LECTURE PRESENTATIONS

For CAMPBELL BIOLOGY, NINTH EDITION

Jane B. Reece, Lisa A. Urry, Michael L. Cain, Steven A. Wasserman, Peter V. Minorsky, Robert B. Jackson

Chapter 43

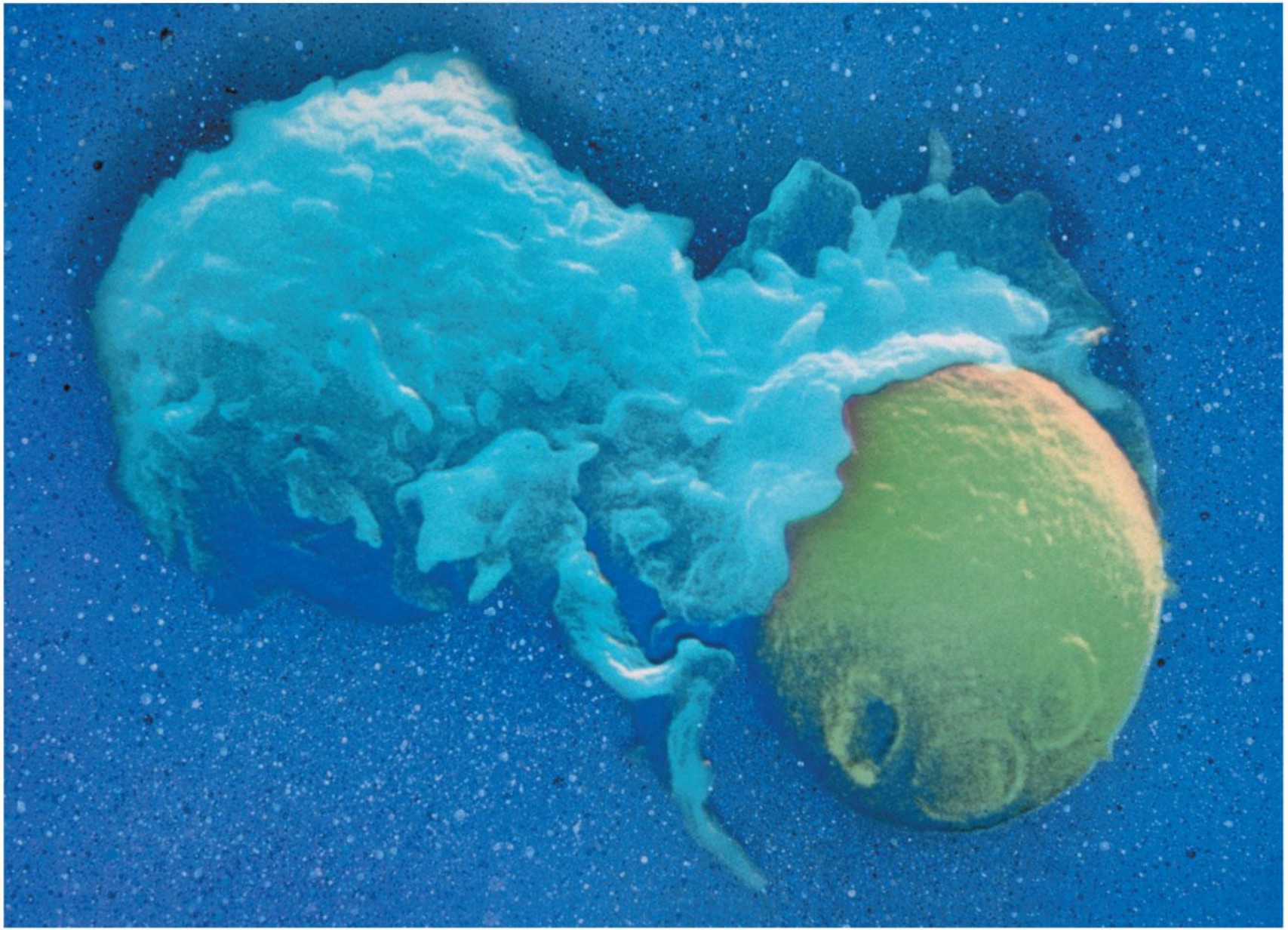
The Immune System

Lectures by
Erin Barley
Kathleen Fitzpatrick

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**

