CAMPBELL
BIOLOGY
TENTH EDITION
Reece • Urry • Cain • Wasserman • Minorsky • Jackson

43 The Immune System

Lecture Presentation by Nicole Tunbridge and Kathleen Fitzpatrick

Recognition and Response

- **Pathogens**, agents that cause disease, infect a wide range of animals, including humans
- The **immune system** recognizes foreign bodies and responds with the production of immune cells and proteins
- All animals have **innate immunity**, a defense active immediately upon infection
- Vertebrates also have **adaptive immunity**

Figure 43.1

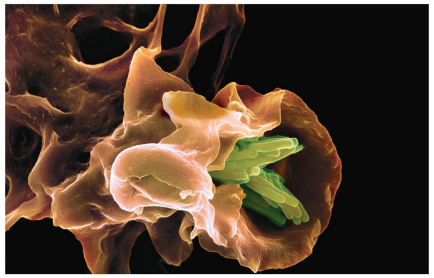
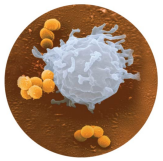


Figure 43.1a

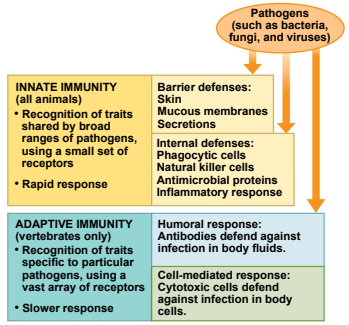


Video: Leukocyte Adhesion and Rolling

- Innate immunity is present before any exposure to pathogens and is effective from the time of birth
- It responds to a broad range of pathogens

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

Figure 43.2



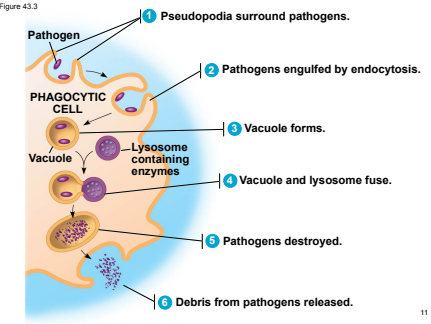
Concept 43.1: In innate immunity, recognition and response rely on traits common to groups of pathogens

- Innate immunity is found in all animals and plants
- In vertebrates, innate immunity is a first response to infections and also serves as the foundation of adaptive immunity

Innate Immunity of Invertebrates

- 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

Figure 43.3

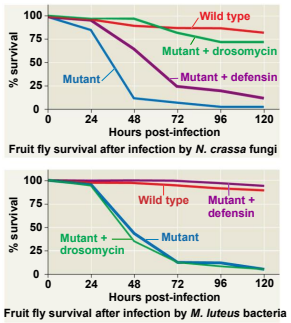


- Hemocytes also secrete antimicrobial peptides that disrupt the plasma membranes of fungi and bacteria

Figure 43.4

- The immune system recognizes bacteria and fungi by structures on their cell walls
- Innate immune responses are distinct for different classes of pathogens

Figure 43.5



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 unique to vertebrates are natural killer cells, interferons, and the inflammatory response

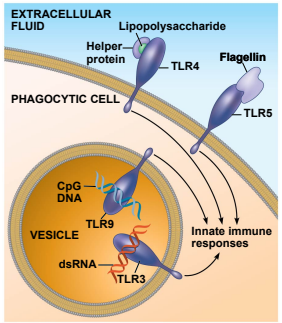
Barrier Defenses

- 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

Cellular Innate Defenses

- Pathogens entering the mammalian body are subject to phagocytosis
- Phagocytic cells recognize groups of pathogens using **TLRs**, **Toll-like receptors**
- TLRs recognize fragments of molecules characteristic of a set of pathogens

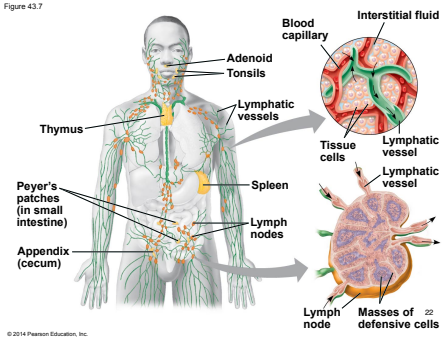
Figure 43.6



- There are two main types of phagocytic cells in the mammalian body
  - **Neutrophils** engulf and destroy pathogens
  - **Macrophages** are found throughout the body
- There are two additional types of phagocytic cells
  - **Dendritic cells** stimulate development of adaptive immunity
  - Eosinophils discharge destructive enzymes

