Overview: Reconnaissance, Recognition, and Response

- Barriers help an animal to defend itself from the many dangerous pathogens it may encounter.
- The immune system recognizes foreign bodies and responds with the production of immune cells and proteins.
- Two major kinds of defense have evolved: innate immunity and acquired immunity.

Innate immunity is present before any exposure to pathogens and is effective from the time of birth.
- It involves nonspecific responses to pathogens.
- Innate immunity consists of external barriers plus internal cellular and chemical defenses.

Acquired immunity, or adaptive immunity, develops after exposure to agents such as microbes, toxins, or other foreign substances.
- It involves a very specific response to pathogens.

<table>
<thead>
<tr>
<th>Innate Immunity</th>
<th>Acquired Immunity</th>
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<tr>
<td>Recognition of traits shared by broad ranges of pathogens, using a small set of receptors.</td>
<td>Recognition of traits specific to particular pathogens, using a vast array of receptors.</td>
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<tr>
<td>Rapid response.</td>
<td>Slower response.</td>
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Pathogens (microorganisms and viruses)

- Barrier defenses: Skin, mucous membranes, secretions.
- Internal defenses: Phagocytic cells, antimicrobial proteins, inflammatory responses, natural killer cells.
- Humoral response: Antibodies defend against infection in body fluids.
- Cell-mediated response: Cytotoxic lymphocytes defend against infection in body cells.
**Concept 43.1: In innate immunity, recognition and response rely on shared traits of pathogens**

- Both invertebrates and vertebrates depend on innate immunity to fight infection
- Vertebrates also develop acquired immune defenses

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**Innate Immunity of Invertebrates**

- In insects, an exoskeleton made of chitin forms the first barrier to pathogens
- The digestive system is protected by low pH and lysozyme, an enzyme that digests microbial cell walls
- Hemocytes circulate within hemolymph and carry out phagocytosis, the ingestion and digestion of foreign substances including bacteria

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- Hemocytes also secrete antimicrobial peptides that disrupt the plasma membranes of bacteria

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- The immune system recognizes bacteria and fungi by structures on their cell walls
- An immune response varies with the class of pathogen encountered
Innate Immunity of Vertebrates

- The immune system of mammals is the best understood of the vertebrates
- Innate defenses include barrier defenses, phagocytosis, antimicrobial peptides
- Additional defenses are unique to vertebrates: the inflammatory response and natural killer cells

Barrier Defenses

- Barrier defenses include the skin and mucous membranes of the respiratory, urinary, and reproductive tracts
- Mucus traps and allows for the removal of microbes
- Many body fluids including saliva, mucus, and tears are hostile to microbes
- The low pH of skin and the digestive system prevents growth of microbes

Cellular Innate Defenses

- White blood cells (leukocytes) engulf pathogens in the body
- Groups of pathogens are recognized by TLR, Toll-like receptors
Antimicrobial Peptides and Proteins

- Peptides and proteins function in innate defense by attacking microbes directly or impeding their reproduction.
- Interferon proteins provide innate defense against viruses and help activate macrophages.
- About 30 proteins make up the complement system, which causes lysis of invading cells and helps trigger inflammation.

Inflammatory Responses

- Following an injury, mast cells release histamine, which promotes changes in blood vessels; this is part of the inflammatory response.
- These changes increase local blood supply and allow more phagocytes and antimicrobial proteins to enter tissues.
- Pus, a fluid rich in white blood cells, dead microbes, and cell debris, accumulates at the site of inflammation.
Inflammation can be either local or systemic (throughout the body)

- Fever is a systemic inflammatory response triggered by pyrogens released by macrophages, and toxins from pathogens
- **Septic shock** is a life-threatening condition caused by an overwhelming inflammatory response

**Natural Killer Cells**

- All cells in the body (except red blood cells) have a class 1 MHC protein on their surface
- Cancerous or infected cells no longer express this protein; **natural killer (NK) cells** attack these damaged cells