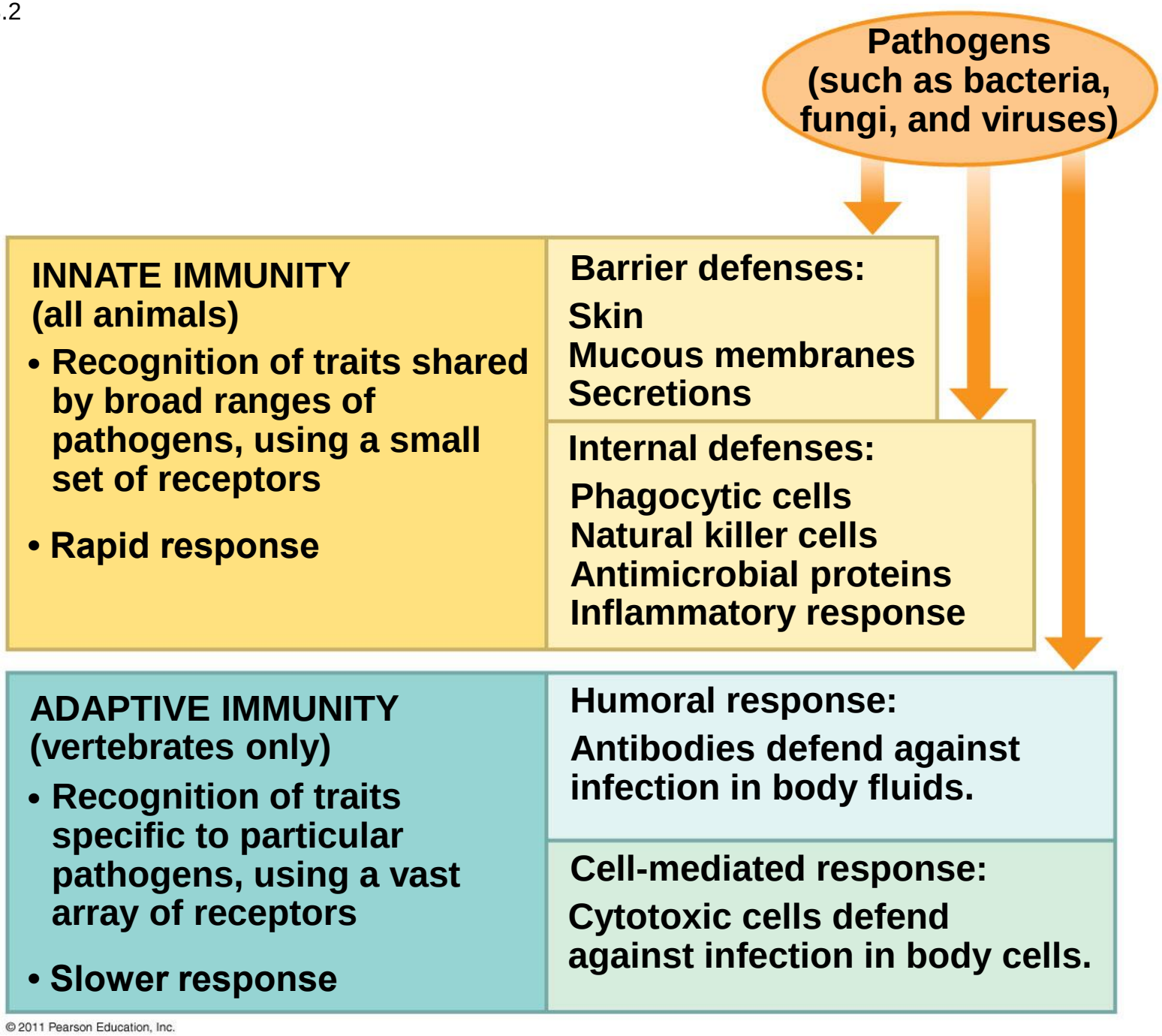
Figure 43.1



- 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



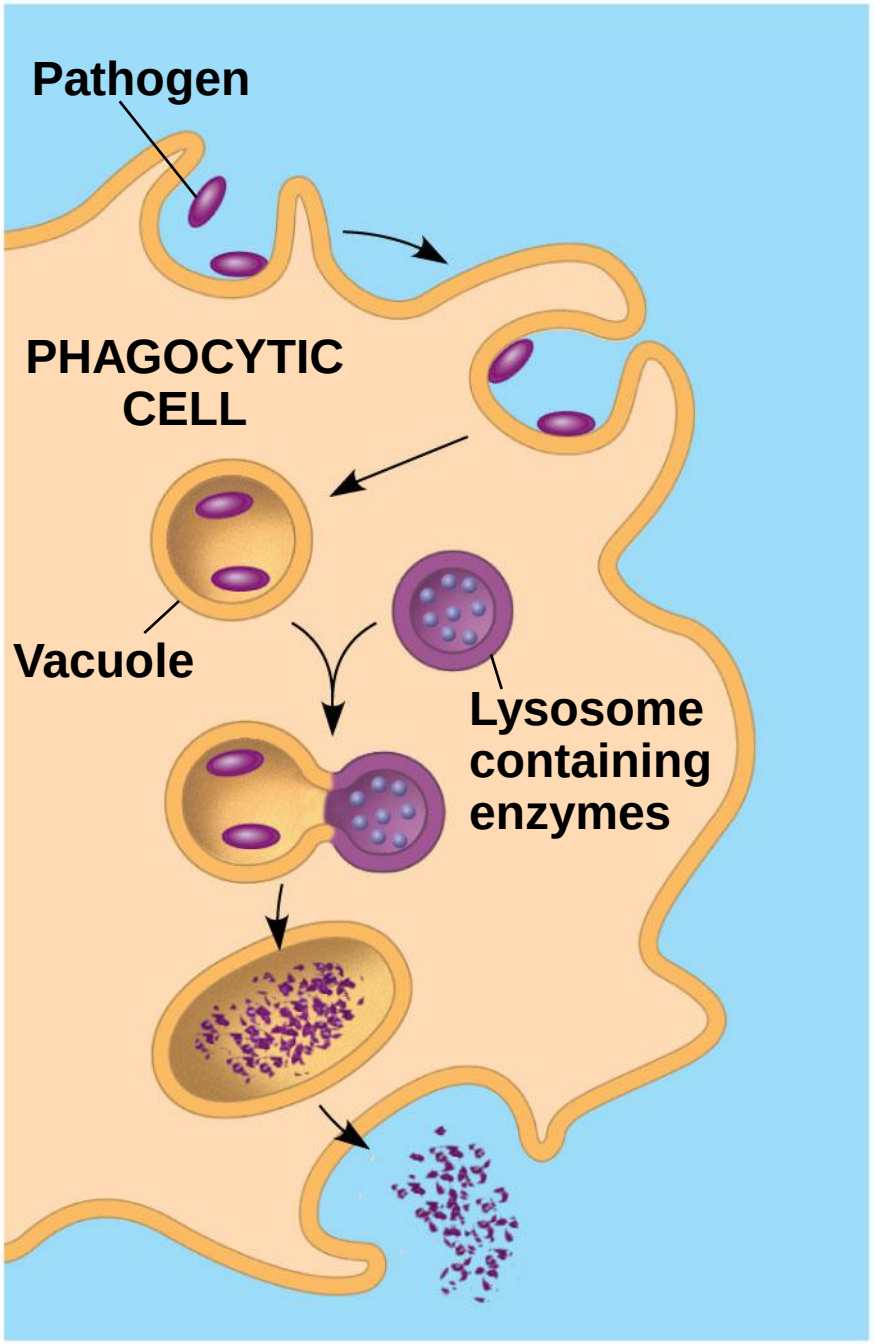
Concept 43.1: In innate immunity, recognition and response rely on traits common to groups of pathogens

- 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

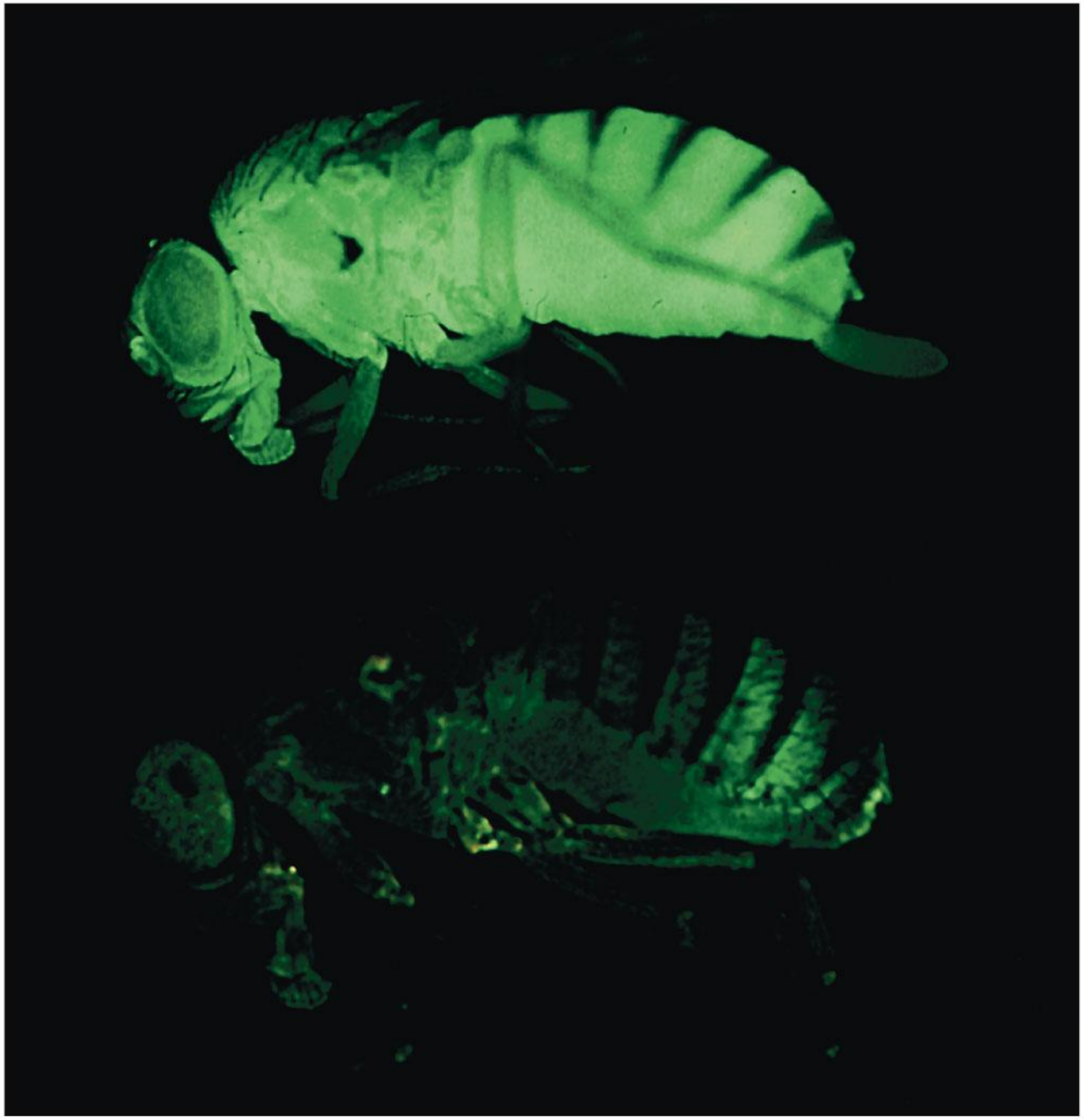
- In insects, an exoskeleton made of chitin forms the first barrier to pathogens
- The digestive system is protected by a chitin-based barrier and **lysozyme**, an enzyme that breaks down bacterial cell walls
- Hemocytes circulate within hemolymph and carry out **phagocytosis**, the ingestion and digestion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

