stimulate the inflammatory response.

3. Neutrophils and monocytes (become macrophages) squeeze through the capillary wall and phagocytize pathogens.

4. Blood clotting walls off capillary and prevents blood loss.

Figure 7.4 Steps of the inflammatory response.
The second line of defense: Protective proteins

- **Complement**
  - Group of blood plasma proteins
  - Involved in the inflammatory response by binding to mast cells, causing them to release histamine
  - Attract phagocytes to pathogens by binding them
  - Form a membrane attack complex that makes holes in some bacteria and viruses, causing them to burst

- **Interferons**
  - Proteins produced by virus-infected cells sent out to warn neighboring healthy cells
The second line of defense: Protective proteins

Figure 7.5 Action of the complement system
What do the specific defenses include?

• Third line of defense
  – Helps protect us against specific pathogens when nonspecific defenses fail
  – Helps protect us against cancer
  – Depends on the action of B and T cells (remember that these are lymphocytes)
What are the types of B and T cells?

• B cells produce plasma cells and memory cells.
  – Plasma cells produce specific antibodies.
  – Memory cells are ready to produce antibodies in the future.
What are the types of B and T cells?

- T cells regulate immune response; produce various types of T cells.
  - Cytotoxic T (T_c) cells kill virus-infected and cancer cells.
  - Helper T (T_H) cells regulate immunity.
  - Memory T (T_c and T_H) cells are ready to kill in the future.
What are the types of B and T cells?

Figure 7.6 Overview of adaptive immune defenses.
What are the characteristics of B cells?

- Antibody-mediated immunity against pathogens
- Produced and mature in bone marrow
- Directly recognize antigen and then undergo clonal selection
- Clonal expansion produces antibody-secreting plasma cells as well as memory B cells
Third line of defense: Antibody-mediated immunity by B cells

- Each B cell has a unique receptor called a BCR that binds a specific antigen.
- This binding and cytokines secreted by helper T cells result in clonal expansion in which this B cell makes copies of itself.
- Most of the cells produced are plasma cells that secrete antibodies.
Third line of defense: Antibody-mediated immunity by B cells

- Other cells become memory cells which result in long-term immunity.

- After an infection has passed, plasma cells undergo apoptosis (programmed cell death) leaving memory cells.
7.3 Adaptive Immune Defenses

Antibody-mediated immunity by B cells

a. Activation: When a B cell receptor binds to an antigen, activation occurs.

b. Clonal expansion – During clonal expansion, cytokines secreted by helper T cells stimulate B cells to clone mostly into plasma cells or memory cells.

c. Apoptosis – Apoptosis, or programmed cell death, occurs to plasma cells left in the system after the infection has passed.

Figure 7.7 B cell clonal selection.
Structure of antibodies

• The basic unit that composes antibody molecules is a Y-shaped protein.

• The trunk of the Y is a constant region that determines the class of the antibody.

• The ends of the arms (Y) are the variable regions where specific antigens bind.
7.3 Adaptive Immune Defenses

Structure of antibodies

Figure 7.8 The structure of an antibody.

a. Antigen binds to binding site. Shape of antigen fits shape of binding site.

b. Courtesy Dr. Arthur J. Olson, Scripps Institute
### What are the 5 classes of antibodies?

<table>
<thead>
<tr>
<th>Class</th>
<th>Presence</th>
<th>Function</th>
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<tbody>
<tr>
<td>IgG</td>
<td>Main antibody type in circulation; crosses the placenta from mother to fetus</td>
<td>Binds to pathogens, activates complement, and enhances phagocytosis by white blood cells</td>
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<tr>
<td>IgM</td>
<td>Antibody type found in circulation; largest antibody; first antibody formed by a newborn; first antibody formed with any new infection</td>
<td>Activates complement; clumps cells</td>
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<tr>
<td>IgA</td>
<td>Main antibody type in secretions such as saliva and milk</td>
<td>Prevents pathogens from attaching to epithelial cells in digestive and respiratory tract</td>
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<tr>
<td>IgD</td>
<td>Antibody type found on surface of immature B cells</td>
<td>Presence signifies readiness of B cell</td>
</tr>
<tr>
<td>IgE</td>
<td>Antibody type found as antigen receptors on mast cells in tissues</td>
<td>Responsible for immediate allergic response and protection against certain parasitic worms</td>
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</tbody>
</table>
How do we make monoclonal antibodies?

