LECTURE PRESENTATIONS

For CAMPBELL BIOLOGY, NINTH EDITION

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Chapter 43

The Immune System

Lectures by
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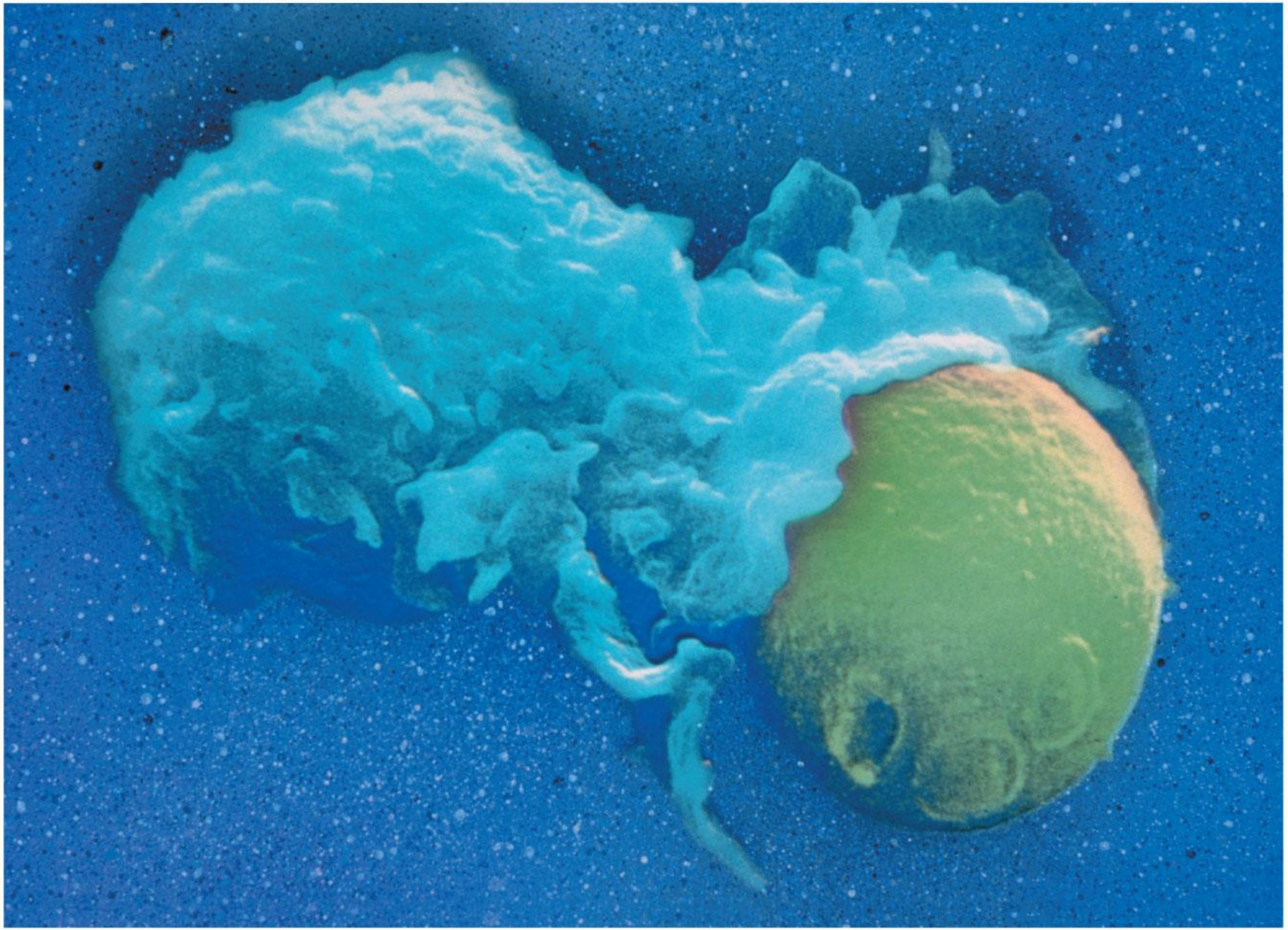
Overview: Recognition and Response

- **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**

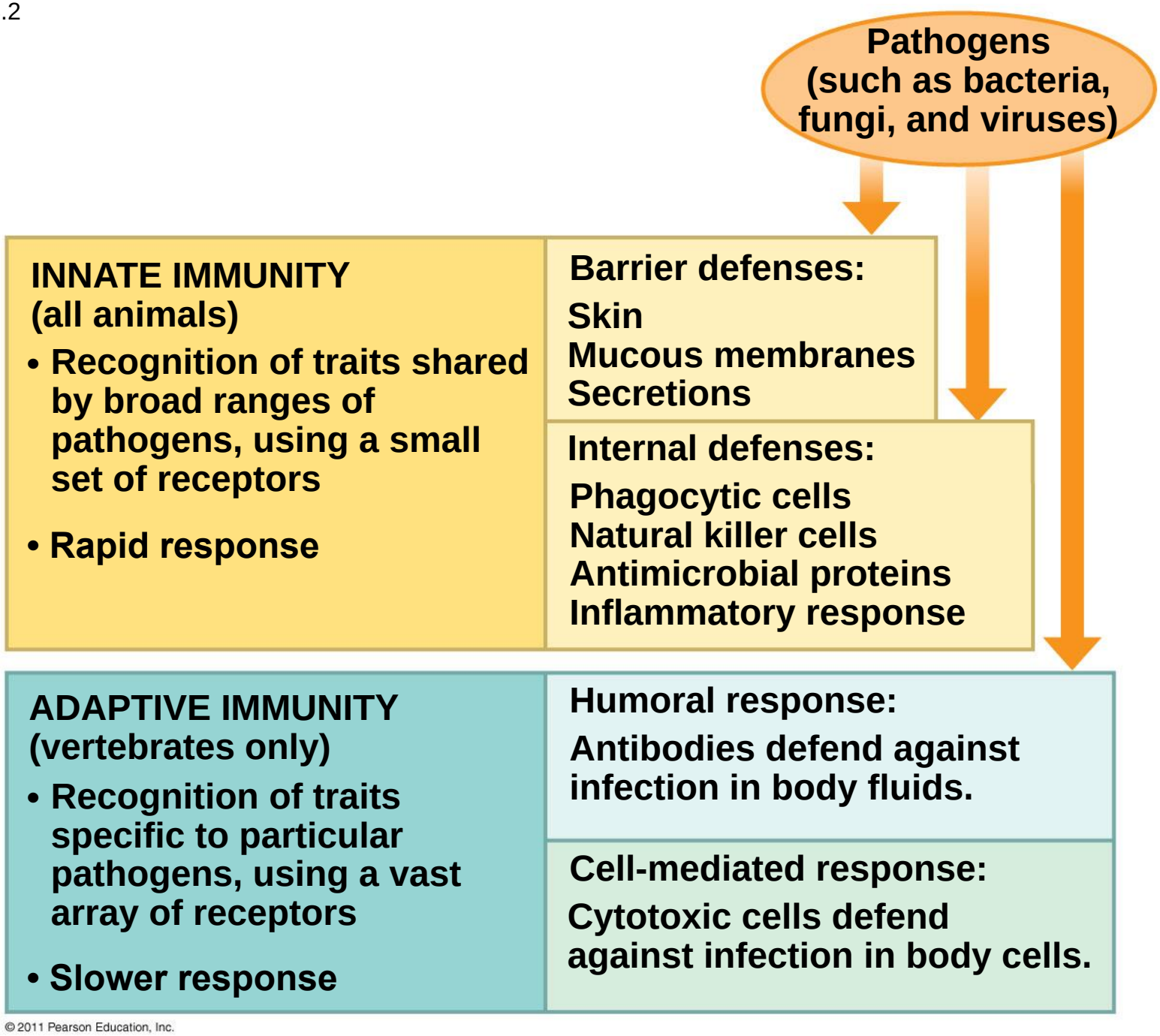
Figure 43.1



- 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

- 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



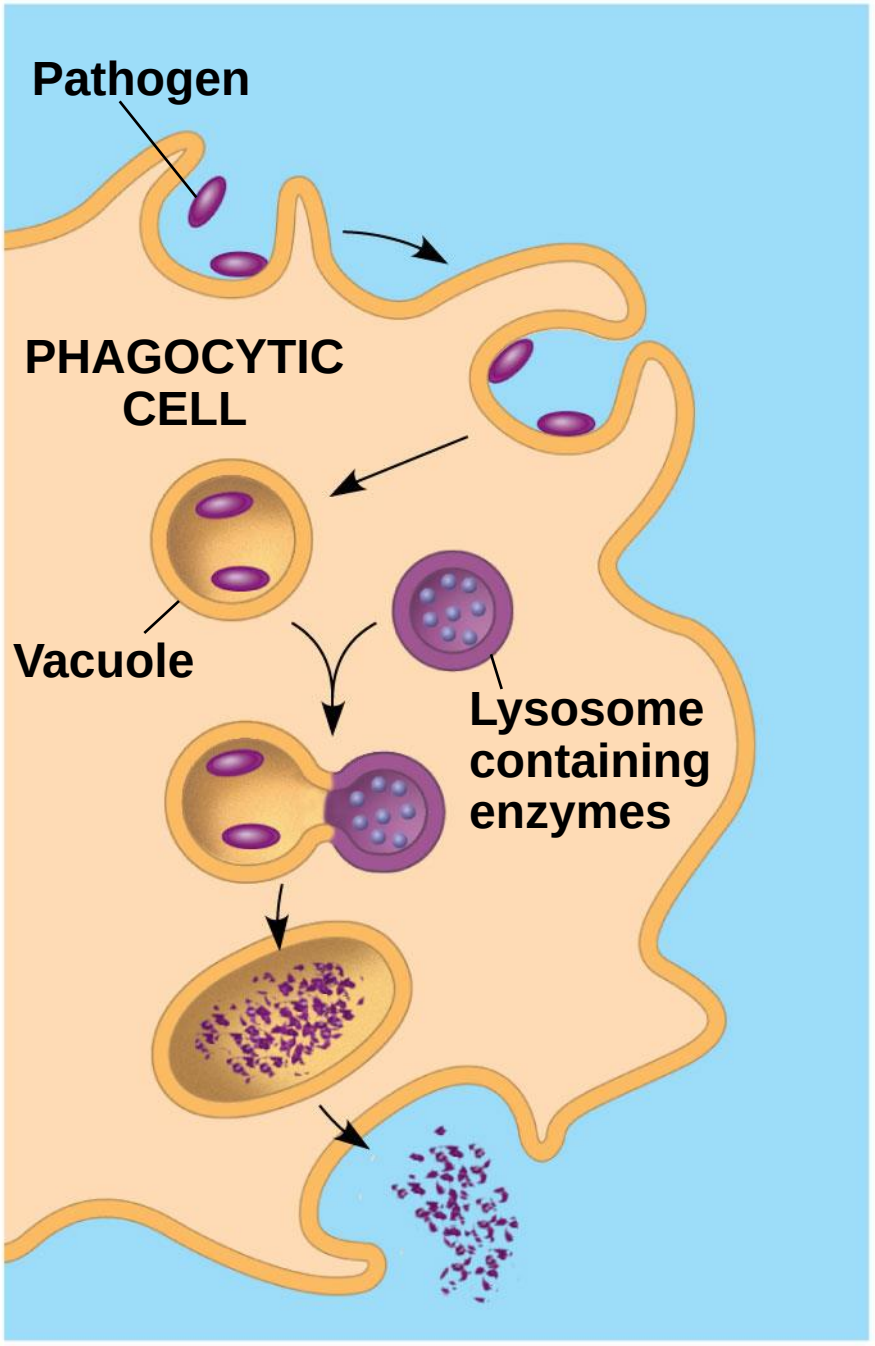
Concept 43.1: In innate immunity, recognition and response rely on traits common to groups of pathogens

