CHAPTER 24

The Immune System

Objectives

Introduction Describe the frequency with which new people are infected with HIV in the United States and the world. Explain what people can do to decrease their risks of acquiring this virus.

Nonspecific Defenses Against Infection

24.1 Describe the nature of nonspecific human defenses against infection.
24.2 Describe the events of the inflammatory response and explain how it helps to prevent the spread of disease.
24.3 Describe the structure and functions of the lymphatic system.

Specific Immunity

24.4 Describe the specific nature of an immune system response. Define antigen, antibody, passive immunity, and active immunity.
24.5 Describe the development and functions of B and T lymphocytes.
24.6 Describe the nature of antigens. Explain how an antigen and its antibody interact.
24.7 Explain how clones of the appropriate B and T cells are produced to fight an infection.
24.8, 24.9 Compare the primary and secondary immune responses. Distinguish between the functions of plasma cells and memory cells.
24.10 Relate the specific structure of an antibody to its functions.
24.11 Describe the effector mechanisms triggered by antibodies binding to antigens.
24.12 Describe the production of and uses for monoclonal antibodies.
24.13 Describe the specific functions of cytotoxic T cells and helper T cells. Note their interactions with other cells.
24.14 Explain how the immune system helps to fight cancer.
24.15 Explain how the immune system identifies the body's own molecules and how this system creates problems for organ transplantations.

Disorders of the Immune System

24.16 Describe examples of how the malfunction or failure of the immune system causes disease.
24.17 Explain why allergies occur and what causes anaphylactic shock.
24.18 Explain the mechanism of HIV infection and the medical consequences.

Key Terms

neutrophil
monocyte
macrophage
natural killer cell
interferon
complement protein
inflammatory response
histamine
lymphatic system
lymph
immune system
antigen

antibody
immunity
vaccination
vaccine
active immunity
passive immunity
lymphocyte
B cell
T cell
humoral immunity
cell-mediated immunity
antigen receptor
antigenic determinant
clonal selection
primary immune response
secondary immune response
memory cell
plasma cell
antigen-binding site
monoclonal antibody
cytotoxic T cell
helper T cell
antigen-presenting cell (APC)
self protein
nonself molecule
perforin
major histocompatibility complex (MHC)
autoimmune disease
immunodeficiency disease
allergy
allergen
mast cell
antihistamine
anaphylactic shock

Word Roots

an- = without; **-aphy** = suck (*anaphylactic shock:* an acute, life-threatening, allergic response)

anti- = against; **-gen** = produce (*antigen:* a foreign macromolecule that does not belong to the host organism and that elicits an immune response)

macro- = large; **-phage** = eat (*macrophage:* an amoeboid cell that moves through tissue fibers, engulfing bacteria and dead cells by phagocytosis)

mono- = one (*monocyte:* an agranular leukocyte that is able to migrate into tissues and transform into a macrophage)

neutro- = neutral; **-phil** = loving (*neutrophil:* the most abundant type of leukocyte; neutrophils tend to self-destruct as they destroy foreign invaders, limiting their life span to but a few days)

perfora- = bore through (*perforin:* a protein that forms pores in a target cell's membrane)

Lecture Outline

Introduction *The Continuing Problem of HIV*

A. Humans and other animals depend on several elaborate systems of defense.
   1. Nonspecific defenses do not distinguish individual infectious agents.
   2. The immune system recognizes specific invaders, and it attacks and eliminates them.

B. The AIDS epidemic.
   1. *Review:* The HIV life cycle, noting that the transfer of HIV occurs in body fluids, including blood and semen (Module 10.21; Figure 10.21A, B).
   2. Acquired immune deficiency syndrome results from HIV infection, eventually undermining the entire immune system, after a latent period of several years.
   3. Most AIDS patients die from other infectious diseases that their ravaged immune systems cannot combat.
   4. The best defense against AIDS is abstinence. For a sexually active person, using condoms and having only one partner who is nonpromiscuous are the best defenses against AIDS.

I. Nonspecific Defenses Against Infection

Module 24.1 Nonspecific defenses against infection include the skin and mucous membranes, phagocytic cells, and antimicrobial proteins.

