1 The Immune System

2 All animals have innate immunity, a defense active immediately upon infection
   Vertebrates also have adaptive immunity

3 Figure 43.2

4 In innate immunity, recognition and response rely on traits common to groups of pathogens
   In insects, an exoskeleton made of chitin forms the first barrier to pathogens
   The digestive system is protected by a chitin-based barrier and lysozyme, an enzyme that breaks down bacterial cell walls
   Hemocytes circulate within hemolymph and carry out phagocytosis, the ingestion and digestion of foreign substances including bacteria
   Hemocytes also secrete antimicrobial peptides that disrupt the plasma membranes of fungi and bacteria

5 Figure 43.4

6 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: natural killer cells, interferons, and the inflammatory response

7 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 many microbes
   The low pH of skin and the digestive system prevents growth of many bacteria

8 Cellular Innate Defenses
   Pathogens entering the mammalian body are subject to phagocytosis
   Phagocytic cells recognize groups of pathogens by TLRs, Toll-like receptors

9 A white blood cell engulfs a microbe, then fuses with a lysosome to destroy the microbe
   There are different types of phagocytic cells
   Neutrophils engulf and destroy pathogens
   Macrophages are found throughout the body
   Dendritic cells stimulate development of adaptive immunity
   Eosinophils discharge destructive enzymes


Cellular innate defenses in vertebrates also involve natural killer cells.

Figure 43.7

**Antimicrobial Peptides and Proteins**
- Function in innate defense by attacking pathogens or impeding their reproduction
- Interferon proteins provide innate defense, interfering with viruses and helping activate macrophages
- About 30 proteins make up the complement system, which causes lysis of invading cells and helps trigger inflammation

**Inflammatory Responses**
- The inflammatory response, such as pain and swelling, is brought about by molecules released upon injury of infection
- Mast cells, a type of connective tissue, release histamine, which triggers blood vessels to dilate and become more permeable
- Activated macrophages and neutrophils release cytokines, signaling molecules that enhance the immune response
- *Pus*, a fluid rich in white blood cells, dead pathogens, and cell debris from damaged tissues

Figure 43.8-1

Figure 43.8-2

Figure 43.8-3

Inflammation can be either local or systemic (throughout the body)
- Fever is a systemic inflammatory response triggered by pyrogens released by macrophages and by toxins from pathogens
- *Septic shock* is a life-threatening condition caused by an overwhelming inflammatory response

**Evasion of Innate Immunity 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

**In adaptive immunity, receptors provide pathogen-specific recognition**
- Lymphocytes that mature in the thymus are called T cells, and those that mature in bone marrow are called B cells
- Antigens can elicit a response from a B or T cell
- Exposure to the pathogen activates B and T cells with antigen receptors specific for parts of that pathogen
- The small accessible part of an antigen that binds to an antigen receptor is called an epitope
Antigen Recognition by B Cells and Antibodies
- Each B cell antigen receptor is a Y-shaped molecule
- The constant regions vary little among B cells, whereas the variable regions differ greatly
- The variable regions provide antigen specificity

Binding of a B cell antigen receptor to an antigen is an early step in B cell activation
- This gives rise to cells that secrete a soluble form of the protein called an antibody or immunoglobulin (Ig)
- Secreted antibodies are similar to B cell receptors but lack transmembrane regions that anchor receptors in the plasma membrane

Antigen Recognition by T Cells
- Each T cell receptor consists of two different polypeptide chains (called α and β)
- The tips of the chain form a variable (V) region; the rest is a constant (C) region
- T cell and B cell antigen receptors are functionally different

T cells bind to antigen fragments displayed or presented on a host cell
- These antigen fragments are bound to cell-surface proteins called MHC molecules
- MHC (major histocompatibility complex) molecules are host proteins that display the antigen fragments on the cell surface
- In infected cells, MHC molecules bind and transport antigen fragments to the cell surface, a process called antigen presentation
- A T cell can then bind both the antigen fragment and the MHC molecule
- This interaction is necessary for the T cell to participate in the adaptive immune response

B Cell and T Cell Development
- The adaptive immune system has four major characteristics
  - Diversity of lymphocytes and receptors
  - Self-tolerance; lack of reactivity against an animal’s own molecules
  - B and T cells proliferate after activation
  - Immunological memory

Generation of B and T Cell Diversity
- By combining variable elements, the immune system assembles a diverse variety of antigen receptors
- The immunoglobulin (Ig) gene encodes one chain of the B cell receptor
- Many different chains can be produced from the same 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
- Some B and T cells with receptors specific for the body’s own molecules are destroyed by apoptosis, or programmed cell death
- The remainder are rendered nonfunctional