- 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

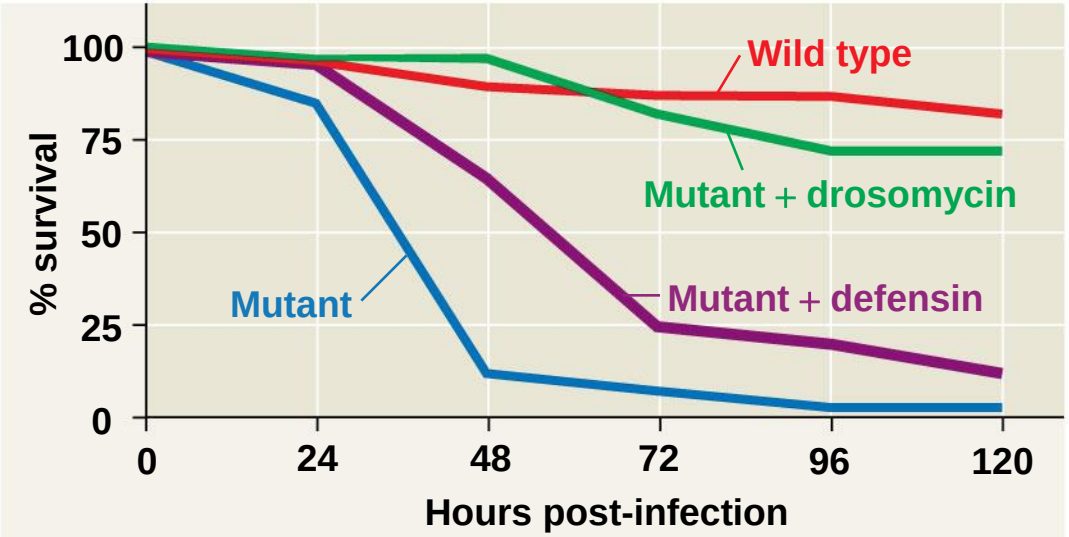


- Hemocytes also secrete antimicrobial peptides that disrupt the plasma membranes of fungi and bacteria

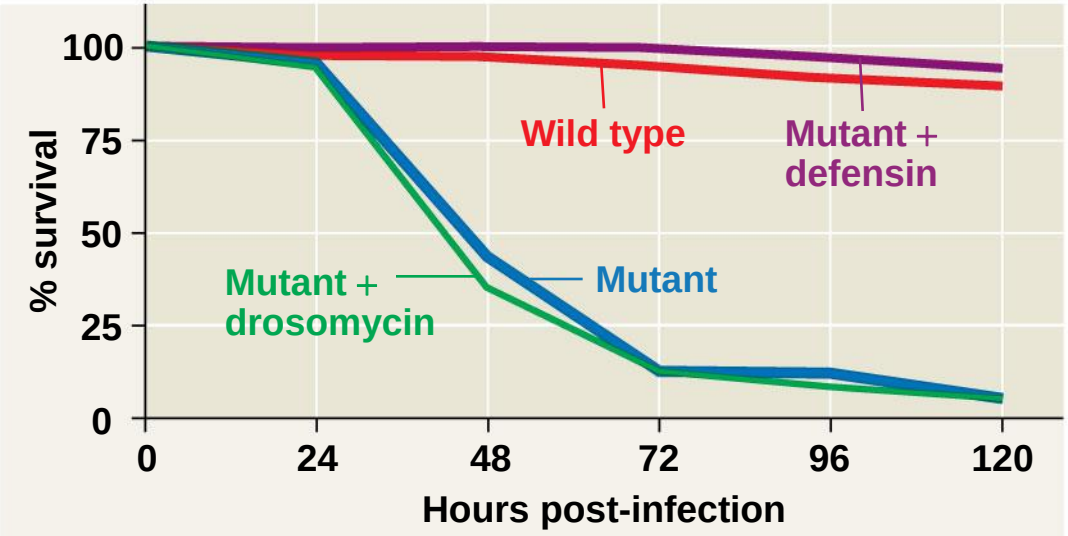
- The immune system recognizes bacteria and fungi by structures on their cell walls
- An immune response varies with the class of pathogen encountered

Figure 43.5

RESULTS



Fruit fly survival after infection by *N. crassa* fungi



Fruit fly survival after infection by *M. luteus* bacteria

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

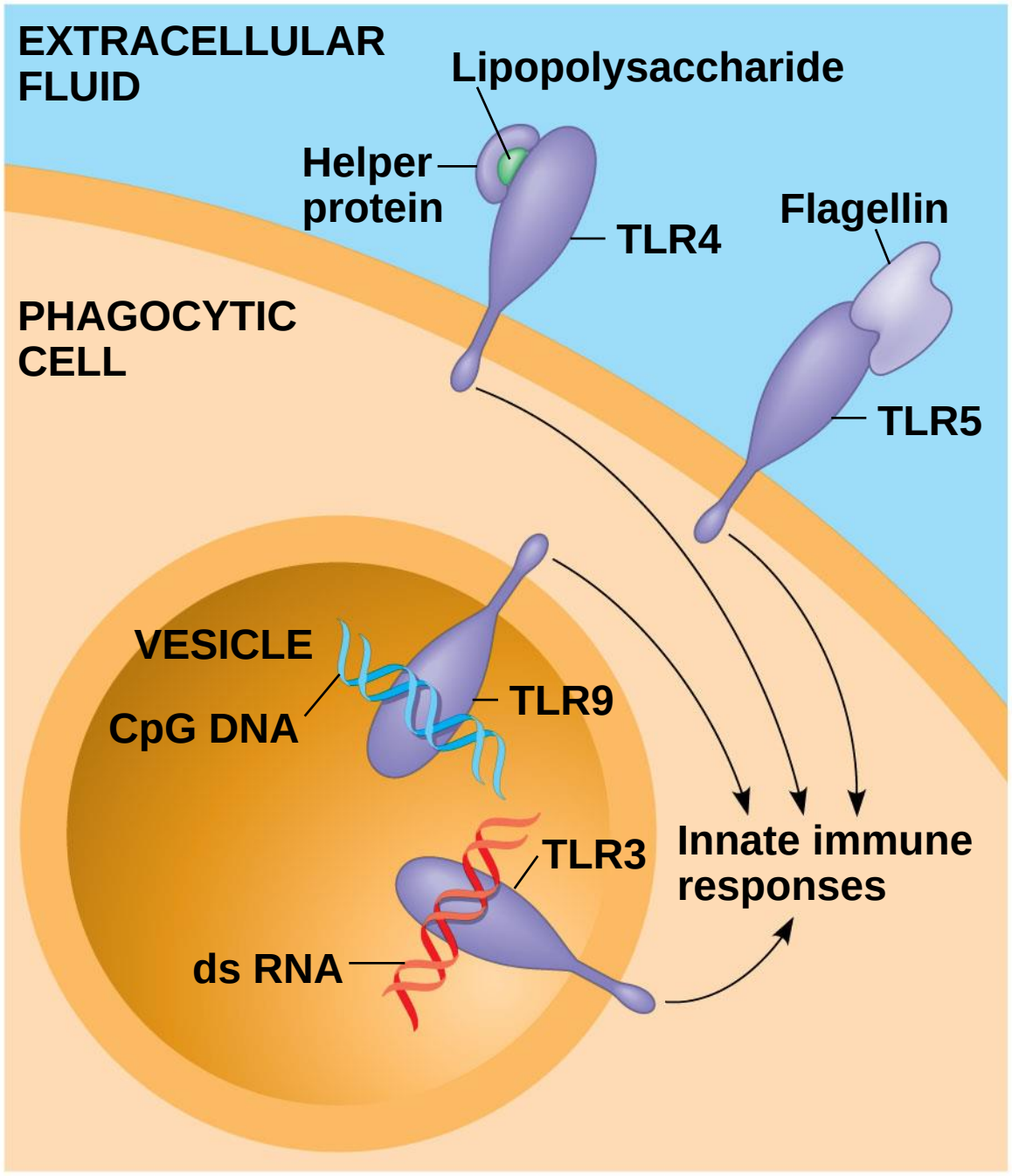
Barrier Defenses

- 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 by **TLRs**, **Toll-like receptors**

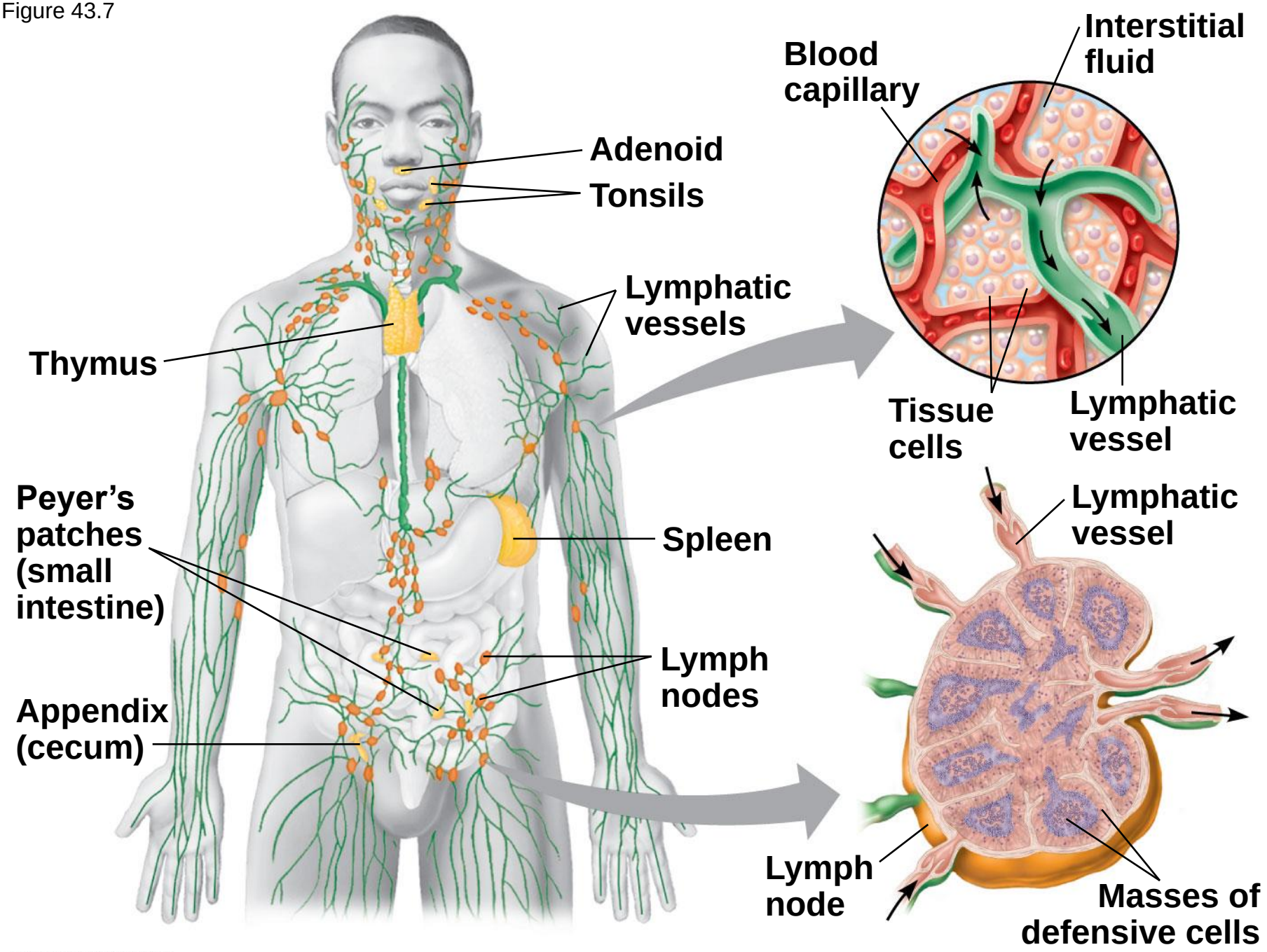
Figure 43.6



- 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**
- 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