A. The skin provides a tough, physical barrier. It also provides general chemical defenses (acidic pH) in the form of glandular secretions (tears, sweat, and other secretions) that inhibit or kill microbes. Sweat, saliva, and tears contain lysozyme.

B. Mucous membranes protect organ systems (digestive and respiratory) that are open to the external environment. Stomach acid kills bacteria that are swallowed. Nose hair filters air and mucous in the respiratory passages traps microbes and debris. Cilia propel the mucous to the throat, where it is swallowed.
Review: The details of the functioning of cilia are discussed in Module 4.18.

C. **Neutrophils** and **monocytes** phagocytize bacteria and viruses in infected tissue. **Macrophages** develop from monocytes and phagocytize bacteria and virus-infected cells (Figure 24.1A). **Natural killer cells** attack cancer cells and virus-infected cells. All of these types of white blood cells leave the blood and scavenge invading cells in the interstitial fluid and body tissues.
Review: White blood cells (Module 23.15).

D. **Interferons** are antimicrobial proteins produced by virus-infected cells that help other cells resist viruses. Interferons produced by recombinant DNA technology may provide an approach to combating viral infections (Figure 24.1B).

E. Other types of antimicrobial proteins are **complement proteins.** Inactive complement proteins circulate in the blood and are activated by the immune system or by microbes. Some coat the microbes, making the microbes more susceptible to attack by macrophages; others lethally damage microbial membranes. Complement also amplifies the inflammatory response.

Module 24.2 The inflammatory response mobilizes nonspecific defense forces.

A. Any infectious agent or break in the barrier triggers the **inflammatory response.**

B. The damaged cells release chemical alarms such as **histamine.** Histamine induces blood vessels to dilate and become leakier, facilitating the flow of blood and fluid to the affected region (Figure 24.2).

C. Other chemicals attract phagocytes.

D. Local clotting reactions seal off the infected region and allow repairs to begin.
Review: Clotting (Module 23.16).

E. Local action of this response is the disinfection and cleaning of injured areas that become hot, red, and swollen as a consequence of the increased blood supply.
NOTE: Swelling presses against nerves and causes pain that is associated with inflammation. The accumulation of fluid also dilutes any toxins that may be present.

F. Systemic action of the response, due to microbes or their toxins circulating in the blood, results in increased white blood cells and fever. Moderate fevers may stimulate phagocytosis and inhibit the growth of microbes.

G. Overwhelming bacterial infection of an organ or an organ system results in systemic shock and often ends in death.

Module 24.3 The lymphatic system becomes a crucial battleground during infection.

A. The **lymphatic system** consists of an open branching network of vessels, lymph nodes, and associated glands. The system has two main functions: to return excess fluid from the interstitial fluid to the circulatory system and to fight infection (Figure 24.3A).

B. Lymph nodes are concentrated areas of branched ducts containing large numbers of lymphocytes (B cells and T cells) and macrophages. During an infection, these areas become activated and swell, causing the tenderness and aches and pains associated with a systemic infection (Figure 24.3A–D).

C. In addition to lymph nodes, other lymph organs include the thymus (the "T" in T cell), tonsils, appendix, adenoids, spleen, and bone marrow.
NOTE: With age, the glandular tissue of the thymus is replaced with connective tissue.

D. **Lymph** (the fluid of the lymphatic system) enters the system through open, lymphatic capillaries. The largest lymph ducts empty into circulatory system veins in the shoulders (Figure 24.3A).

E. Lymph is similar to interstitial fluid, except that it is lower in oxygen and contains fewer nutrients. As it circulates through the lymphatic organs, microbes from infected sites and cancer cells may be phagocytized by macrophages. Also, within these lymphoid organs, lymphocytes may be activated to mount a specific immune response.

F. Swollen and tender lymph nodes are an overt sign that your body is responding to an infection.

II. Specific Immunity

Module 24.4 The immune response counters specific invaders.

A. The **immune system** recognizes specific invaders more efficiently than the nonspecific defenses, and it amplifies the inflammatory and complement responses. Extreme specificity, memory, and prompt response on second exposure to an antigen characterize the immune system.