- We make **monoclonal antibodies** (derived from plasma cells that originated from the same B cell) in glassware outside the body (in vitro).

- This is done through fusion of plasma cells with myeloma cells that allow them to divide indefinitely.

- This fusion results in a cell called a hybridoma.
7.3 Adaptive Immune Defenses

How do we make monoclonal antibodies?

Figure 7.9 The production of monoclonal antibodies.
What are the characteristics of T cells?

- Cell-mediated immunity against virus-infected cells and cancer cells
- Produced in bone marrow, mature in thymus
- Antigen must be presented in groove of an HLA (MHC) molecule
- Cytotoxic T cells destroy nonself antigen-bearing cells
- Helper T cells secrete cytokines that control the immune response
Third line of defense: Cell-mediated immunity by T cells

- Each T cell has a unique receptor called a TCR that will recognize a piece of an antigen with the help of an antigen-presenting cell (APC).

- An APC engulfs an antigen, breaks it down, and presents it on its surface in association with a membrane protein called an MHC (called human leukocyte antigens in humans or HLA) then presents it to T cells in the lymph node or spleen.
Third line of defense: Cell-mediated immunity by T cells

- The T cell will specifically recognize the combination of the HLA protein and the piece of antigen.

- Clonal expansion will occur leading to mostly helper T cells, cytotoxic T cells, and a few memory T cells.

- After an infection has passed, helper and cytotoxic T cells undergo apoptosis, leaving memory cells.
Cell-mediated immunity by T cells

**Figure 7.10** The clonal selection model for T cells.
Helper and cytotoxic T cells

• **Helper T cells**
  – secrete cytokines that help many immune cells function.

• **Cytotoxic T cells**
  – have vacuoles containing granzymes and perforins.
  – Perforins punch holes in target cells, followed by granzymes that cause the cell to undergo apoptosis.

*Figure 7.11* How cytotoxic T cells kill infected cells.
Immunity

• **Immunity** is the ability to combat diseases and cancer.

• It can be brought about naturally through an infection or artificially through medical intervention.

• There are 2 types of immunity, **active** and **passive**.
Active immunity

- The individual’s body makes antibodies against a particular antigen.
- This can happen through natural infection or through immunization involving vaccines.
- Primary exposure is shorter-lived and slower to respond while a secondary exposure is a rapid, strong response.
- This type of immunity is usually long-lasting.
- It depends on memory B and T cells.
Immunization: A type of active immunity

Figure 7.12 How immunizations cause active immunity.
Passive immunity

- An individual is given antibodies against a particular antigen.
- This type of immunity is short-lived.
- This can happen naturally as antibodies are passed across the placenta or during breastfeeding, or artificially via an injection of antibodies.

Figure 7.13 Delivery mechanisms of passive immunity.
How can the immune system harm the body?

- Allergies
- Tissue rejection
- Immune system disorders
Allergies are hypersensitivities to harmless substances such as pollen, food, or animal hair.

An immediate allergic response is caused by the IgE antibodies that attach to mast cells and basophils. When allergens attach to these IgE molecules, histamine is released and we see allergy symptoms.

An immediate allergic response that occurs when the allergen enters the bloodstream is anaphylactic shock, in which the blood pressure drops and is life-threatening.

Delayed allergic responses (such as the reaction to poison ivy) are initiated by memory T cells.
Tissue rejection

- Tissue rejection can occur when cytotoxic T cells respond to tissue that is not recognized as “self.”

- This can be controlled by giving patients immunosuppressive drugs and by transplanting organs that have the same MHC proteins in the donor and recipient.

- Currently, we are trying to grow organs in the lab that can be transplanted with less rejection.
Disorders of the immune system

- **Autoimmune disease**
  - A disease in which cytotoxic T cells or antibodies attack the body’s own cells as if they were foreign
  - Examples: multiple sclerosis, lupus, myasthenia gravis, and rheumatoid arthritis

- **Immunodeficiency disease**
  - A disease in which the immune system is compromised and thus unable to defend the body against disease
  - Examples: AIDS and SCID