Figure 43.3



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

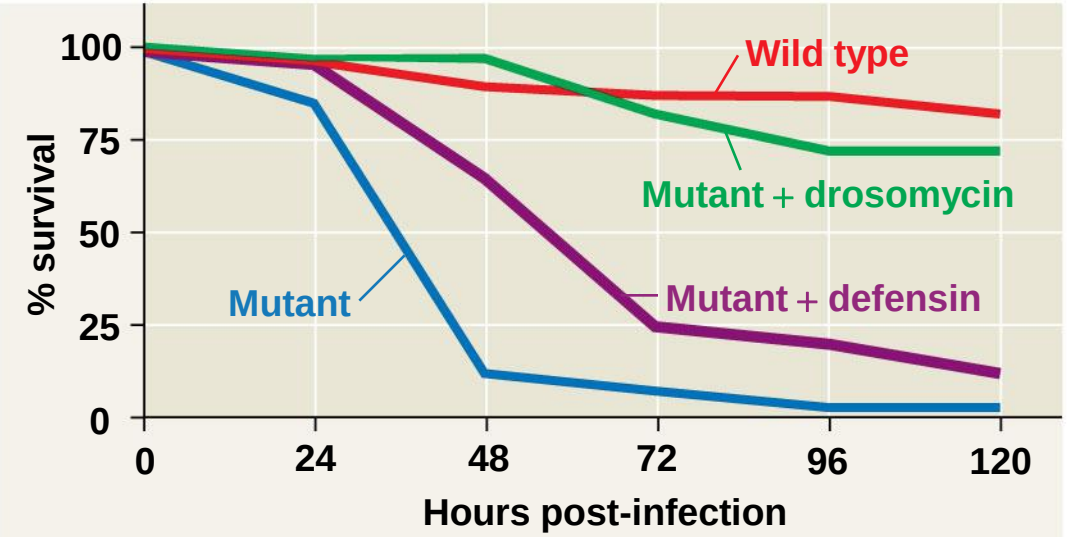
Figure 43.4



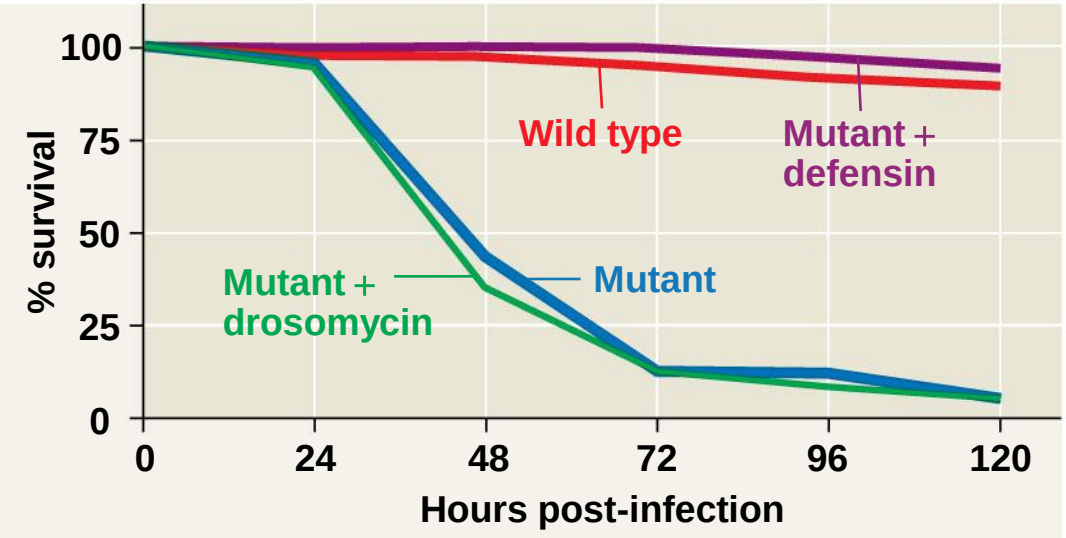
- The immune system recognizes bacteria and fungi by structures on their cell walls