Proliferation of B Cells and T Cells
- In the body there are few lymphocytes with antigen receptors for any particular epitope
- In the lymph nodes, an antigen is exposed to a steady stream of lymphocytes until a match is made
- This binding of a mature lymphocyte to an antigen initiates events that activate the lymphocyte
- Once activated, a B or T cell undergoes multiple cell divisions
- This proliferation of lymphocytes is called clonal selection
- Two types of clones are produced: short-lived activated effector cells that act immediately against the antigen and long-lived memory cells that can give rise to effector cells if the same antigen is encountered again

Immunological memory is responsible for long-term protections against diseases, due to either a prior infection or vaccination
- The first exposure to a specific antigen represents the primary immune response
- During this time, selected B and T cells give rise to their effector forms
- In the secondary immune response, memory cells facilitate a faster, more efficient response

Adaptive immunity defends against infection of body fluids and body cells
- Acquired immunity has two branches: the humoral immune response and the cell-mediated immune response
- In the humoral immune response antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph
- In the cell-mediated immune response specialized T cells destroy affected host cells

Helper T Cells: A Response to Nearly All Antigens
- A type of T cell called a helper T cell triggers both the humoral and cell-mediated immune responses
- Signals from helper T cells initiate production of antibodies that neutralize pathogens and activate T cells that kill infected cells
- Antigen-presenting cells have class I and class II MHC molecules on their surfaces
Class II MHC molecules are the basis upon which antigen-presenting cells are recognized.

Antigen receptors on the surface of helper T cells bind to the antigen and the class II MHC molecule; then signals are exchanged between the two cells.

The helper T cell is activated, proliferates, and forms a clone of helper T cells, which then activate the appropriate B cells.

**Figure 43.16**

**Cytotoxic T Cells: A Response to Infected Cells**

- Cytotoxic T cells are the effector cells in the cell-mediated immune response.
- Cytotoxic T cells recognize fragments of foreign proteins produced by infected cells and possess an accessory protein that binds to class I MHC molecules.
- The activated cytotoxic T cell secretes proteins that disrupt the membranes of target cells and trigger apoptosis.

**Figure 43.17-1**

**Figure 43.17-2**

**Figure 43.17-3**

**B Cells and Antibodies: A Response to Extracellular Pathogens**

- The humoral response is characterized by secretion of antibodies by B cells.
- Activation of the humoral immune response involves B cells and helper T cells as well as proteins on the surface of pathogens.
- In response to cytokines from helper T cells and an antigen, a B cell proliferates and differentiates into memory B cells and antibody-secreting effector cells called plasma cells.

**Antibody Function**

- Antibodies do not kill pathogens; instead they mark pathogens for destruction.
- In neutralization, antibodies bind to viral surface proteins preventing infection of a host cell.
- Antibodies may also bind to toxins in body fluids and prevent them from entering body cells.

- In opsonization, antibodies bind to antigens on bacteria creating a target for macrophages or neutrophils, triggering phagocytosis.
- Antigen-antibody complexes may bind to a complement protein—which triggers a cascade of complement protein activation.
- Ultimately, a membrane attack complex forms a pore in the membrane of the foreign cell, leading to its lysis.

**Figure 43.19 Antibody-mediated mechanisms of antigen disposal.**

B cells can express five different forms (or classes) of immunoglobulin (Ig) with similar antigen-binding specificity but different heavy chain C regions.
IgD: Membrane bound
IgM: First soluble class produced
IgG: Second soluble class; most abundant
IgA and IgE: Remaining soluble classes

**Summary of the Humoral and Cell-Mediated Immune Responses**
- Both the humoral and cell-mediated responses can include primary and secondary immune response
- Memory cells enable the secondary response

**Active and Passive Immunization**
- Active immunity develops naturally when memory cells form clones 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

**Figure 43.20**

Antibodies as Tools
- Antibody specificity and antigen-antibody binding have been harnessed in research, diagnosis, and therapy

**Immune Rejection**
- Cells, tissues, and organs
- MHC molecules are different among genetically nonidentical individuals

**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)

**Disruptions in immune system function can elicit or exacerbate disease**
- Some pathogens have evolved to diminish the effectiveness of host immune responses
- If the delicate balance of the immune system is disrupted, effects range from minor to sometimes fatal

**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
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, 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 immune system regulation by altering the interactions of the hormonal, nervous, and immune systems.
Sufficient rest is also important for immunity.

**Immunodeficiency Diseases**

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

**Pathogens have evolved mechanisms to thwart 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 adaptive immunity is impaired
- 20% of all human cancers involve viruses
- The immune system can act as a defense against viruses that cause cancer and cancer cells that harbor viruses
- In 2006, a vaccine was released that acts against human papillomavirus (HPV), a virus associated with cervical cancer