B. An **antigen** is any molecule that elicits an immune response. Such molecules include those found on the surfaces of viruses, bacteria, mold, etc.
Preview: An autoimmune response occurs when the antigen(s) that elicit(s) an immune response is (are) that body's own molecule(s). Autoimmune diseases include Type I diabetes and rheumatoid arthritis (Module 24.16).

C. The system responds to antigens by producing **antibodies** that attach to the antigen and help counter its effects.

D. In the future, the primed system remembers the antigen and reacts to it.

E. **Immunity** refers to resistance to specific invaders. **Active immunity** is achieved by exposure to the invader or to parts of the invader incorporated in **vaccinations** in the form of an injection called a **vaccine. Passive immunity** is achieved by a person's getting the antibodies from someone else. For instance, a fetus may achieve passive immunity to antigens from its mother through the placenta.

Module 24.5 Lymphocytes mount a dual defense (Figure 24.5).

A. **Lymphocytes** arise from stem cells in the bone marrow (Modules 23.15 and 30.5).

B. **Humoral immunity** is defense against bacteria and viruses free in the blood or interstitial fluid. It is mounted by B (mature in the bone) lymphocytes, or **B cells.** B cells release antibodies that function when dissolved in the blood.
Preview: (Module 24.9) B cells produce a clone of cells, plasma cells, which secrete antibodies in much higher quantity than B cells.

C. Humoral immunity can be transferred passively by transferring antibody-containing plasma from an immune individual to a nonimmune individual (or by antibodies moving across the placenta: see Module 24.4).

D. **Cell-mediated immunity** is defense against bacteria and viruses inside body cells, against fungi and protozoans, and against cancer cells. It is mounted by T lymphocytes, or **T cells.** T cells circulate in the blood and mount a cellular attack on repeated foreign invaders and promote phagocytosis by other white blood cells. Furthermore, by promoting antibody secretion by B cells, T cells also play a role in humoral immunity.
Preview: There are several different types of T cell (Module 24.13).
Preview: The functioning of the thymus gland is also discussed in Module 26.3.

E. Both B cells and T cells must mature before they are able to function in defense of the body. This involves a process by which these cells become capable of recognizing and responding to a specific antigen. Such mature cells are said to be competent and have surface molecules called **antigen receptors** that can bind antigens.

F. A human has 100 million to 100 billion different kinds of B cells and T cells.

NOTE: Modules 24.6–24.11 describe humoral immunity and Module 24.13 describes cell-mediated immunity.

Module 24.6 Antigens have specific regions where antibodies bind to them.

A. Antigens are usually proteins or large polysaccharides.

B. Antibodies usually identify localized regions, called **antigenic determinants,** on part of the antigen molecule, by means of a "lock-and-key" fit (Figure 24.6).

C. An antigen may have several antigenic determinants. Each antibody has two identical antigen-binding sites.

Module 24.7 Clonal selection musters defensive forces against specific antigens.

A. Each B cell has a specific antigen receptor on its surface before it is exposed to an antigen.

B. The functioning of the immune system is dependent on the diversity of antigen receptors.

C. Upon exposure to an antigen, a tiny fraction of the lymphocytes are able to bind to it and are activated (Figure 24.7).

D. These cells proliferate, forming a clone of genetically identical effector cells.

E. These effector cells secrete antibodies specific to the antigen. The process described is referred to as **clonal selection.**

Module 24.8 The initial immune response results in a type of "memory."

A. The effect of the proliferation of the effector cells is the **primary immune response.** There is a delay between exposure to the antigen and the secretion of antibodies, and this first exposure results in the release of modest levels of antibodies (Figure 24.8A).

B. The **secondary immune response** occurs when the body is exposed again to the same antigen. This response is faster than the primary response, lasts longer, and produces much higher levels of antibodies that may be more effective than those antibodies produced during the primary response.

C. During the primary response, some of the cloned cells function as effector cells, and some become **memory cells.** The memory cells remain in the lymph nodes ready to be activated by a second exposure to the antigen (Figure 24.8B).

Module 24.9 Overview: B cells are the main warriors of humoral immunity.