- An immune response varies with the class of pathogen encountered

Figure 43.5

RESULTS



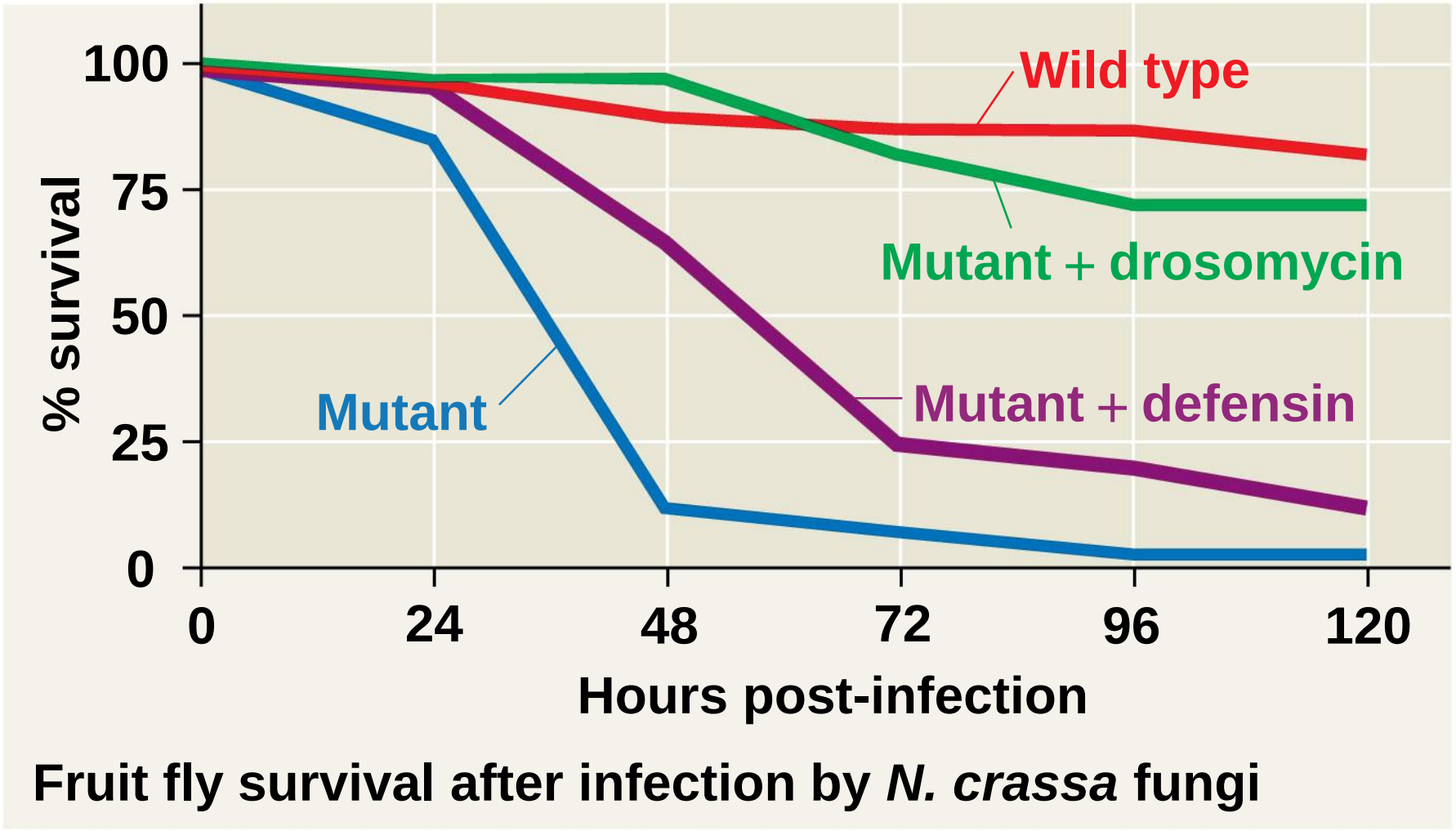
Fruit fly survival after infection by *N. crassa* fungi