- Cellular innate defenses in vertebrates also involve **natural killer cells**
- These circulate through the body and detect abnormal cells
- They release chemicals leading to cell death, inhibiting the spread of virally infected or cancerous cells
- Many cellular innate defenses involve the lymphatic system

Figure 43.7



Antimicrobial Peptides and Proteins

- 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
- Enhanced blood flow to the site helps deliver antimicrobial peptides that result in an accumulation of *pus,* a fluid rich in white blood cells, dead pathogens, and cell debris from damaged tissues

Figure 43.8-1

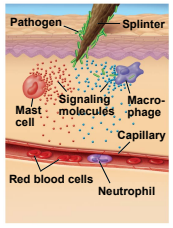


Figure 43.8-2

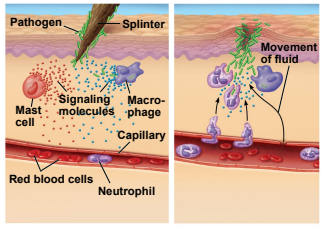
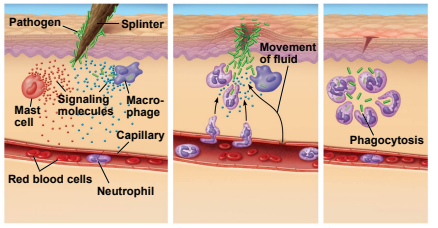
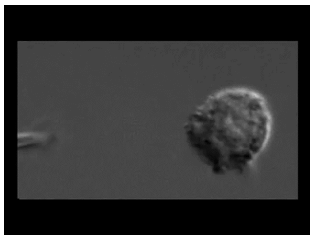


Figure 43.8-3



Video: Chemotaxis of a Neutrophil



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

Evasion of Innate Immunity by Pathogens

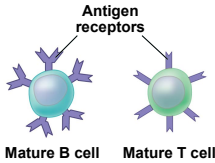
- Some pathogens avoid destruction by modifying their surface to prevent recognition or by resisting breakdown following phagocytosis
- Tuberculosis (TB), one such disease, kills more than a million people a year

Concept 43.2: In adaptive immunity, receptors provide pathogen-specific recognition

- The adaptive response relies on two types of **lymphocytes**, or white blood cells
- Lymphocytes that mature in the **thymus** above the heart are called **T cells**, and those that mature in bone marrow are called **B cells**

- **Antigens** are substances that can elicit a response from a B or T cell
- T or B cells bind to antigens via **antigen receptors** specific to part of one molecule of that pathogen

Figure 43.UN01

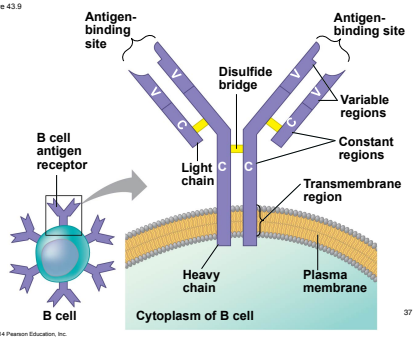


- The small accessible part of an antigen that binds to an antigen receptor is called an **epitope**
- Each individual B or T cell is specialized to recognize a specific type of molecule
- The antigen receptors of B cells and T cells have similar components but they encounter antigens in different ways

Antigen Recognition by B Cells and Antibodies

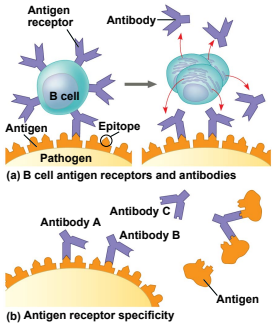
- Each B cell antigen receptor is a Y-shaped molecule with two identical **heavy chains** and two identical **light chains**
- The constant regions of the chains vary little among B cells, whereas the variable regions differ greatly
- The variable regions provide antigen specificity

Figure 43.9



- 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)**
- Antibodies have the same Y shape as B cell antigen receptors but are secreted, not membrane bound