A. *Review:* The role of the B-cell system in attacking free antigenic molecules and those on the surfaces of bacteria and viruses free in body fluids (Module 24.5).

B. Overall, the system works by combining clonal selection and immunological memory. A clone is composed of some effector plasma cells that immediately produce antibodies to the antigen (primary response), and a smaller number of memory cells that prepare the immune system for a secondary response (Figure 24.9).

C. **Plasma cells** may secrete up to 2000 antibody molecules per second during their 4-to-5-day lifetime.

D. Using a military metaphor, plasma cells are "front-line" warriors, the antibodies are their weapons, memory cells are "reservists," and the lymphatic system (indeed, the whole body) is the battleground.

E. During a secondary response memory cells bind antigens and then rapidly produce a new clone of plasma cells.

Module 24.10 Antibodies are the weapons of humoral immunity.

A. *Review:* Tertiary and quaternary structures of proteins (Figures 3.17 and 3.18).

B. Each antibody is made of two "heavy" polypeptide chains and two "light" polypeptide chains. The quaternary structure of these chains results in a Y shape (Figure 24.10B).

C. Each of the four chains of the antibody has a C (constant) region and a V (variable) region. A pair of V regions, at the tip of each arm of the Y, forms the **antigen-binding site.**
NOTE: Genetically, these variable regions are assembled following transcription and translation of combinations of a few each of several dozen genes. Each B-cell or T-cell line activates one set of such genes and continues to activate the same set over its lifetime.

D. The C region of the heavy chains helps eliminate the antigens.

E. Based on the nature of the C region, human antibodies are divided into five major classes, each with a particular role.

Module 24.11 Antibodies mark antigens for elimination.

A. Antibody-antigen complexes are eliminated by several mechanisms (Figure 24.11). All mechanisms involve a specific recognition phase (the antibodies of humoral immunity) followed by a nonspecific destruction phase (phagocytosis and complement proteins).

B. Neutralization physically blocks harmful antigens, making them harmless.

C. Agglutination clumps groups of cells (or viruses) to ease their capture by phagocytes.

D. Precipitation clumps dissolved antigens together so they precipitate out of solution and can be captured by phagocytes.

E. Antigen-antibody complexes activate complement proteins. Activated complement proteins attach to foreign cells and lyse (rupture) them.

Module 24.12 Connection: Monoclonal antibodies are powerful tools in the lab and clinic.

A. Antibodies used in diagnosis and research were first produced in animals by injecting the antigen and removing the mixture of B cells, some of which produced the right antibodies.

B. Techniques were developed to separate the one B-cell type specific to an antigen. This cell is fused with an immortal tumor cell to form a hybrid cell that can be cultured indefinitely and produce the desired **monoclonal antibody** (Figure 24.12A).

C. Monoclonal antibodies are useful in medical diagnoses, such as pregnancy tests (which test for the presence of a specific hormone, HCG), and provide a way to target drugs to certain cells that cause disease (including cancer).
NOTE: They are also used with fluorochromes, such as fluorescein, thus allowing the molecular (antigen) positions to be determined within a cell by a technique called immunofluorescence.

Module 24.13 T cells mount the cell-mediated defense and aid humoral immunity.

Review: The role of T cells in attacking antigens from bacteria and viruses inside body cells and those of protozoans and fungi (Module 24.5).

A. The mechanism of the T-cell system results from the close cooperation of a number of cell types.

B. **Cytotoxic T cells** attack pathogen-infected cells.

C. **Helper T cells** play a role in the activation of cytotoxic T cells and macrophages, stimulate the release of antibodies by B cells, and interact with **antigen-presenting cells (APCs).**

D. APCs are macrophages that combine with and display on their cell surface **"self proteins"** and a **nonself molecule** consisting of a small peptide, from an antigen that it has ingested and processed.

E. Helper T cells recognize only one combination of a self protein and a foreign antigen as presented by an APC (Figure 24.13A). The binding to a self-nonself complex is one of the ways helper T cells are activated. Other signals, such as the secretion of interleukin-1 by the APC, enhance the activation of helper T cells. Either way, the result is activation of the helper T cell via signal-transduction pathways (Module 11.13).