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

Figure 43.5a

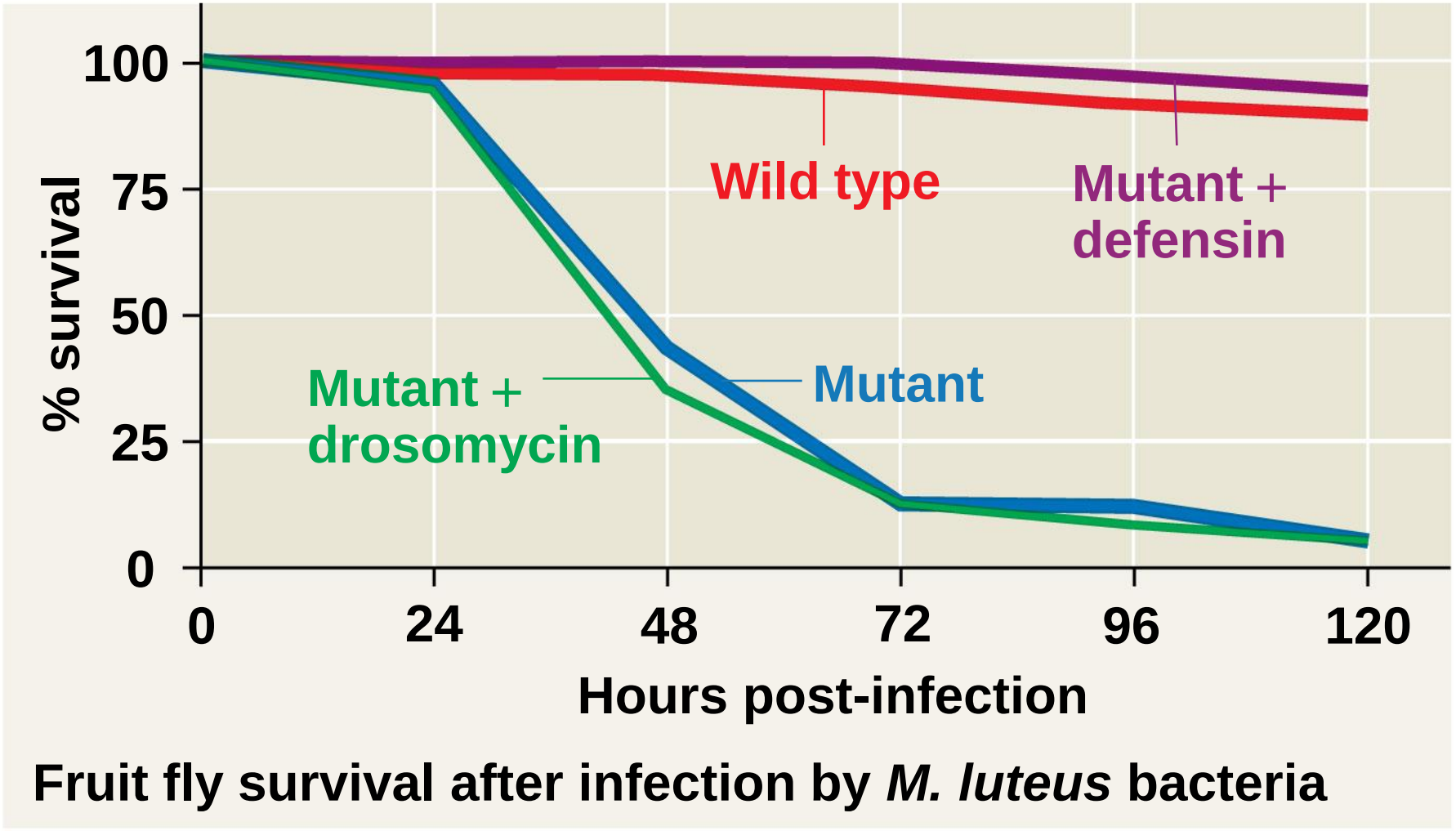
RESULTS (part 1)



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

Figure 43.5b

RESULTS (part 2)