**Innate Immune System Evasion by Pathogens**

- Some pathogens avoid destruction by modifying their surface to prevent recognition or by resisting breakdown following phagocytosis
- Tuberculosis (TB) is one such disease and kills more than a million people a year

**Concept 43.2: In acquired immunity, lymphocyte receptors provide pathogen-specific recognition**

- White blood cells called **lymphocytes** recognize and respond to antigens, foreign molecules
- Lymphocytes that mature in the **thymus** above the heart are called **T cells**, and those that mature in bone marrow are called **B cells**

**Acquired Immunity: An Overview**

- Lymphocytes contribute to immunological memory, an enhanced response to a foreign molecule encountered previously
- **Cytokines** are secreted by macrophages and dendritic cells to recruit and activate lymphocytes
- B cells and T cells have receptor proteins that can bind to foreign molecules
- Each individual lymphocyte is specialized to recognize a specific type of molecule
Antigen Recognition by Lymphocytes

- An antigen is any foreign molecule to which a lymphocyte responds
- A single B cell or T cell has about 100,000 identical antigen receptors

The Antigen Receptors of B Cells and T Cells

- Secreted antibodies, or immunoglobulins, are structurally similar to B cell receptors but lack transmembrane regions that anchor receptors in the plasma membrane

- B cell receptors bind to specific, intact antigens
- The B cell receptor consists of two identical heavy chains and two identical light chains
- The tips of the chains form a constant (C) region, and each chain contains a variable (V) region, so named because its amino acid sequence varies extensively from one B cell to another

- All antigen receptors on a single lymphocyte recognize the same epitope, or antigenic determinant, on an antigen
- B cells give rise to plasma cells, which secrete proteins called antibodies or immunoglobulins
Each T cell receptor consists of two different polypeptide chains.

- The tips of the chain form a variable (V) region; the rest is a constant (C) region.
- T cells can bind to an antigen that is free or on the surface of a pathogen.

T cells bind to antigen fragments presented on a host cell.

- These antigen fragments are bound to cell-surface proteins called MHC molecules.
- MHC molecules are so named because they are encoded by a family of genes called the major histocompatibility complex.

The Role of the MHC

- In infected cells, MHC molecules bind and transport antigen fragments to the cell surface, a process called antigen presentation.
- A nearby T cell can then detect the antigen fragment displayed on the cell’s surface.
- Depending on their source, peptide antigens are handled by different classes of MHC molecules.

Class I MHC molecules are found on almost all nucleated cells of the body.

- They display peptide antigens to cytotoxic T cells.

Fig. 43-11

Top view: binding surface exposed to antigen receptors

Antigen

Class I MHC molecule

Plasma membrane of infected cell

Fig. 43-12

Infected cell

Antigen fragment

Class I MHC molecule

T cell receptor

(a) Cytotoxic T cell

Class II MHC molecule

T cell receptor

(b) Helper T cell

Microbe

Antigen-presenting cell

Antigen fragment

Antigen associates with MHC molecule

T cell recognizes combination
Class II MHC molecules are located mainly on dendritic cells, macrophages, and B cells. Dendritic cells, macrophages, and B cells are antigen-presenting cells that display antigens to cytotoxic T cells and helper T cells.

Lymphocyte Development

The acquired immune system has three important properties:
- Receptor diversity
- A lack of reactivity against host cells
- Immunological memory

Generation of Lymphocyte Diversity by Gene Rearrangement

- Differences in the variable region account for specificity of antigen receptors
- The immunoglobulin (Ig) gene encodes one chain of the B cell receptor
- Many different chains can be produced from the same Ig chain gene by rearrangement of the DNA
- Rearranged DNA is transcribed and translated and the antigen receptor formed

Origin of Self-Tolerance

- Antigen receptors are generated by random rearrangement of DNA
- As lymphocytes mature in bone marrow or the thymus, they are tested for self-reactivity
- Lymphocytes with receptors specific for the body’s own molecules are destroyed by apoptosis, or rendered nonfunctional