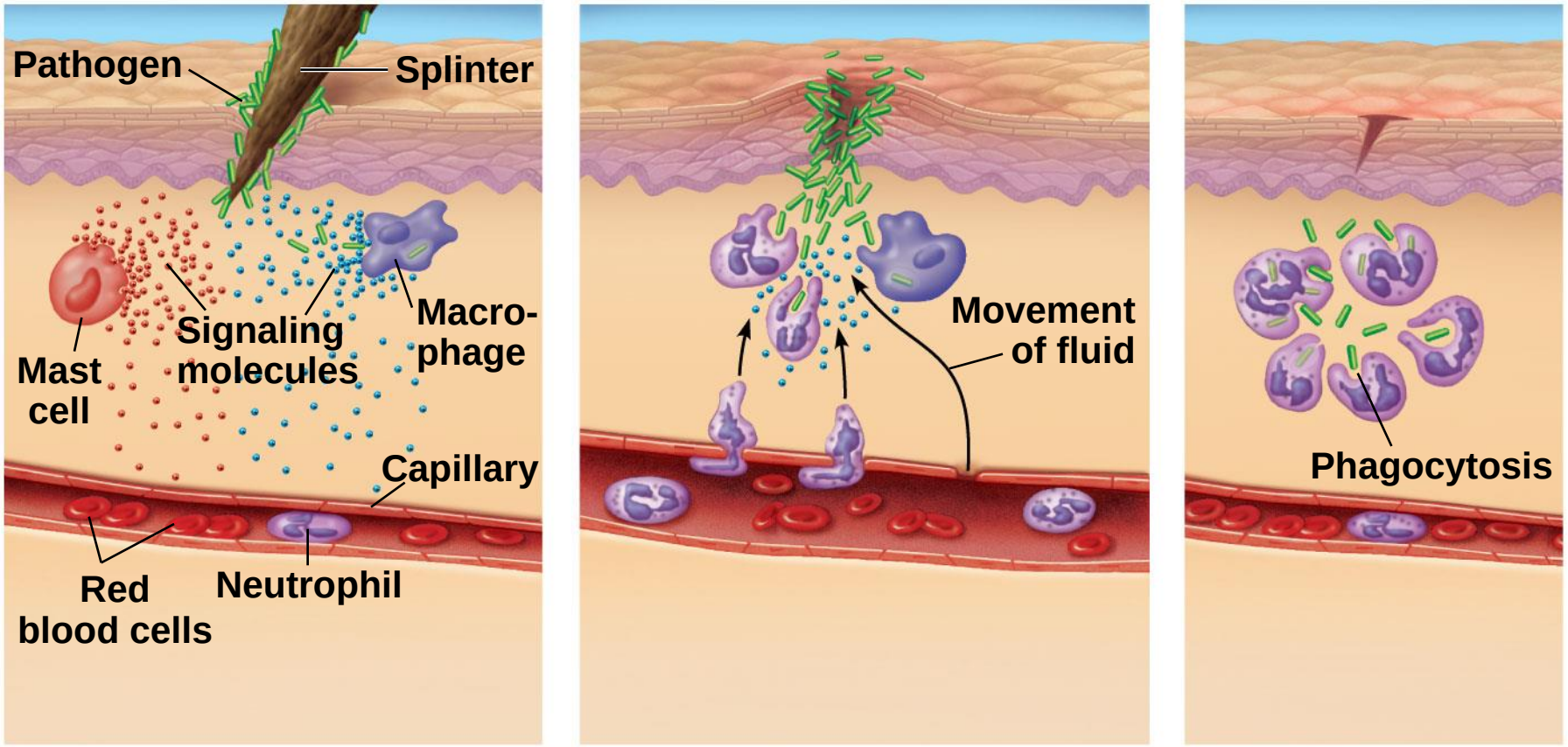
- Peptides and proteins function in innate defense by attacking pathogens or impeding their reproduction
- **Interferon** proteins provide innate defense, interfering with viruses and helping activate macrophages
- About 30 proteins make up the **complement system**, which causes lysis of invading cells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

- *Pus,* a fluid rich in white blood cells, dead pathogens, and cell debris from damaged tissues

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

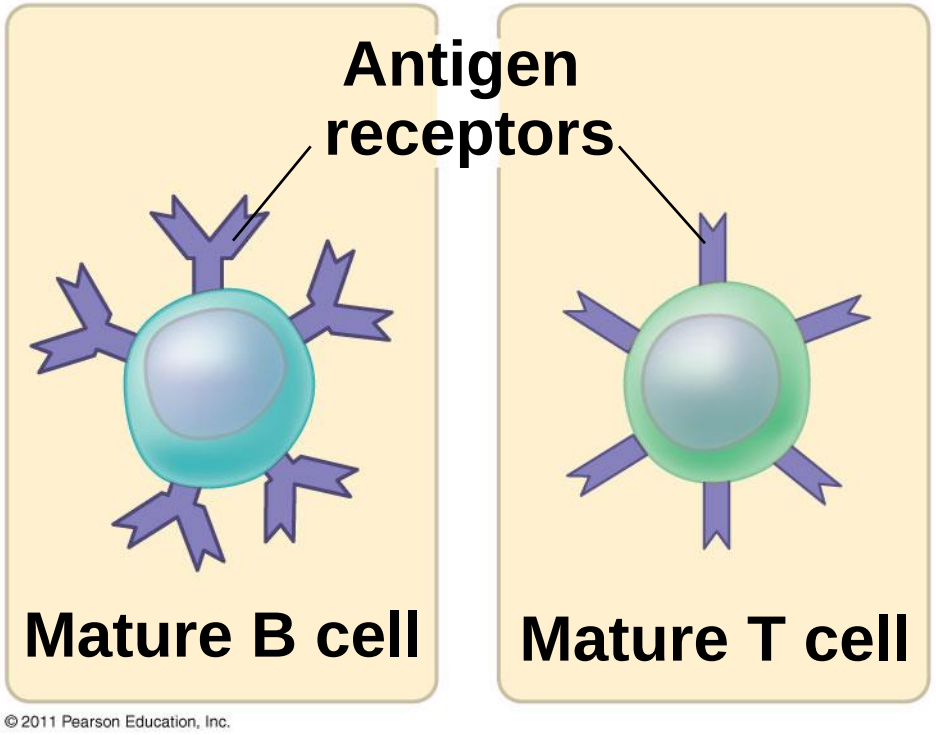
- Some pathogens avoid destruction by modifying their surface to prevent recognition or by resisting breakdown following phagocytosis
- Tuberculosis (TB) is one such disease and kills more than a million people a year

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
- 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**

Figure 43.UN01

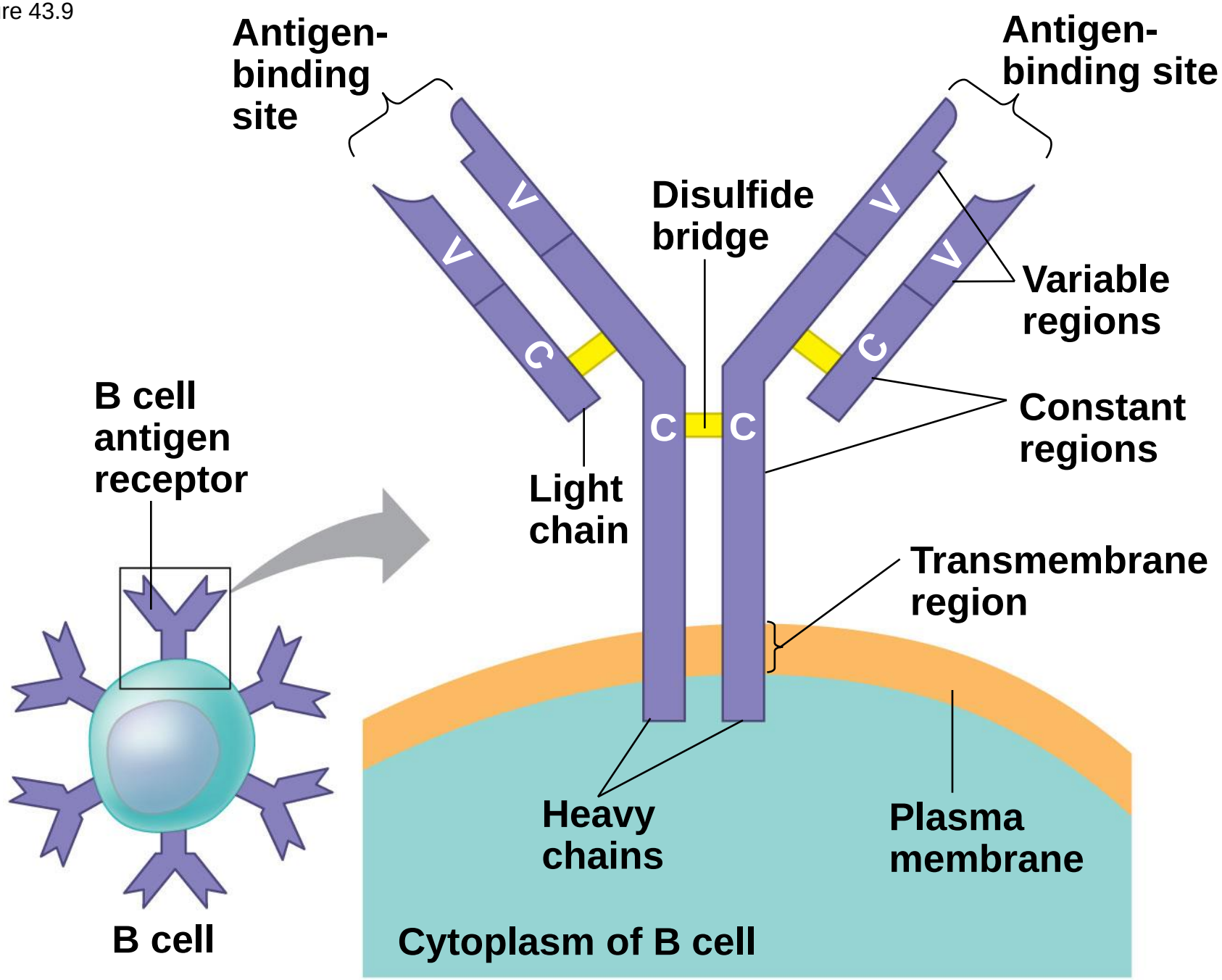


- B cells and T cells have receptor proteins that can bind to foreign molecules
- Each individual lymphocyte is specialized to recognize a specific type of molecule