F. Activated helper T cells secrete proteins that promote an immune response. For example, interleukin-2 has three major effects:
   1. It stimulates helper T cells to grow and divide, producing both memory cells and helper T cells (cell-mediated immunity).
   2. It stimulates cytotoxic T cells (cell-mediated immunity).
   3. It stimulates B cells (humoral immunity). (Figure 24.13B).

G. Cytotoxic T cells are the only T cells that actually kill other cells. Activated cytotoxic T cells recognize and bind to infected body cells in much the same way that helper T cells bind to APCs: They recognize only a combination of a self protein (different from the APC self protein) and the foreign antigen as presented by the infected cell. The cytotoxic T cells then secrete **perforin,** a protein that makes holes in the target cell, causing lysis (Figure 24.13C). Another T-cell protein enters the infected cell and triggers apoptosis (programmed cell death), causing cell death and lysis (Module 27.13).

Module 24.14 Cytotoxic T cells may help prevent cancer.

Review: The molecular and cellular bases of cancer (Modules 8.10, 8.23, 11.15–11.19).

A. Changes that occur in cancer cells can involve the outer membrane.

B. If these changes result in the cancer cell's not appearing as "self" to the T-cell system, they may be eliminated by the cytotoxic T-cell fraction (Figure 24.14).

C. How often this built-in system functions and why it sometimes fails are the subjects of considerable research on possible cancer cures.

Module 24.15 The immune system depends on our molecular fingerprints.

A. The ability of our immune system to distinguish self from nonself enables it to battle foreign invaders without harming healthy body cells.

B. There are two types of self proteins. Class I proteins occur on all nucleated body cells. Class II proteins are found only on B cells, activated T cells, and macrophages. Both are unique to each individual.

C. The main self proteins are determined by 6 chromosomal loci, each with hundreds of alleles. Thus, with the exception of identical twins, it is (effectively) impossible for two individuals to have an identical set of self proteins. Self proteins are coded for by **MHC (major histocompatibility complex)** genes.

D. This diversity can cause problems when a person receives an organ transplant. The donated organ displays different self proteins and is recognized as foreign, thus subject to immune attack and organ rejection.

E. The risk of rejection is minimized by finding a donor whose self proteins match the recipient's as closely as possible and by using drugs that suppress the immune response against the transplant. Most such drugs interfere with the beneficial effects of the system. Cyclosporine suppresses only the cell-mediated response.
NOTE: Cloning (Module 11.5) has the potential to make possible autologous organ transplants.

F. Approaches that have yet to be perfected would:
1. Use monoclonal antibodies to target and eliminate the T cells that attack transplants.
2. Find a way to use isolated stem cells to establish a new, second immune system that would recognize the new tissue as self (Module 23.17).

III. Disorders of the Immune System

Module 24.16 Connection: Malfunction or failure of the immune system causes diseases.

A. In **autoimmune diseases,** the immune system turns against its own body cells. Such diseases include insulin-dependent diabetes (insulin-producing cells are subjected to a cell-mediated response; Module 26.9), rheumatoid arthritis (antibody-mediated damage to joints, bones, and cartilage; Module 30.4), lupus (production of antibodies against molecules such as histones and DNA), and multiple sclerosis (T cells attack myelin; Module 28.2).
NOTE: Autoimmune diseases, such as Type I diabetes, appear to be triggered by an infection.

B. In **immunodeficiency diseases,** part or all of the immune system is lacking. SCID (severe combined immunodeficiency) is an inherited disorder in which both T cells and B cells are absent or inactive. Hodgkin's disease is a cancer of lymphocytes; treatment of this disease can suppress the immune system. HIV infection, leading to AIDS, is discussed in Module 24.18).
NOTE: A version of SCID, *X*-SCID, is an *X*-linked disorder (Modules 9.22 and 9.23).

C. Physical and emotional stress may also weaken the immune system.

Module 24.17 Connections: Allergies are overreactions to certain environmental antigens.