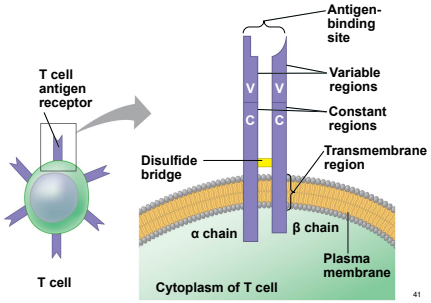
Figure 43.10



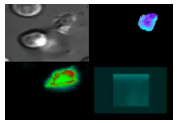
Antigen Recognition by T Cells

- 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

Figure 43.11



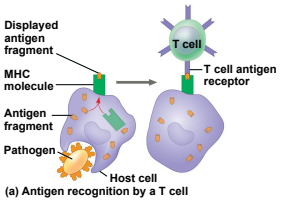
Video: T Cell Receptors



- 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

Figure 43.12



B Cell and T Cell Development

- The adaptive immune system has four major characteristics
  - Immense 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

Figure 43.13

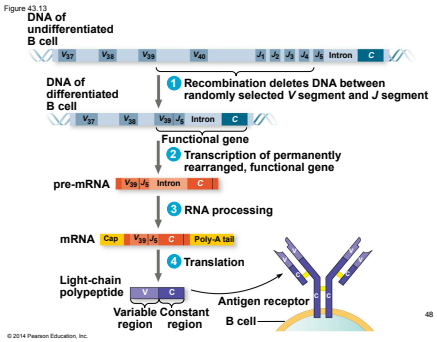


Figure 43.13a

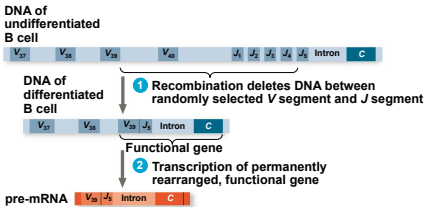
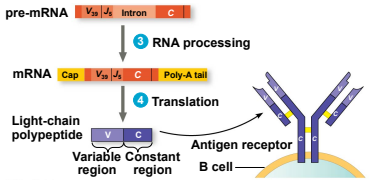


Figure 43.13b



Origin of Self-Tolerance

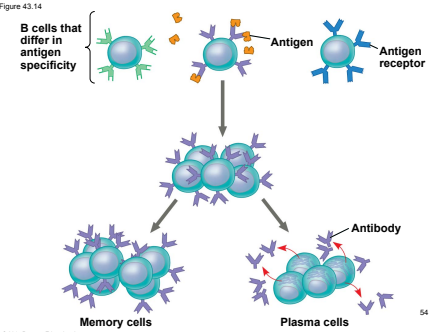
- Antigen receptors are generated by random rearrangement of DNA
- As lymphocytes mature in bone marrow or the thymus, they are tested for self-reactivity
- Some B and T cells with receptors specific for the body's own molecules are destroyed by apoptosis, or programmed cell death
- The remainder are rendered nonfunctional

Proliferation of B Cells and T Cells

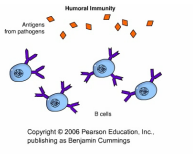
- In the body there are few lymphocytes with antigen receptors for any particular epitope
- In the lymph nodes, an antigen is exposed to a steady stream of lymphocytes until a match is made
- This binding of a mature lymphocyte to an antigen initiates events that activate the lymphocyte

- Once activated, a B or T cell undergoes multiple cell divisions (**clonal selection**) to produce a clone of identical cells
- Some cells from the clone become short-lived **effector cells** that act immediately against the antigen
- Effector cells are **plasma cells** that secrete antibodies
- Some cells from the clone become long-lived **memory cells** that can give rise to effector cells if the same antigen is encountered again

Figure 43.14



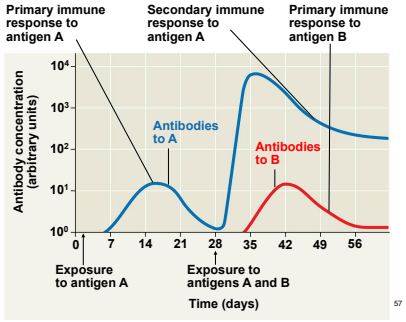
Animation: Role of B Cells



Immunological Memory

- Immunological memory is responsible for long-term protections against diseases
- 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

Figure 43.15



Concept 43.3: Adaptive immunity defends against infection of body fluids and body cells

- The defenses provided by B and T lymphocytes can be divided into 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