Antigen Recognition by B Cells and Antibodies

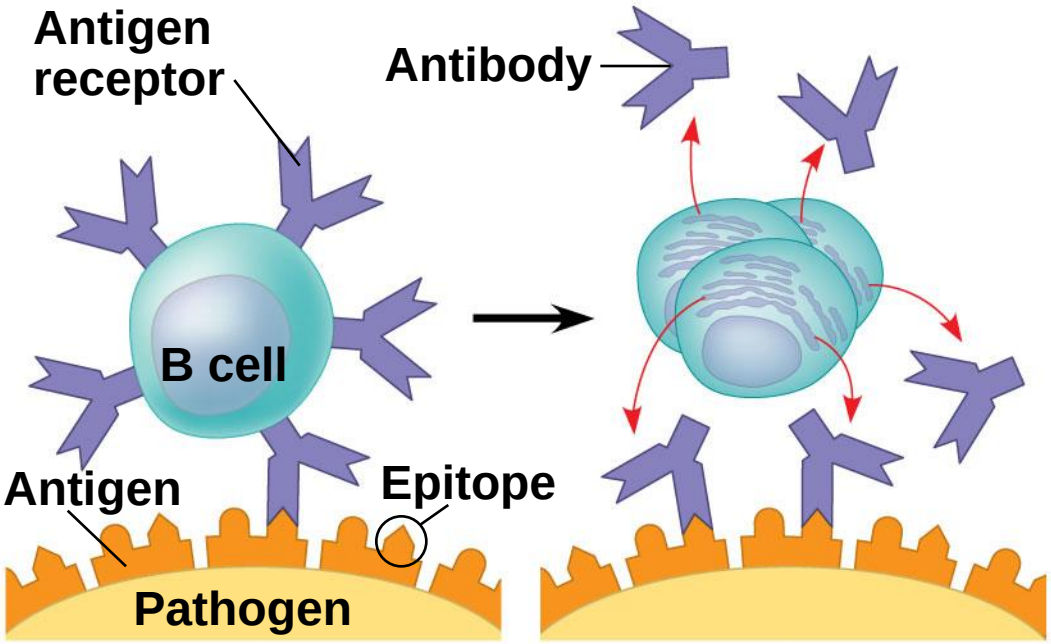
- Each B cell antigen receptor is a Y-shaped molecule with two identical **heavy chains** and two identical **light chains**
- The constant regions of the chains vary little among B cells, whereas the variable regions differ greatly
- The variable regions provide antigen specificity

Figure 43.9

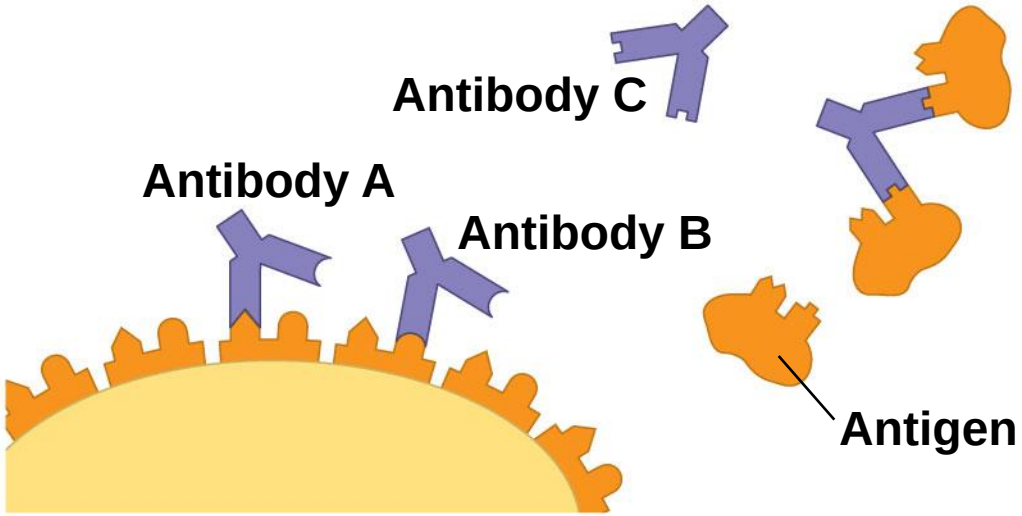


- Binding of a B cell antigen receptor to an antigen is an early step in B cell activation
- This gives rise to cells that secrete a soluble form of the protein called an **antibody** or **immunoglobulin (Ig)**
- Secreted antibodies are similar to B cell receptors but lack transmembrane regions that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

Figure 43.10



(a) B cell antigen receptors and antibodies

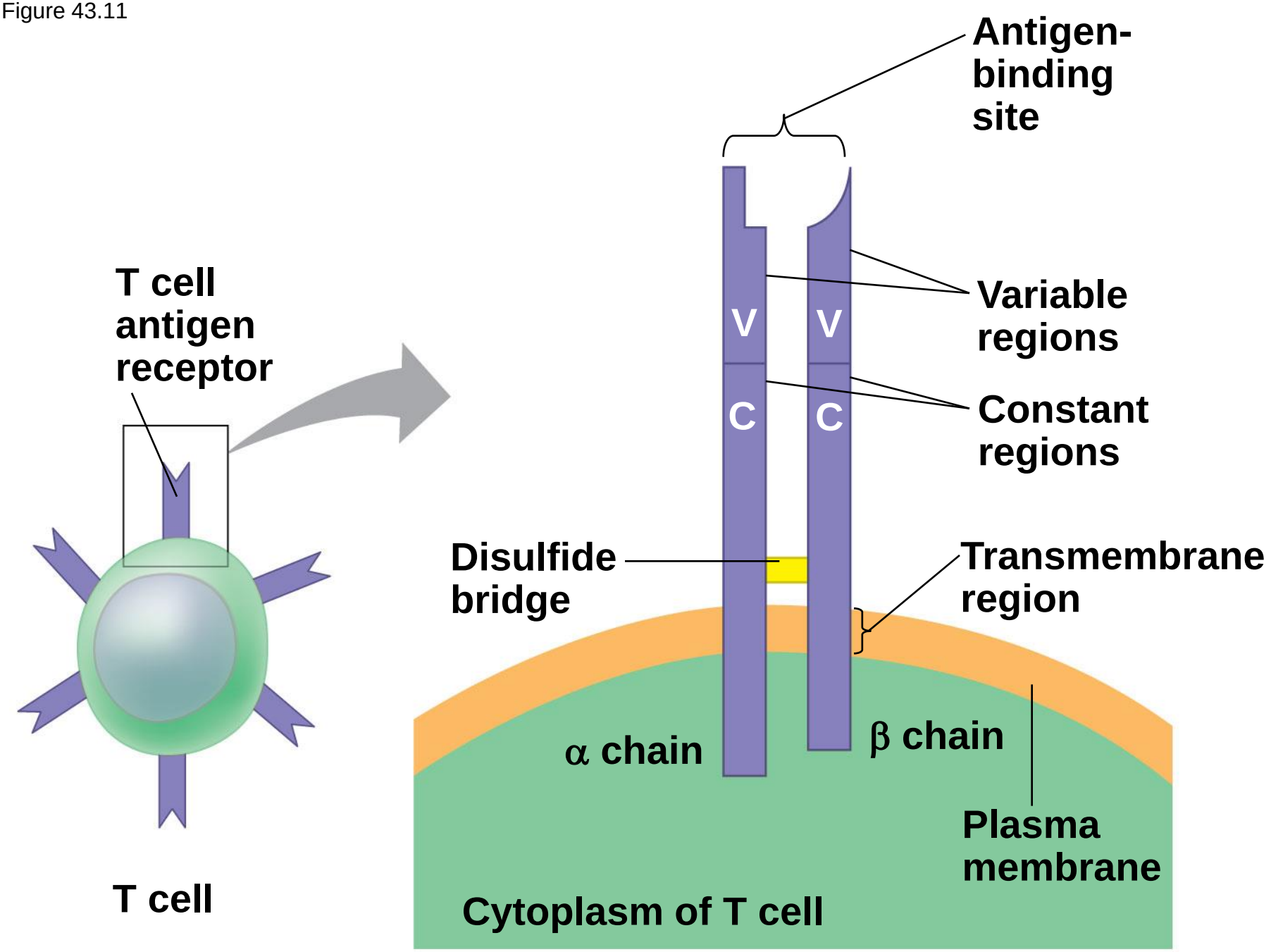


(b) Antigen receptor specificity

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

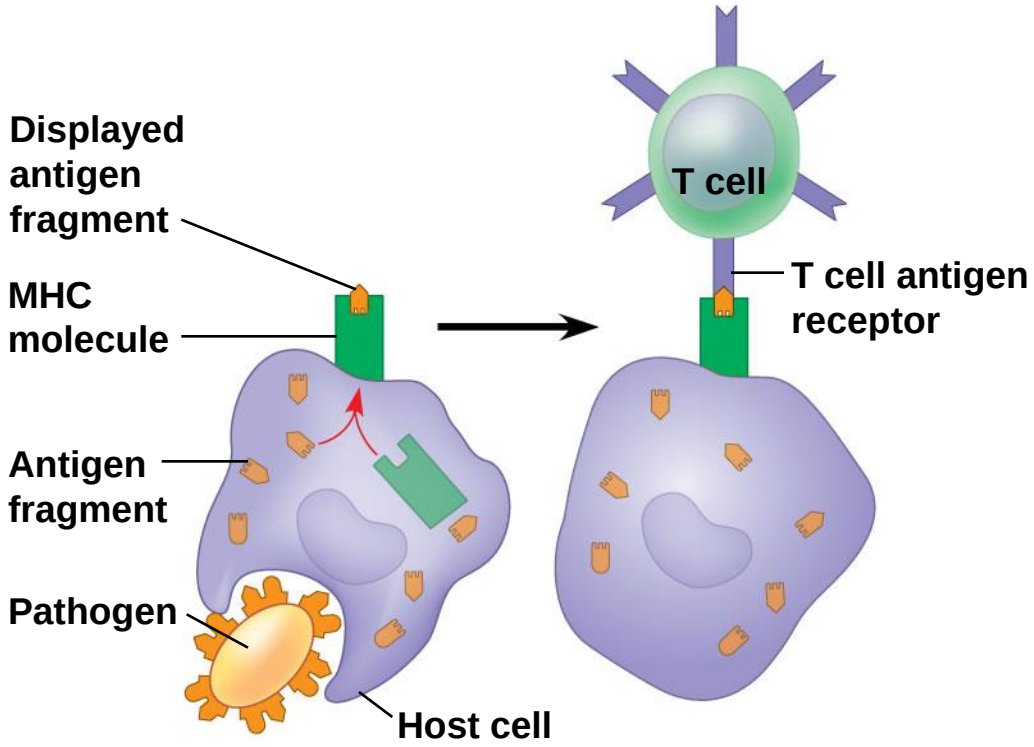
Figure 43.11



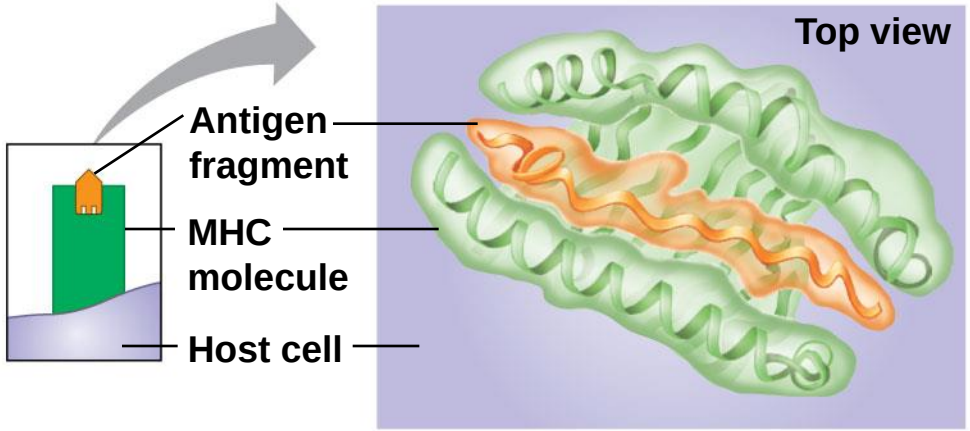
- T cells bind to antigen fragments displayed or presented on a host cell
- These antigen fragments are bound to cell-surface proteins called MHC molecules
- **MHC (major histocompatibility complex)** molecules are host proteins that display the antigen fragments on the cell surface