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

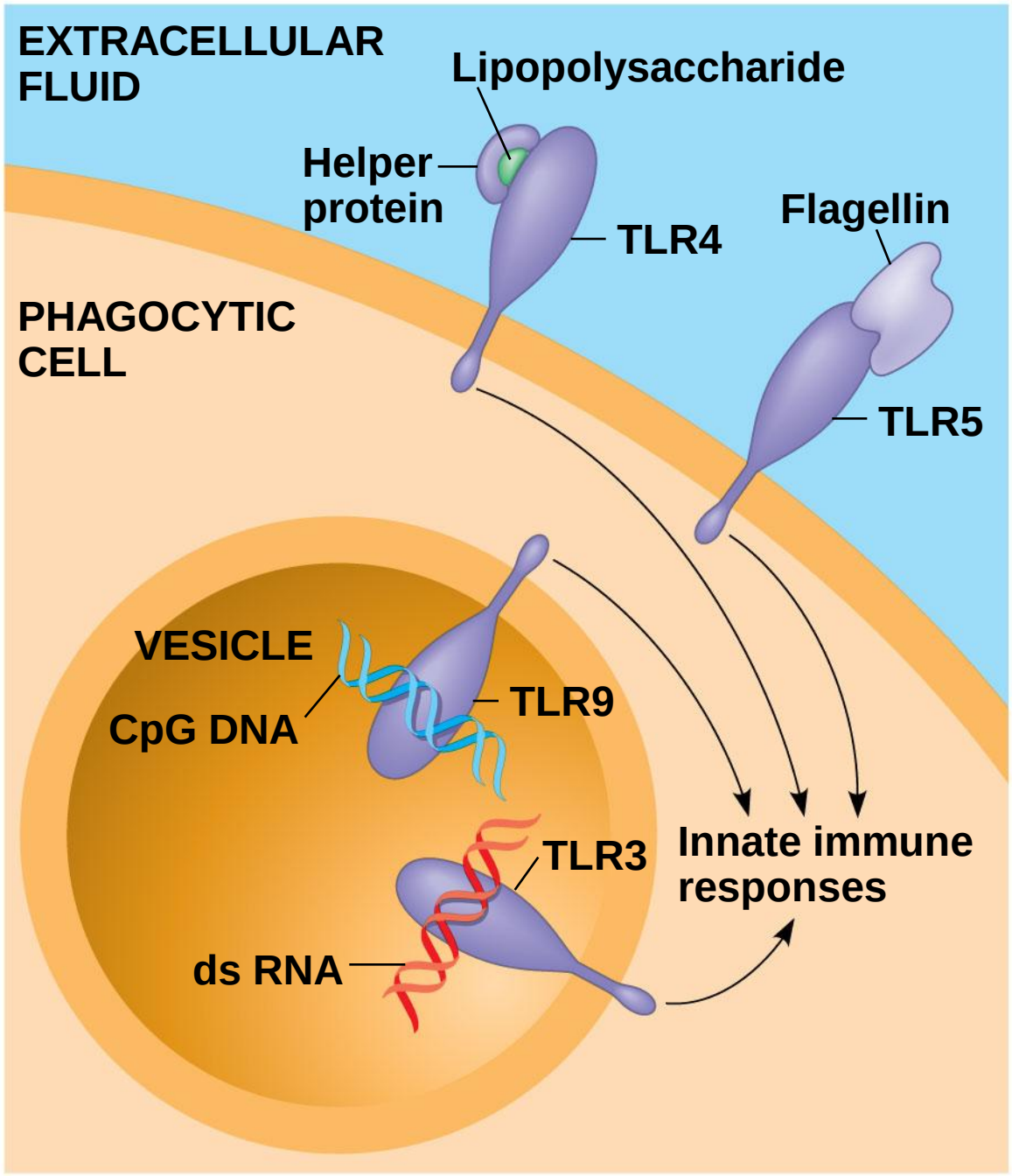
Barrier Defenses

- 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**