Amplifying Lymphocytes by Clonal Selection

- In the body there are few lymphocytes with antigen receptors for any particular epitope
- The binding of a mature lymphocyte to an antigen induces the lymphocyte to divide rapidly
- This proliferation of lymphocytes is called clonal selection
- Two types of clones are produced: short-lived activated effector cells and long-lived memory cells
• The first exposure to a specific antigen represents the primary immune response.
• During this time, effector B cells called plasma cells are generated, and T cells are activated to their effector forms.
• In the secondary immune response, memory cells facilitate a faster, more efficient response.

Concept 43.3: Acquired immunity defends against infection of body cells and fluids.
• Acquired immunity has two branches: the humoral immune response and the cell-mediated immune response.
• Humoral immune response involves activation and clonal selection of B cells, resulting in production of secreted antibodies.
• Cell-mediated immune response involves activation and clonal selection of cytotoxic T cells.
• Helper T cells aid both responses.
Helper T Cells: A Response to Nearly All Antigens

- A surface protein called CD4 binds the class II MHC molecule
- This binding keeps the helper T cell joined to the antigen-presenting cell while activation occurs
- Activated helper T cells secrete cytokines that stimulate other lymphocytes

Cytotoxic T Cells: A Response to Infected Cells

- Cytotoxic T cells are the effector cells in cell-mediated immune response
- Cytotoxic T cells make CD8, a surface protein that greatly enhances interaction between a target cell and a cytotoxic T cell
- Binding to a class I MHC complex on an infected cell activates a cytotoxic T cell and makes it an active killer
- The activated cytotoxic T cell secretes proteins that destroy the infected target cell
B Cells: A Response to Extracellular Pathogens

- The humoral response is characterized by secretion of antibodies by B cells
- Activation of B cells is aided by cytokines and antigen binding to helper T cells
- Clonal selection of B cells generates antibody-secreting plasma cells, the effector cells of humoral immunity

Antibody Classes

- The five major classes of antibodies, or immunoglobulins, differ in distribution and function
- Polyclonal antibodies are the products of many different clones of B cells following exposure to a microbial antigen
- Monoclonal antibodies are prepared from a single clone of B cells grown in culture

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<tr>
<th>Class of Immunoglobulin (Antibody)</th>
<th>Distribution</th>
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<td>IgM (pentamer)</td>
<td>First Ig class produced after initial exposure to antigen; then its concentration in the blood declines</td>
<td>Promotes neutralization and cross-linking of antigens; very effective in complement system activation</td>
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### The Role of Antibodies in Immunity

- **Neutralization** occurs when a pathogen can no longer infect a host because it is bound to an antibody.
- **Opsonization** occurs when antibodies bound to antigens increase phagocytosis.
- Antibodies together with proteins of the complement system generate a **membrane attack complex** and cell lysis.
Active and Passive Immunization

- **Active immunity** develops naturally in response to an infection
  - It can also develop following **immunization**, also called **vaccination**
  - In immunization, a nonpathogenic form of a microbe or part of a microbe elicits an immune response to an immunological memory

- **Passive immunity** provides immediate, short-term protection
  - It is conferred naturally when IgG crosses the placenta from mother to fetus or when IgA passes from mother to infant in breast milk
  - It can be conferred artificially by injecting antibodies into a nonimmune person

Immune Rejection

- Cells transferred from one person to another can be attacked by immune defenses
  - This complicates blood transfusions or the transplant of tissues or organs

Blood Groups

- Antigens on red blood cells determine whether a person has blood type A (A antigen), B (B antigen), AB (both A and B antigens), or O (neither antigen)
  - Antibodies to nonself blood types exist in the body
  - Transfusion with incompatible blood leads to destruction of the transfused cells
  - Recipient-donor combinations can be fatal or safe

Tissue and Organ Transplants

- MHC molecules are different among genetically nonidentical individuals
  - Differences in MHC molecules stimulate rejection of tissue grafts and organ transplants

- Chances of successful transplantation increase if donor and recipient MHC tissue types are well matched
  - Immunosuppressive drugs facilitate transplantation
  - Lymphocytes in bone marrow transplants may cause the donor tissue to reject the recipient
**Concept 43.4: Disruption in immune system function can elicit or exacerbate disease**

- Some pathogens have evolved to diminish the effectiveness of host immune responses.