- 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



(a) Antigen recognition by a T cell



(b) A closer look at antigen presentation

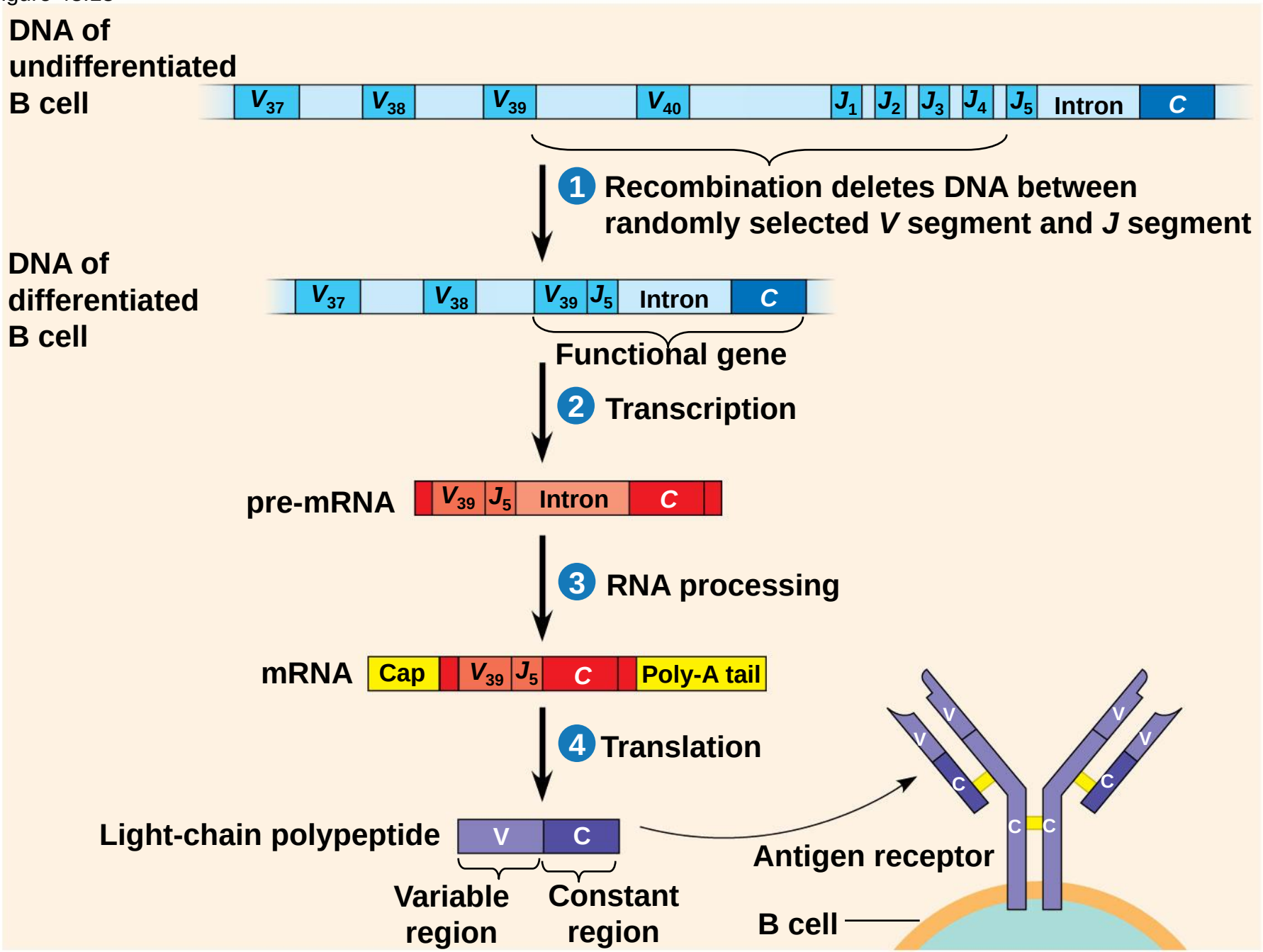
B Cell and T Cell Development

- 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

Figure 43.13



Origin of Self-Tolerance

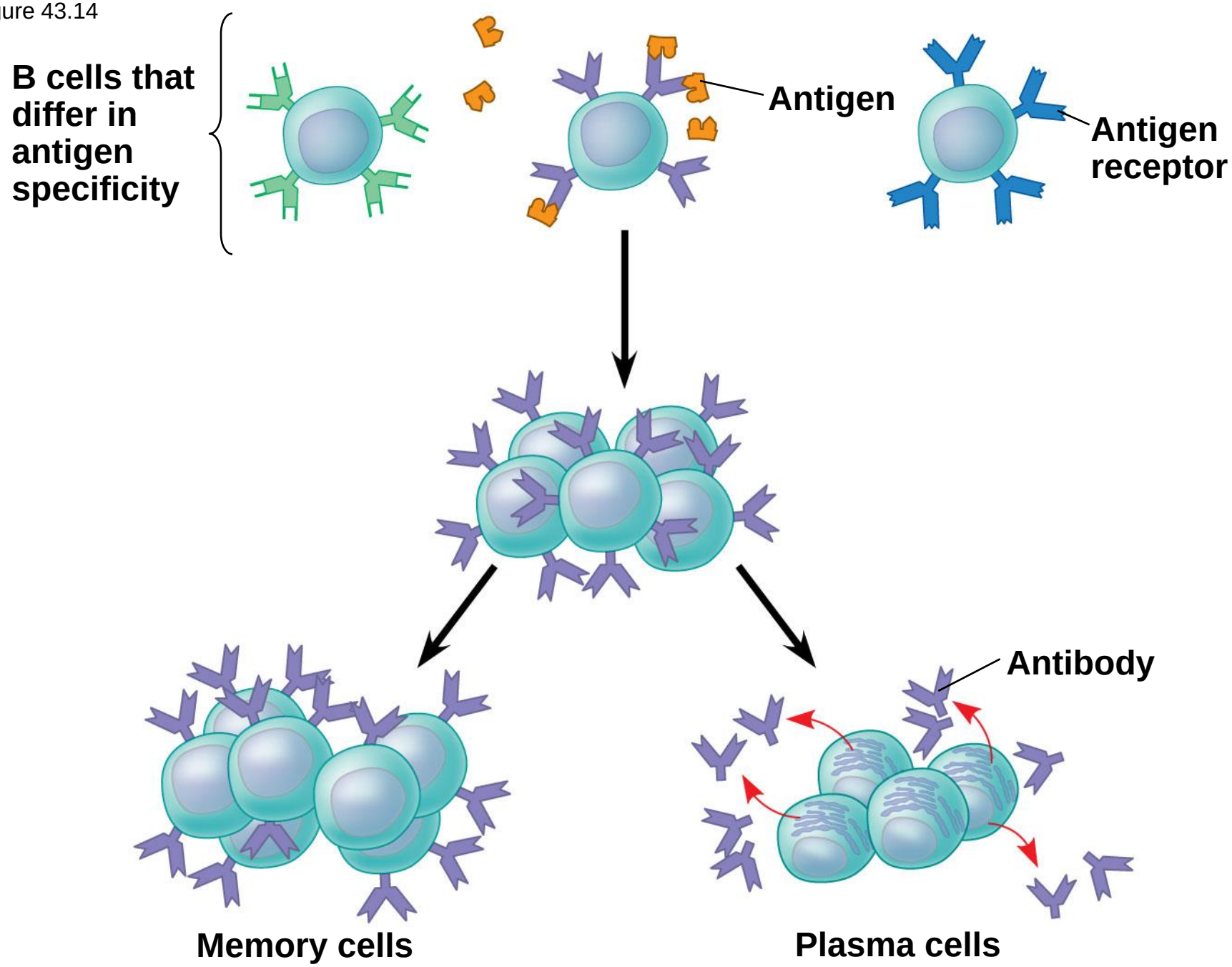
- Antigen receptors are generated by random rearrangement of DNA
- As lymphocytes mature in bone marrow or the thymus, they are tested for self-reactivity
- Some B and T cells with receptors specific for the body's own molecules are destroyed by apoptosis, or programmed cell death
- The remainder are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