A. These antigens are **allergens** (pollen, dust, insect toxins, cat saliva, proteins).
NOTE: Children subjected to cigarette smoke as well as children who were prenatally exposed to cigarette smoke are more likely to develop **allergies.** Also, feeding young children nuts or peanuts (a legume) may increase the risk of the development of allergies in susceptible individuals.

B. Allergic reactions follow two stages:
   1. A person is first exposed to the allergen, eliciting B cells to form an immunologic clone against the allergen, and the antibodies produced attach to histamine-producing **mast cells.**
   2. The person is secondarily exposed to the same allergen. The antibody-mast cell unions join with the allergen and produce histamine in greater amounts than in a normal inflammatory response, causing the symptoms of allergies: nasal irritation, itchiness, and tears (Figure 24.17).

C. **Antihistamines** interfere with histamine action and give temporary relief.

D. The precipitous release of histamine can cause **anaphylactic shock** in some people.

Module 24.18 Connection: AIDS leaves the body defenseless.

Review: AIDS is an RNA virus (Module 10.21).

A. HIV has a preference for helper T cells. Once HIV has reproduced and attacked all of these, the body has neither humoral nor cell-mediated immunity.

B. HIV infection and AIDS are incurable. But the use of drugs may postpone the development of AIDS, and the use of several drugs in combination shows particular promise.

C. Approaches to the treatment of AIDS that are being studied include injecting patients with HIV-resistant stem cells and the development of a vaccine.

D. Treatment of an HIV infection is particularly difficult because the virus is continually mutating and a single individual may contain several variants of the virus.

E. The best current weapons are abstinence, safer sex, and education.

Class Activities

1. Have your students consider why emerging viruses are so dangerous. Based on what they have learned about the functioning of the immune system, is it possible that there is a naturally existing pathogen that can evade everyone's immune system? Is it possible to genetically engineer a pathogen that can evade the immune system?
2. Inflammation is a normal part of the nonspecific response against infection. It is also very uncomfortable, so people tend to take analgesics to reduce inflammation. In terms of dealing with the infection, is it always a good idea to reduce inflammation?

Transparency Acetates

Figure 24.1B	The interferon mechanism against viruses
Figure 24.2	The inflammatory response
Figure 24.3A	The human lymphatic system
Figure 24.3B	A lymphatic vessel and capillaries
Figure 24.3C	A lymph node
Figure 24.5	The development of B cells and T cells
Figure 24.6	The binding of antibodies to antigenic determinants

Figure 24.7	Clonal selection of B cells
Figure 24.8A	Immunological memory
Figure 24.8B	The cellular basis of immunological memory
Figure 24.9	An overview of humoral immunity (Layer 1)
Figure 24.9	An overview of humoral immunity (Layer 2)
Figure 24.10B	Antibody structure
Figure 24.11	Effector mechanisms of humoral immunity
Figure 24.12A	The procedure for making monoclonal antibodies
Figure 24.13A	Development of an APC and its interaction with a helper T cell
Figure 24.13B	The activation of a helper T cell and its roles in immunity
Figure 24.13C	How a cytotoxic T cell kills an infected cell
Figure 24.17	The two stages of an allergic reaction

Media

See the beginning of this book for a complete description of all media available for instructors and students. Animations and videos are available in the Campbell Image Presentation Library. Media Activities and Thinking as a Scientist investigations are available on the student CD-ROM and web site.

Animations and Videos	File Name
Role of B Cells Animation	24-07-RoleOfBCellsAnim.mov
Antibodies Animation	24-11-AntibodiesAnim.mov
T Cell Receptors Video	24-13-TCellReceptorsVideo-S.mov
Helper T Cells Animation	24-13B-HelperTCellsAnim.mov
Cytotoxic T Cells Animation	24-13C-CytotoxicTCellsAnim.mov

Activities and Thinking as a Scientist	Module Number
Web/CD Activity 24A: *Immune Responses*	24.13
Web/CD Activity 24B: *HIV Reproductive Cycle*	24.18
Web/CD Thinking as a Scientist: *Connection: What Causes Infections in AIDS Patients?*	24.18
Web/CD Thinking as a Scientist: *Connection: Why Do AIDS Rates Differ Across the U.S.?*	24.18