**Exaggerated, Self-Directed, and Diminished Immune Responses**

- If the delicate balance of the immune system is disrupted, effects range from minor to often fatal.

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**Allergies**

- Allergies are exaggerated (hypersensitive) responses to antigens called **allergens**.
- In localized allergies such as hay fever, IgE antibodies produced after first exposure to an allergen attach to receptors on mast cells.

**Fig. 43-23**

- The next time the allergen enters the body, it binds to mast cell–associated IgE molecules.
- Mast cells release histamine and other mediators that cause vascular changes leading to typical allergy symptoms.
- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction that can occur within seconds of allergen exposure.

**Autoimmune Diseases**

- In individuals with **autoimmune diseases**, the immune system loses tolerance for self and turns against certain molecules of the body.
- Autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, insulin-dependent diabetes mellitus, and multiple sclerosis.
Exertion, Stress, and the Immune System

- Moderate exercise improves immune system function
- Psychological stress has been shown to disrupt hormonal, nervous, and immune systems

Immunodeficiency Diseases

- Inborn immunodeficiency results from hereditary or developmental defects that prevent proper functioning of innate, humoral, and/or cell-mediated defenses
- Acquired immunodeficiency results from exposure to chemical and biological agents
- Acquired immunodeficiency syndrome (AIDS) is caused by a virus

Acquired Immune System Evasion by Pathogens

- Pathogens have evolved mechanisms to attack immune responses

Antigenic Variation

- Through antigenic variation, some pathogens are able to change epitope expression and prevent recognition
- The human influenza virus mutates rapidly, and new flu vaccines must be made each year
- Human viruses occasionally exchange genes with the viruses of domesticated animals
- This poses a danger as human immune systems are unable to recognize the new viral strain
Latency

- Some viruses may remain in a host in an inactive state called latency
- Herpes simplex viruses can be present in a human host without causing symptoms

Attack on the Immune System: HIV

- Human immunodeficiency virus (HIV) infects helper T cells
- The loss of helper T cells impairs both the humoral and cell-mediated immune responses and leads to AIDS
- HIV eludes the immune system because of antigenic variation and an ability to remain latent while integrated into host DNA

Cancer and Immunity

- The frequency of certain cancers increases when the immune response is impaired
- Two suggested explanations are
  - Immune system normally suppresses cancerous cells
  - Increased inflammation increases the risk of cancer
You should now be able to:

1. Distinguish between innate and acquired immunity
2. Name and describe four types of phagocytic cells
3. Describe the inflammation response
4. Distinguish between the following pairs of terms: antigens and antibodies; antigen and epitope; B lymphocytes and T lymphocytes; antibodies and B cell receptors; primary and secondary immune responses; humoral and cell-mediated response; active and passive immunity
5. Explain how B lymphocytes and T lymphocytes recognize specific antigens
6. Explain why the antigen receptors of lymphocytes are tested for self-reactivity
7. Describe clonal selection and distinguish between effector cells and memory cells
8. Describe the cellular basis for immunological memory
9. Explain how a single antigen can provoke a robust humoral response
10. Compare the processes of neutralization and opsonization
11. Describe the role of MHC in the rejection of tissue transplants
12. Describe an allergic reaction, including the roles of IgE, mast cells, and histamine
13. Describe some of the mechanisms that pathogens have evolved to thwart the immune response of their hosts
14. List strategies that can reduce the risk of HIV transmission