Figure 43.14

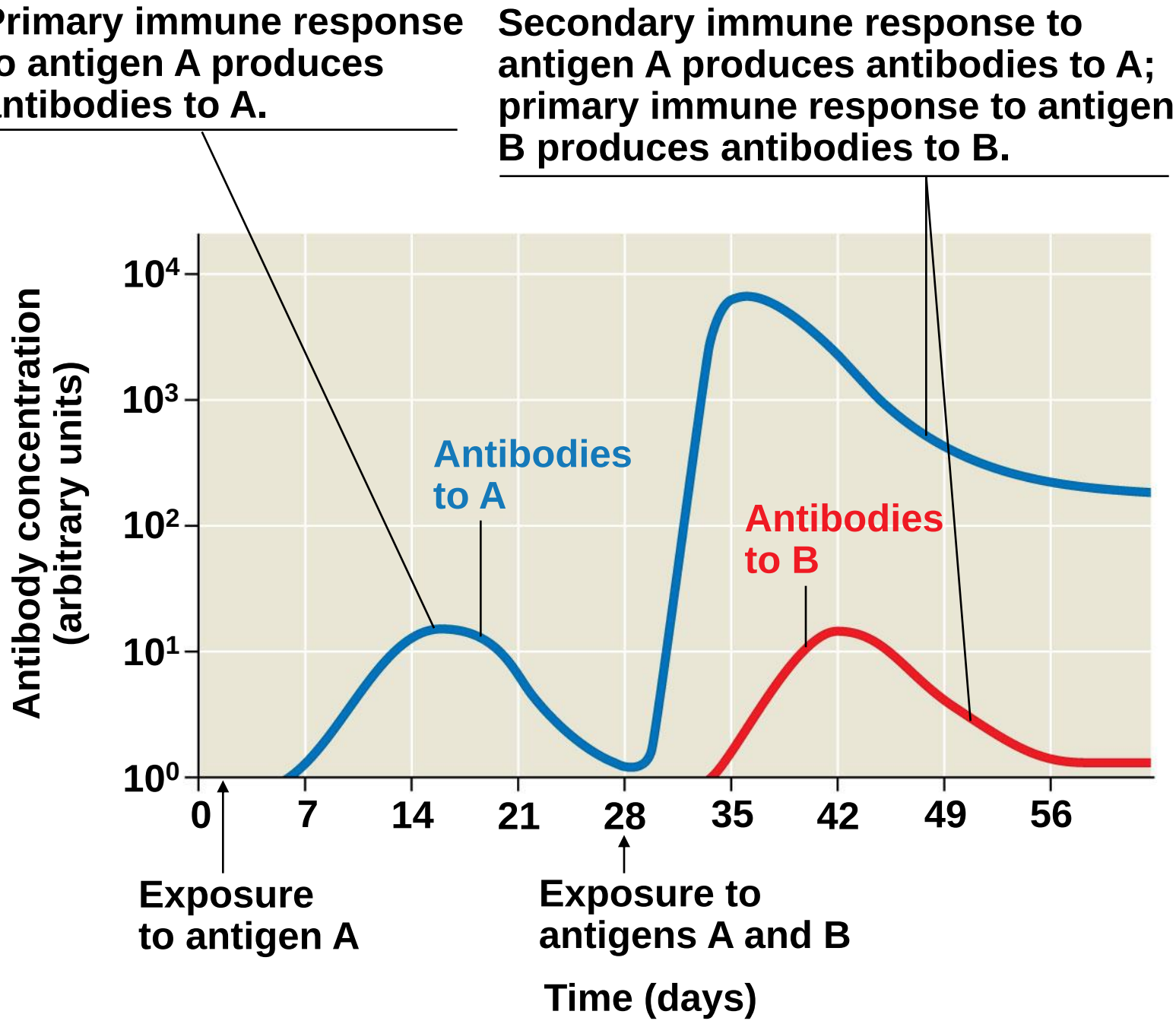


Immunological Memory

- 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

Animation: Role of B Cells

Figure 43.15



Concept 43.3: 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

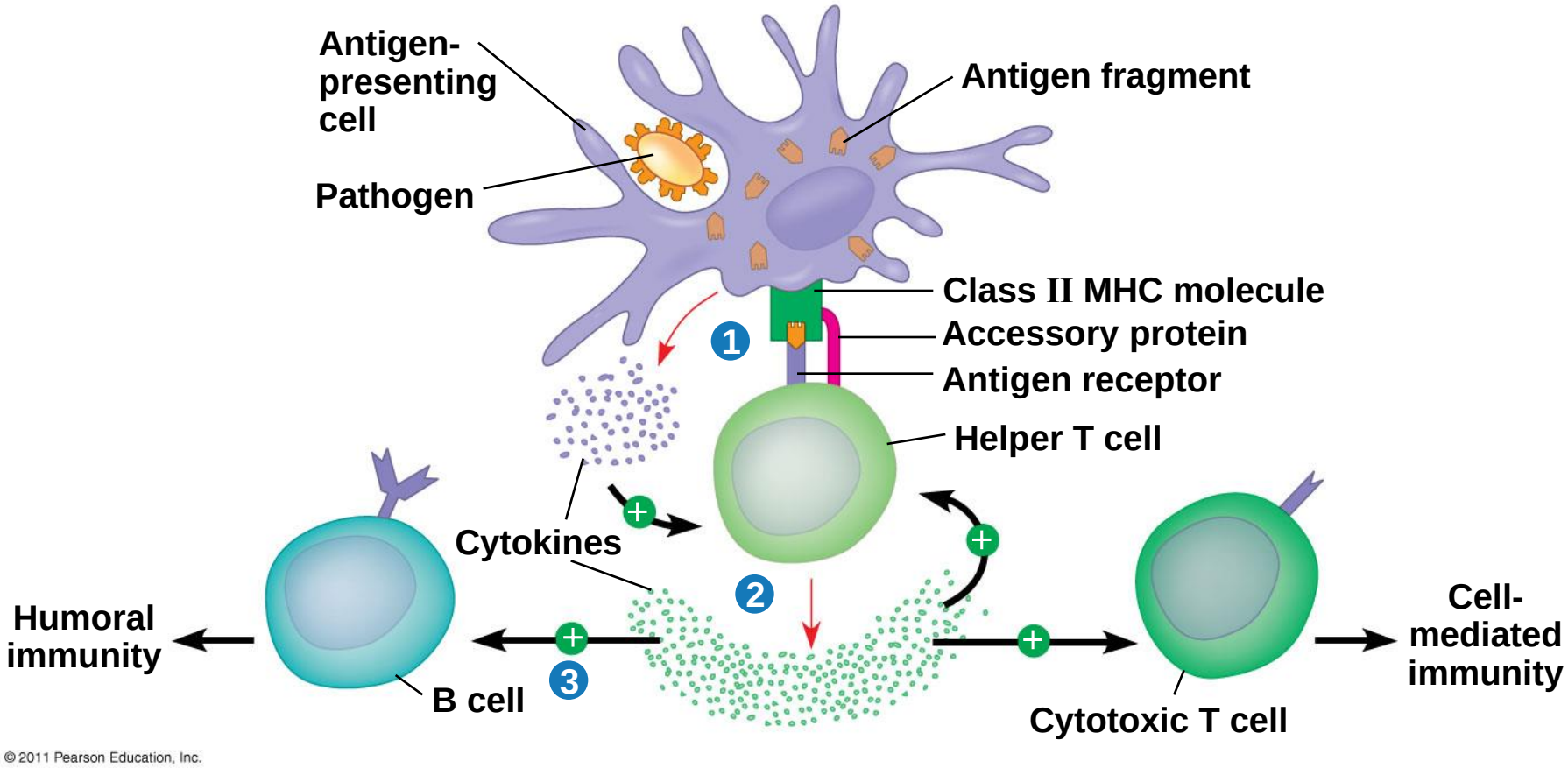
Helper T Cells: A Response to Nearly All Antigens

- 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

Animation: Helper T Cells

Figure 43.16

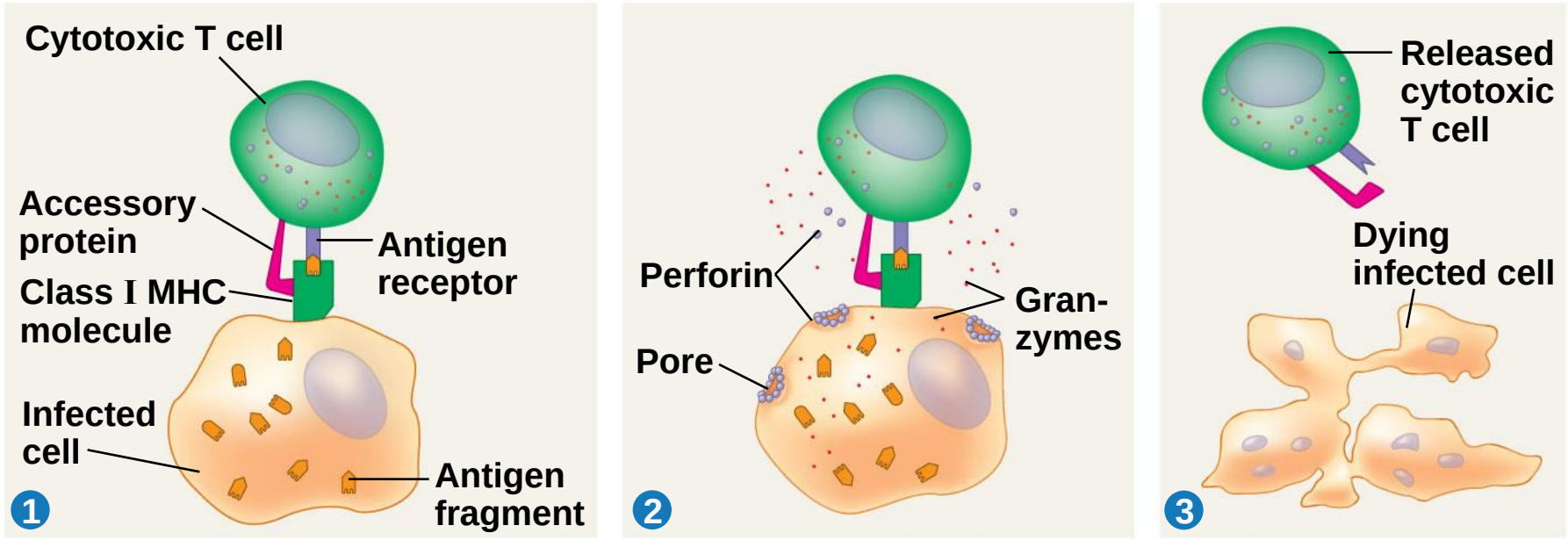


Cytotoxic T Cells: A Response to Infected Cells

- **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

Animation: Cytotoxic T Cells

Figure 43.17-3



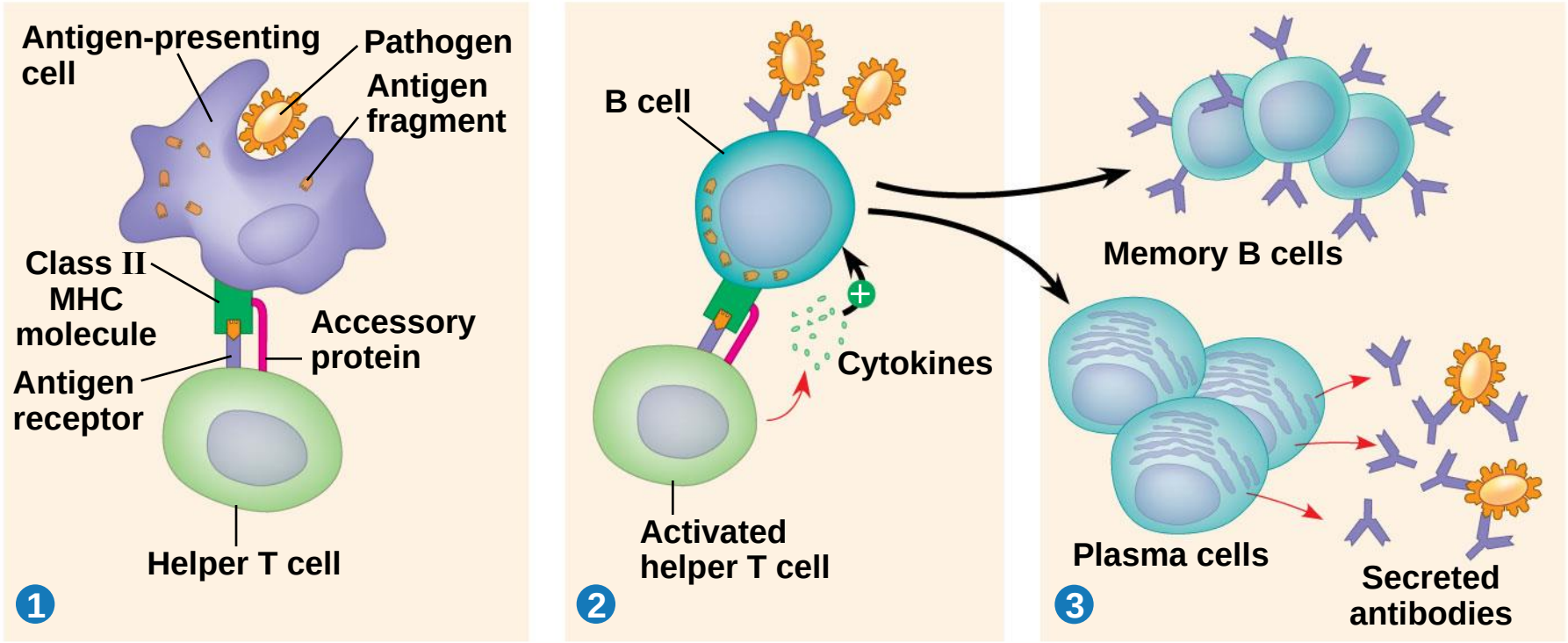
B Cells and Antibodies: A Response to Extracellular Pathogens