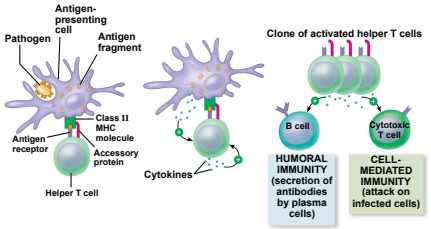


Figure 43.16a

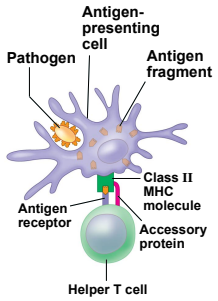


Figure 43.16b

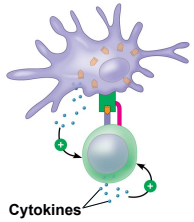
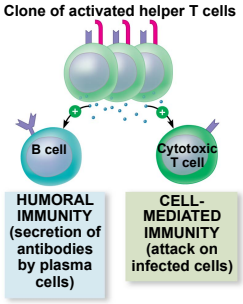
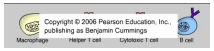


Figure 43.16c



Animation: Helper T Cells



Cytotoxic T Cells: A Response to Infected Cells

- **Cytotoxic T cells** use toxic proteins to kill cells infected by viruses or other intracellular pathogens
- Cytotoxic T cells recognize fragments of foreign proteins produced by infected cells
- The activated cytotoxic T cell secretes proteins that disrupt the membranes of target cells and trigger apoptosis

Figure 43.17-1

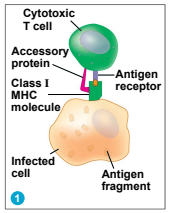


Figure 43.17-2

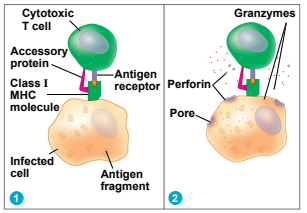
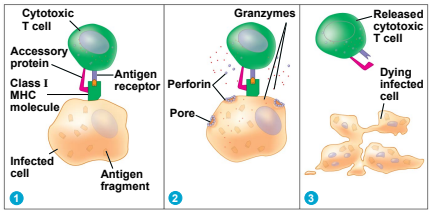
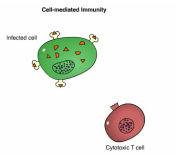


Figure 43.17-3



Animation: Cytotoxic T Cells



B Cells and Antibodies: A Response to Extracellular Pathogens

- The humoral response is characterized by secretion of antibodies by B cells

Activation of B Cells

- Activation of B cells involves helper T cells as well as proteins on the surface of pathogens
- When an antigen binds a B cell, the cell takes in a few foreign molecules by receptor-mediated endocytosis
- The class II MHC protein of the B cell then presents an antigen fragment to a helper T cell, a process that is critical to B cell activation

- An activated B cell gives rise to thousands of identical plasma cells
- These begin producing and secreting antibodies
- Most antigens recognized by B cells contain multiple epitopes
- A variety of B cells activated by one antigen will give rise to plasma cells producing antibodies directed against different epitopes of the common antigen

Figure 43.18-1

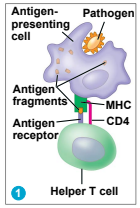


Figure 43.18-2

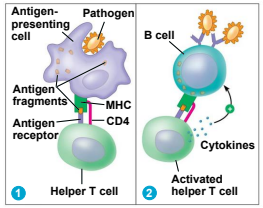
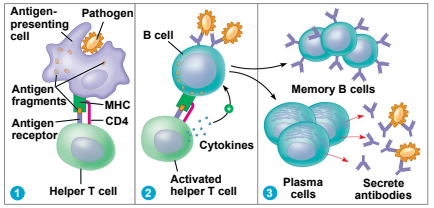


Figure 43.18-3



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, 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