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

Activation of 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**

Figure 43.18-3

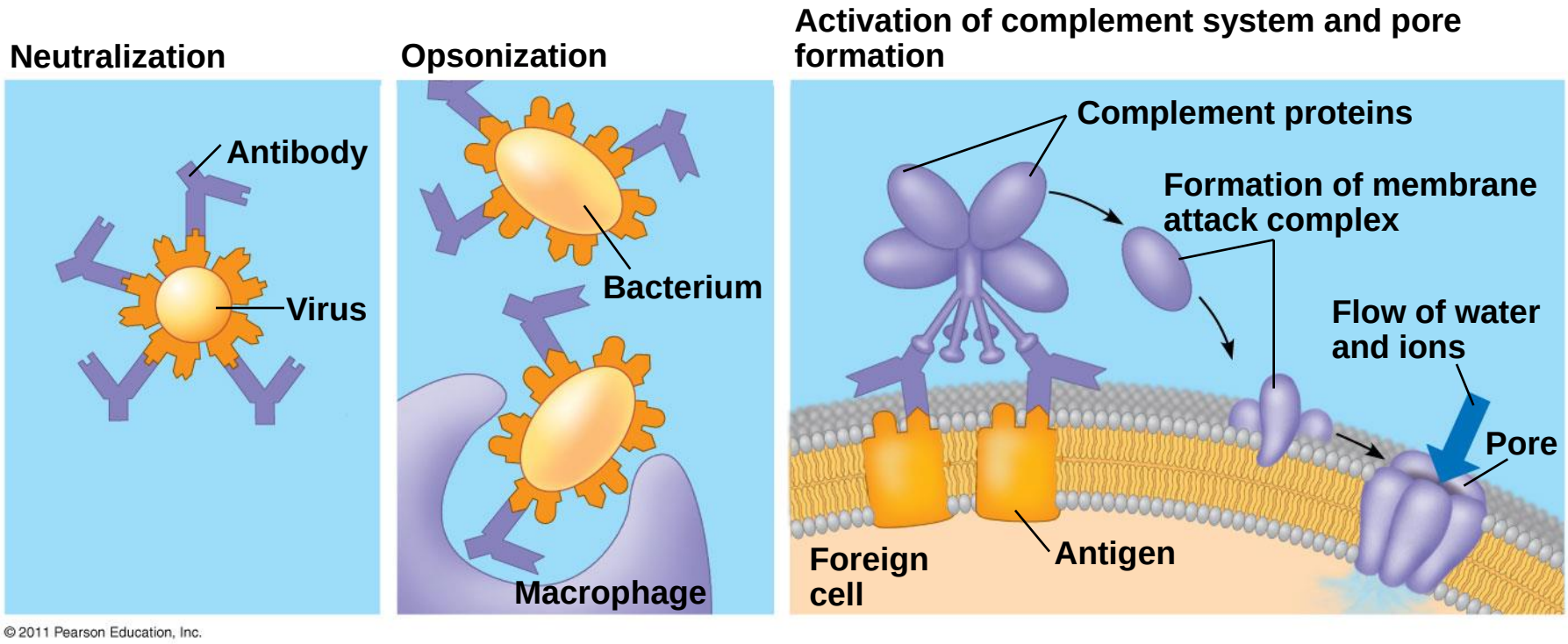


Antibody Function

- 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 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



- 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

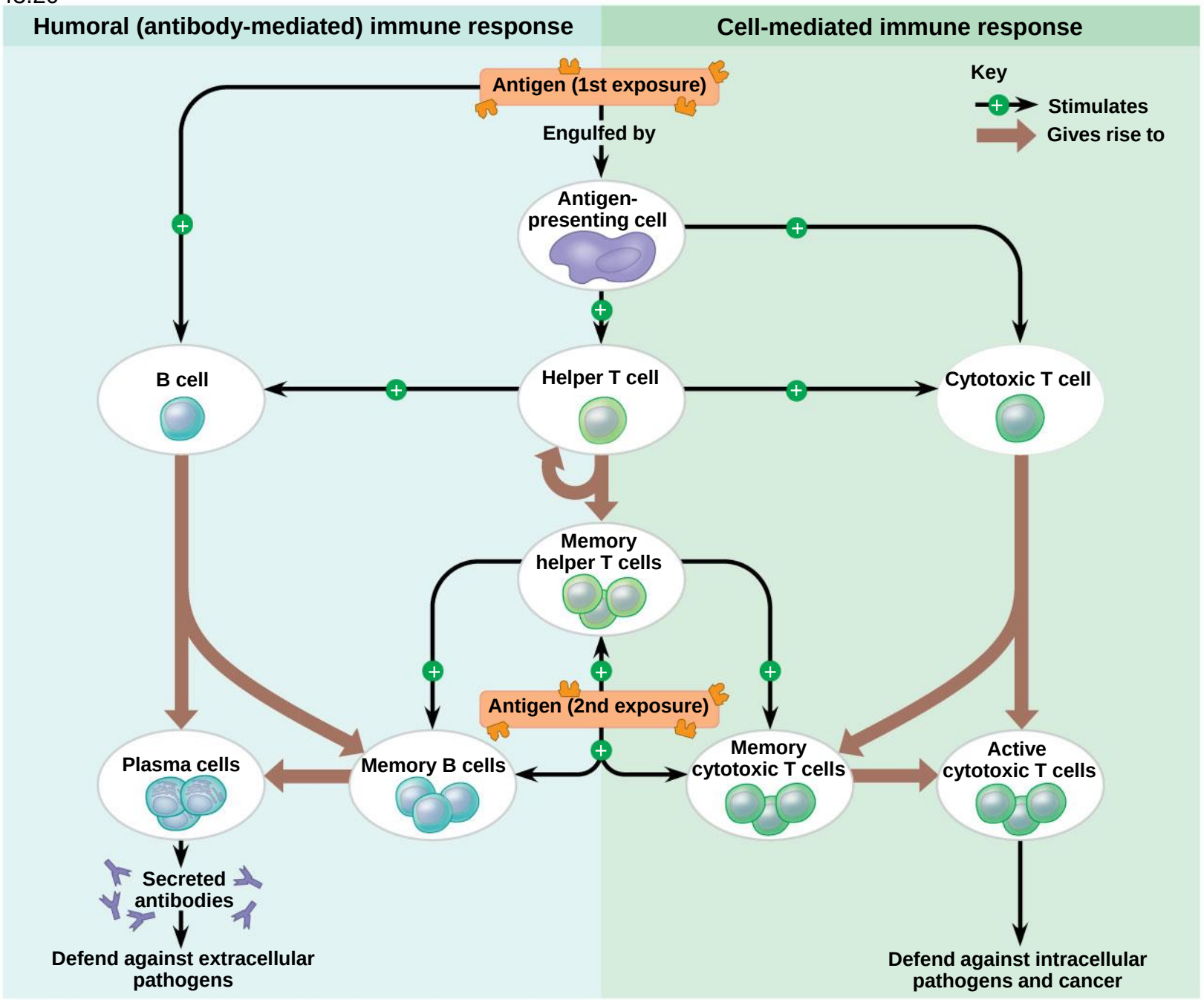
- Both the humoral and cell-mediated responses can include primary and secondary immune response
- Memory cells enable the secondary response

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

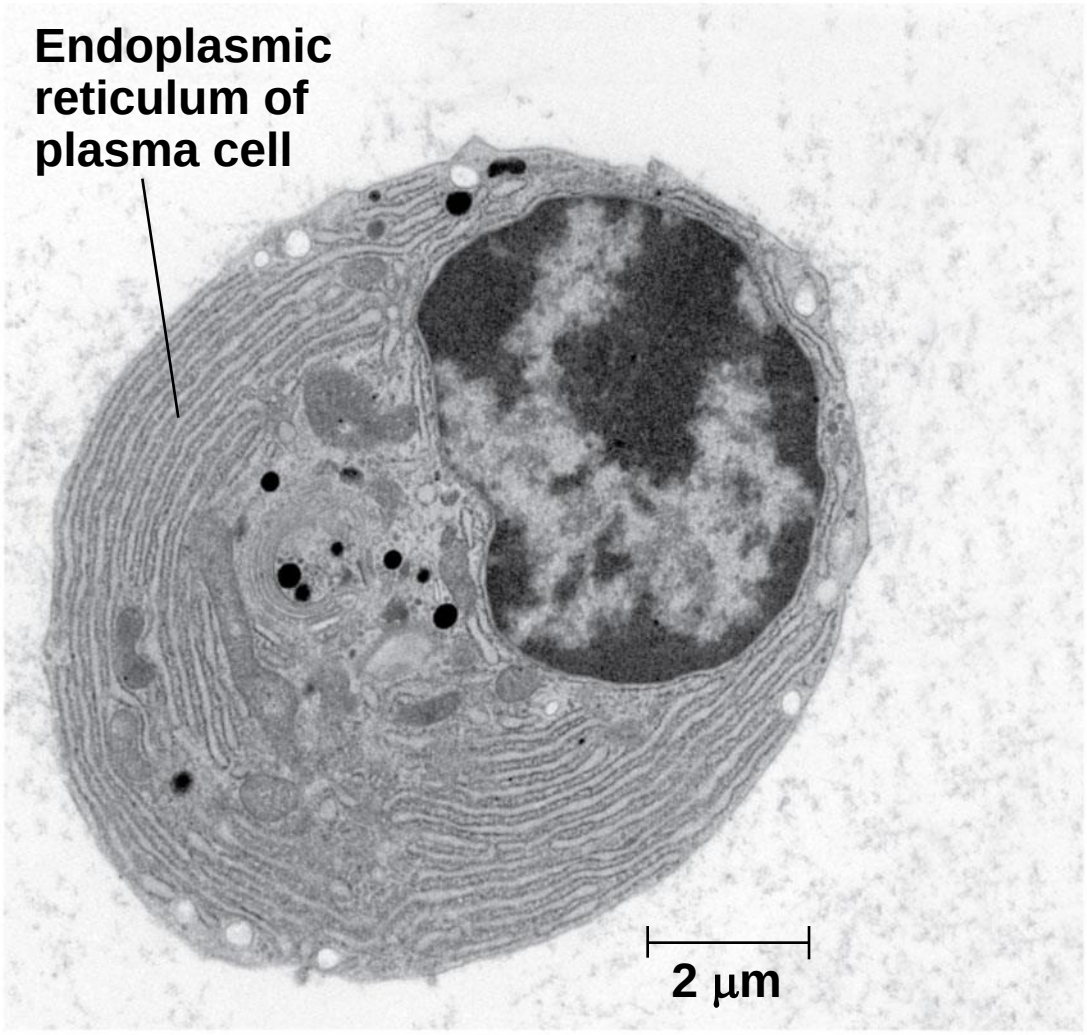
Figure 43.20



Antibodies as Tools

- Antibody specificity and antigen-antibody binding have been harnessed in research, diagnosis, and therapy
- Polyclonal antibodies, produced following exposure to a microbial antigen, are products of many different clones of plasma cells, each specific for a different epitope
- **Monoclonal antibodies** are prepared from a single clone of B cells grown in culture

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
- 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: Disruptions in immune system function can elicit or exacerbate disease

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

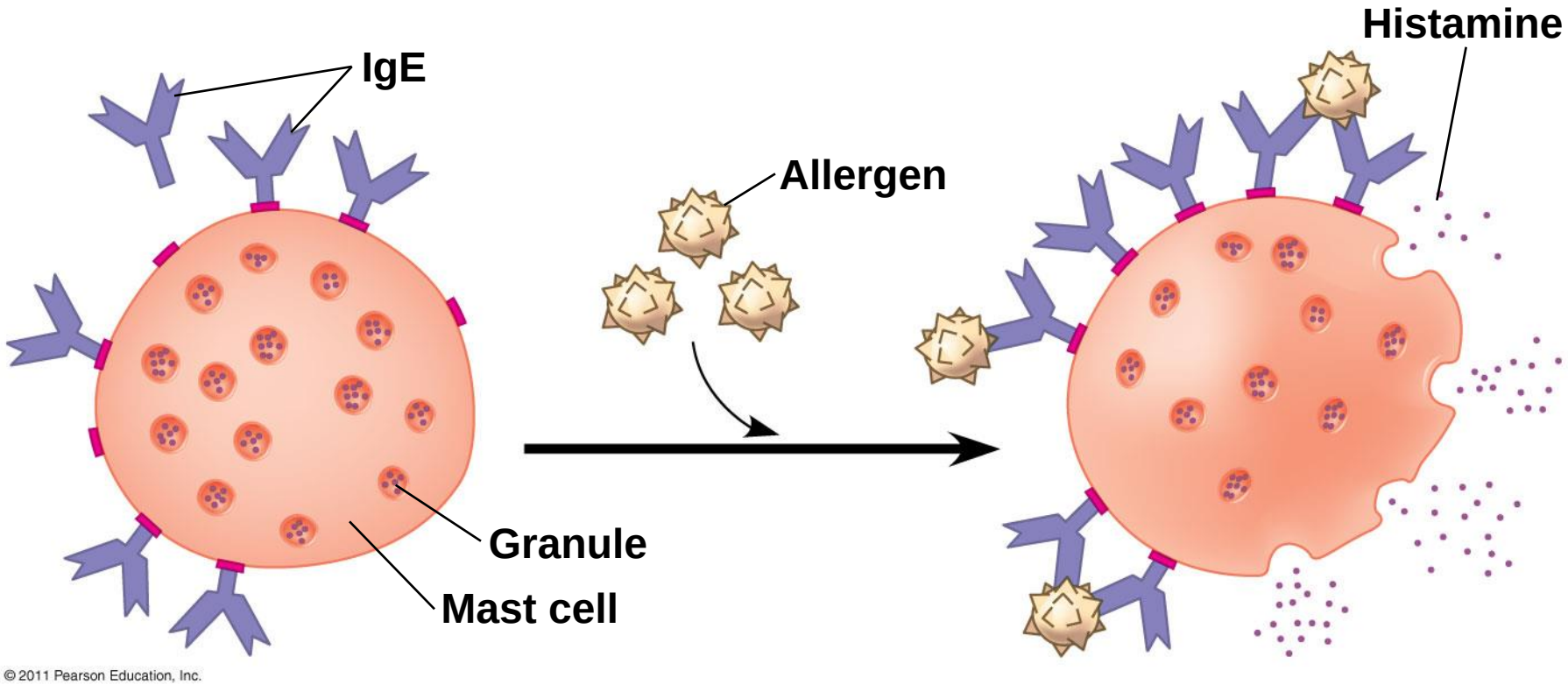
Exaggerated, Self-Directed, and Diminished Immune Responses