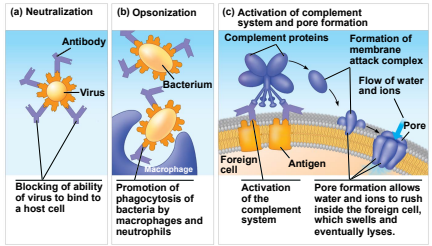


Figure 43.19a

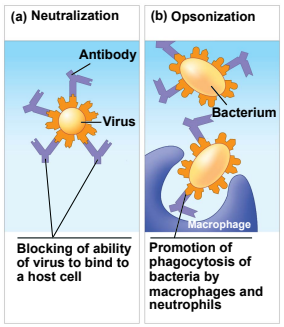
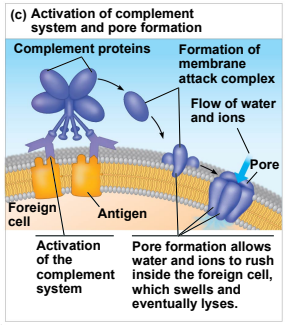
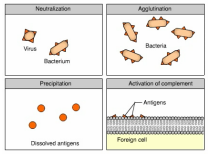


Figure 43.19b



Animation: Antibodies



- B cells can express five different forms (or classes) of immunoglobulin (Ig) with similar antigen-binding specificity but different heavy chain C regions
- IgD is membrane bound, while the other four, IgA, IgE, IgG, and IgM are soluble

Summary of the Humoral and Cell-Mediated Immune Responses

- Both the humoral and cell-mediated responses can include primary and secondary immune responses
- Memory cells enable the secondary response

Figure 43.20

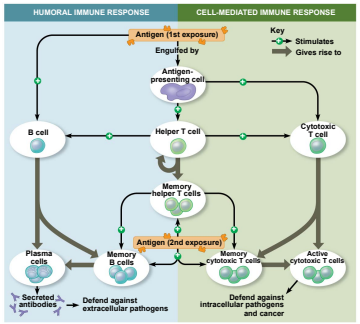


Figure 43.20a

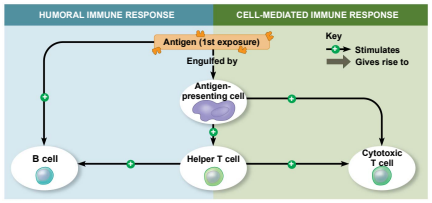
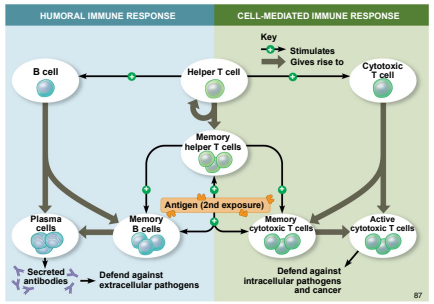
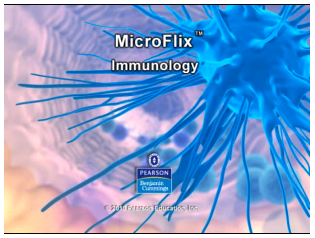


Figure 43.20b



BioFlix: Immunology



Active and Passive Immunity

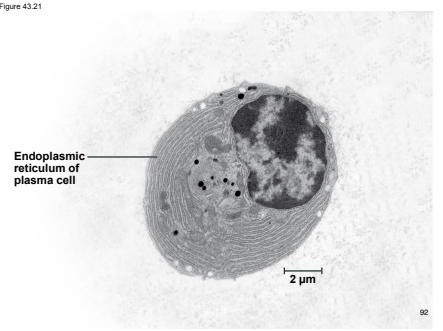
- **Active immunity** develops naturally a pathogen invades the body and elicits a primary or secondary immune response
- **Passive immunity** provides immediate, short-term protection
- It is conferred naturally when IgG crosses the placenta from mother to fetus or when IgA passes from mother to infant in breast milk

- Both active and passive immunity can be induced artificially
- Active immunity can develop following **immunization**, introduction of antigens into the body
- In artificial passive immunization, antibodies from an immune animal are injected into a nonimmune animal

Antibodies as Tools

- Antibodies produced by an animal after exposure to an antigen are the products of many different clones of plasma cells
- However, **monoclonal antibodies** can be prepared from a single clone of B cells grown in culture
- These antibodies are identical and specific for one epitope
- Monoclonal antibodies are used in many types of medical diagnoses and treatments

Figure 43.21



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

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: Disruptions in immune system function can elicit or exacerbate disease

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

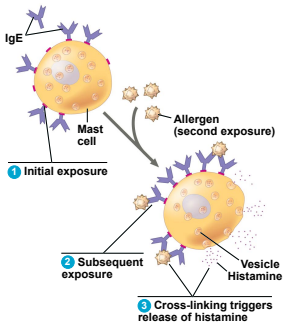
Exaggerated, Self-Directed, and Diminished Immune Responses

- If the delicate balance of the immune system is disrupted, effects can be severe

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

Figure 43.22



- 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

Figure 43.23

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 a genetic or developmental defect in the innate or adaptive defenses, or both
- Acquired immunodeficiency develops later in life due to exposure to chemical and biological agents

Evolutionary Adaptations of Pathogens That Underlie Immune System Avoidance

- 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

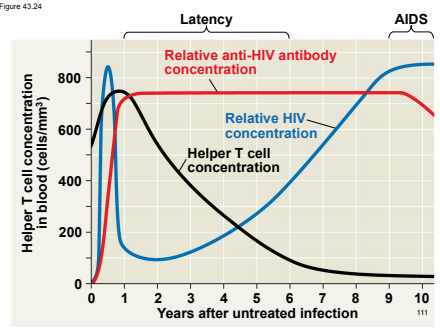
- Some viruses may remain in a host in an inactive state called latency
- Herpes simplex viruses can be present in a human host without causing symptoms

Attack on the Immune System: HIV

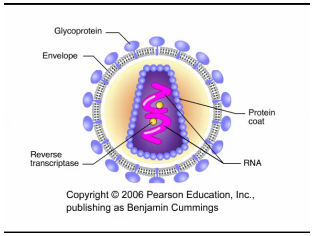
- **Human immunodeficiency virus** (**HIV**) infects helper T cells
- HIV persists in the host—despite an immune response—because it has a high mutation rate that promotes antigen variation
- Over time an untreated HIV infection not only avoids the adaptive immune response, but abolishes it

- HIV infection leads to **acquired immune deficiency syndrome** (**AIDS**)
- People with AIDS are highly susceptible to opportunistic infections and cancers that take advantage of an immune system in collapse
- The spread of HIV is a worldwide problem
- The best approach for slowing this spread is education about practices that transmit the virus

Figure 43.24



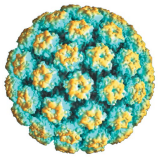
Animation: HIV Reproductive Cycle



Cancer and Immunity

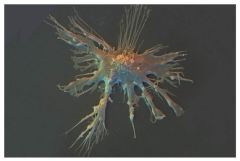
- The frequency of certain cancers increases when adaptive immunity is inactivated
- 15–20% of all human cancers involve viruses
- The immune system can act as a defense against viruses that cause cancer and cancer cells that harbor viruses
- In 2006, a vaccine was released that acts against human papillomavirus (HPV), a virus associated with cervical cancer

Figure 43.UN05



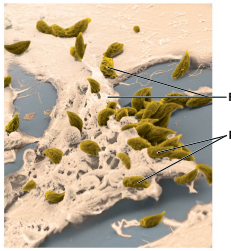
Human papillomavirus

Figure 43.UN02



A dendritic cell (colorized SEM)

Figure 43.UN03



A dying infected cell (colorized SEM).

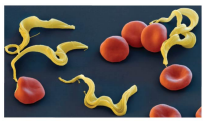
Figure 43.UN04a

Day	Number of Parasites (in millions) per mL of Blood
4	0.1
6	0.3
8	1.2
10	0.2
12	0.2
14	0.9
16	0.6
18	0.1
20	0.7
22	1.2
24	0.2

Figure 43.UN04b

Day	Antibody Specific to Glycoprotein Variant A	Antibody Specific to Glycoprotein Variant B
4	0	0
6	0	0
8	0.2	0
10	0.5	0
12	1	0
14	1	0.1
16	1	0.3
18	1	0.9
20	1	1
22	1	1
24	1	1

Figure 43.UN04c



Trypanosomes (yellow) and red blood cells

Figure 43.UN06

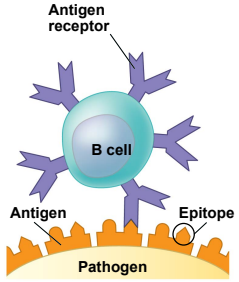


Figure 43.UN07

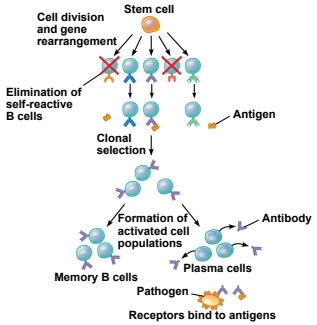


Figure 43.UN08