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

Figure 43.22

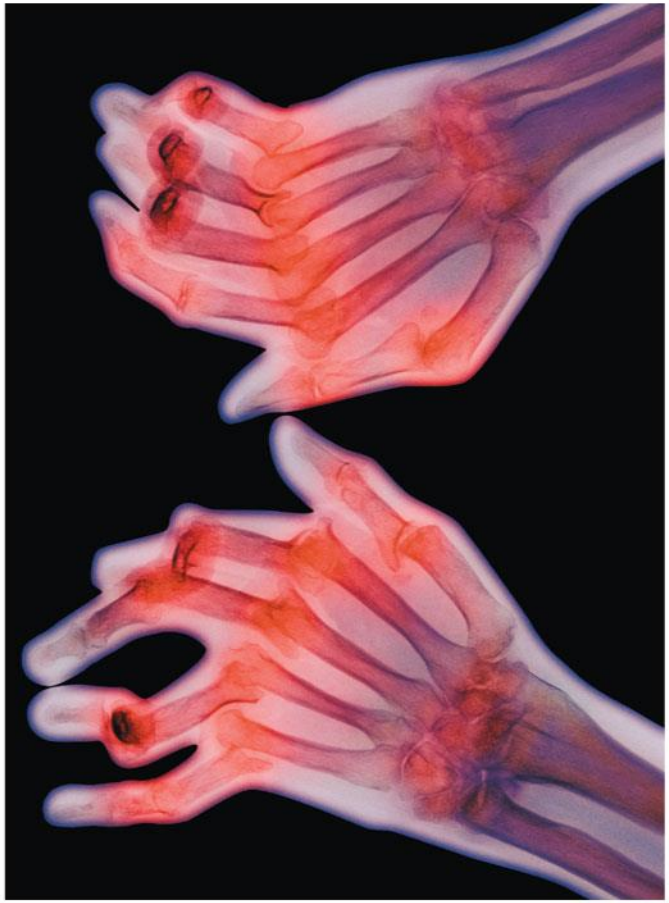


- The next time the allergen enters the body, it binds to mast cell–associated IgE molecules
- Mast cells release histamine and other mediators that cause vascular changes leading to typical allergy symptoms
- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction, within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

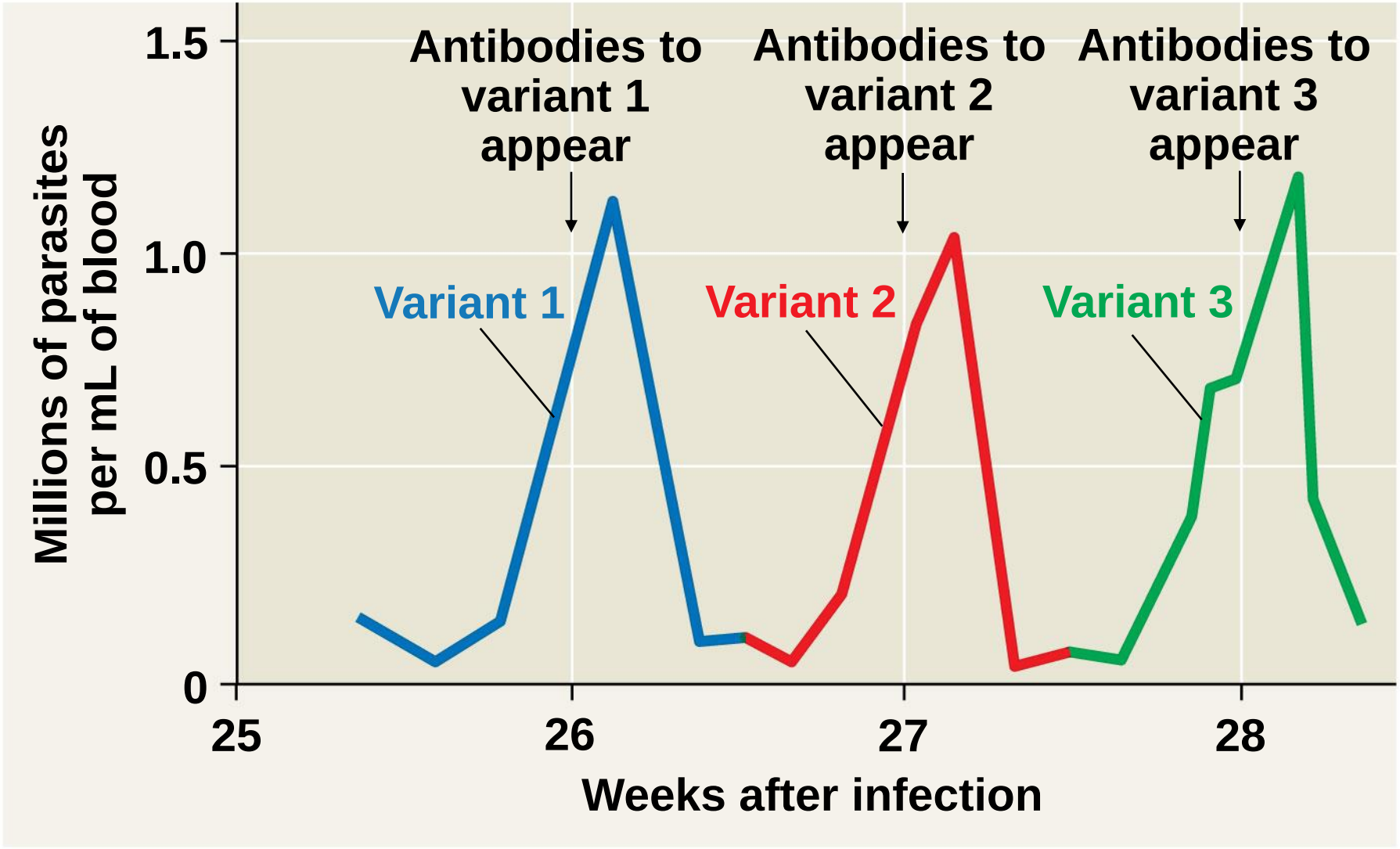
Evolutionary Adaptations of Pathogens That Underlie Immune System Avoidance

- 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

Figure 43.24



Latency

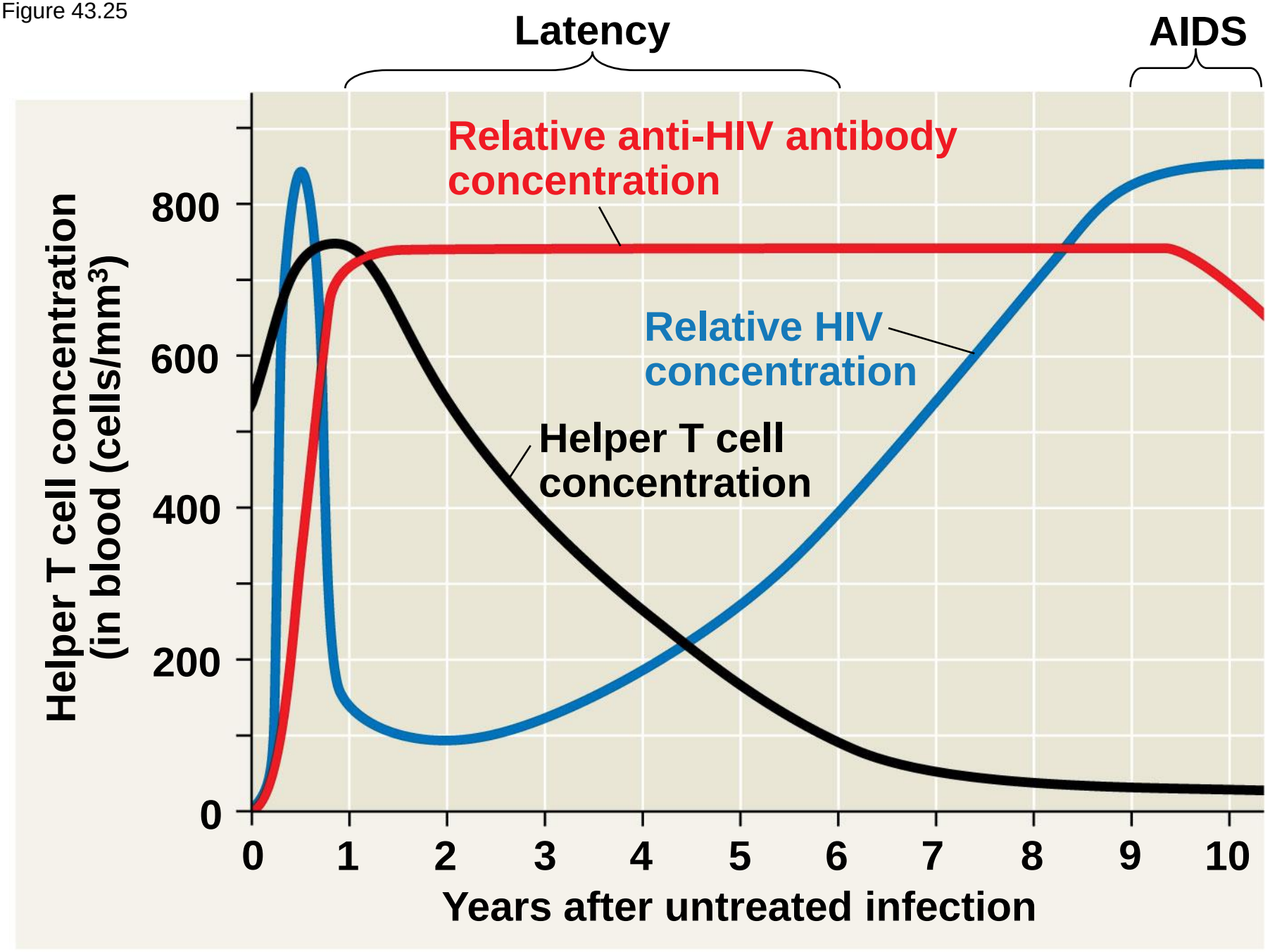
- Some viruses may remain in a host in an inactive state called latency
- Herpes simplex viruses can be present in a human host without causing symptoms

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

Animation: HIV Reproductive Cycle

Figure 43.25



- 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

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