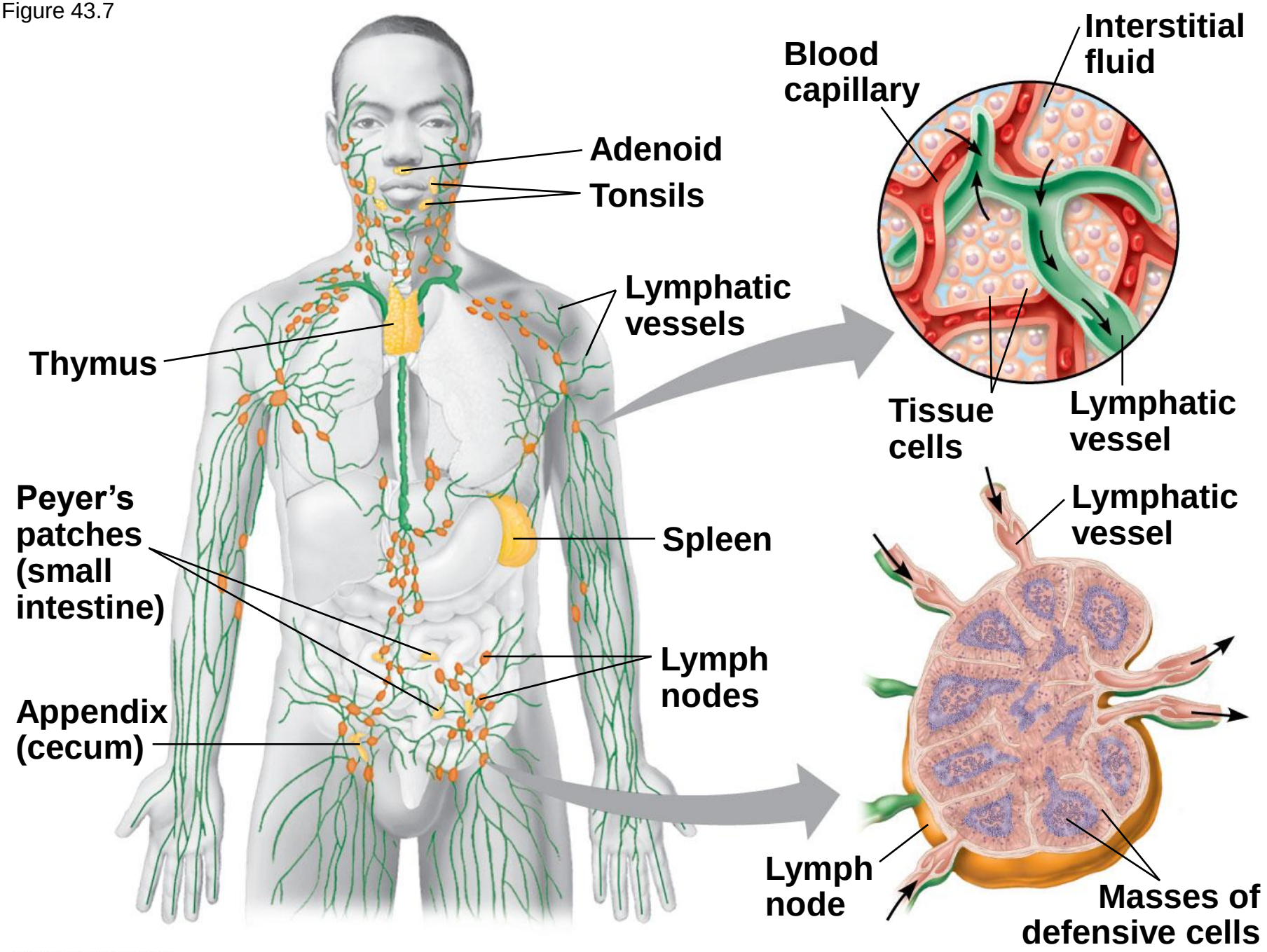
Figure 43.6



- 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 43.8-1

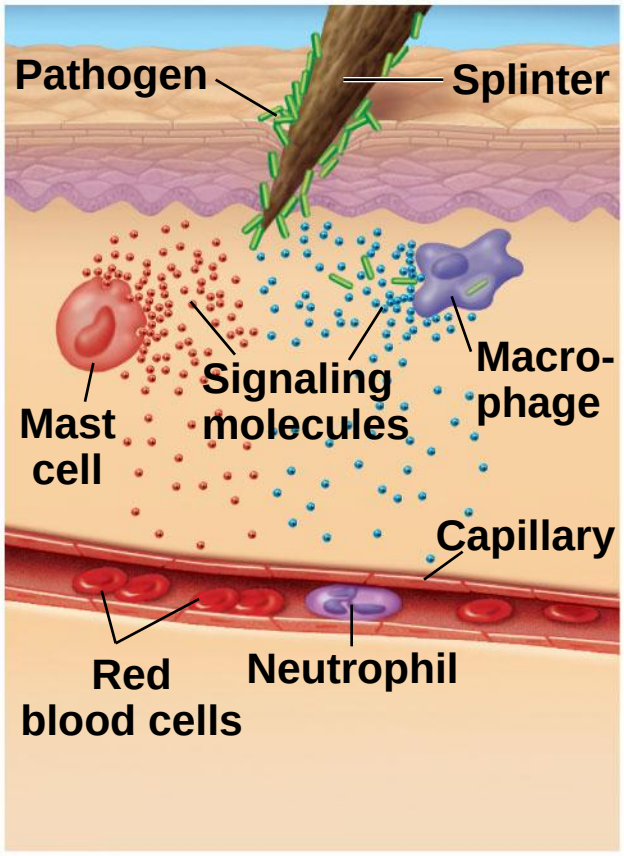


Figure 43.8-2

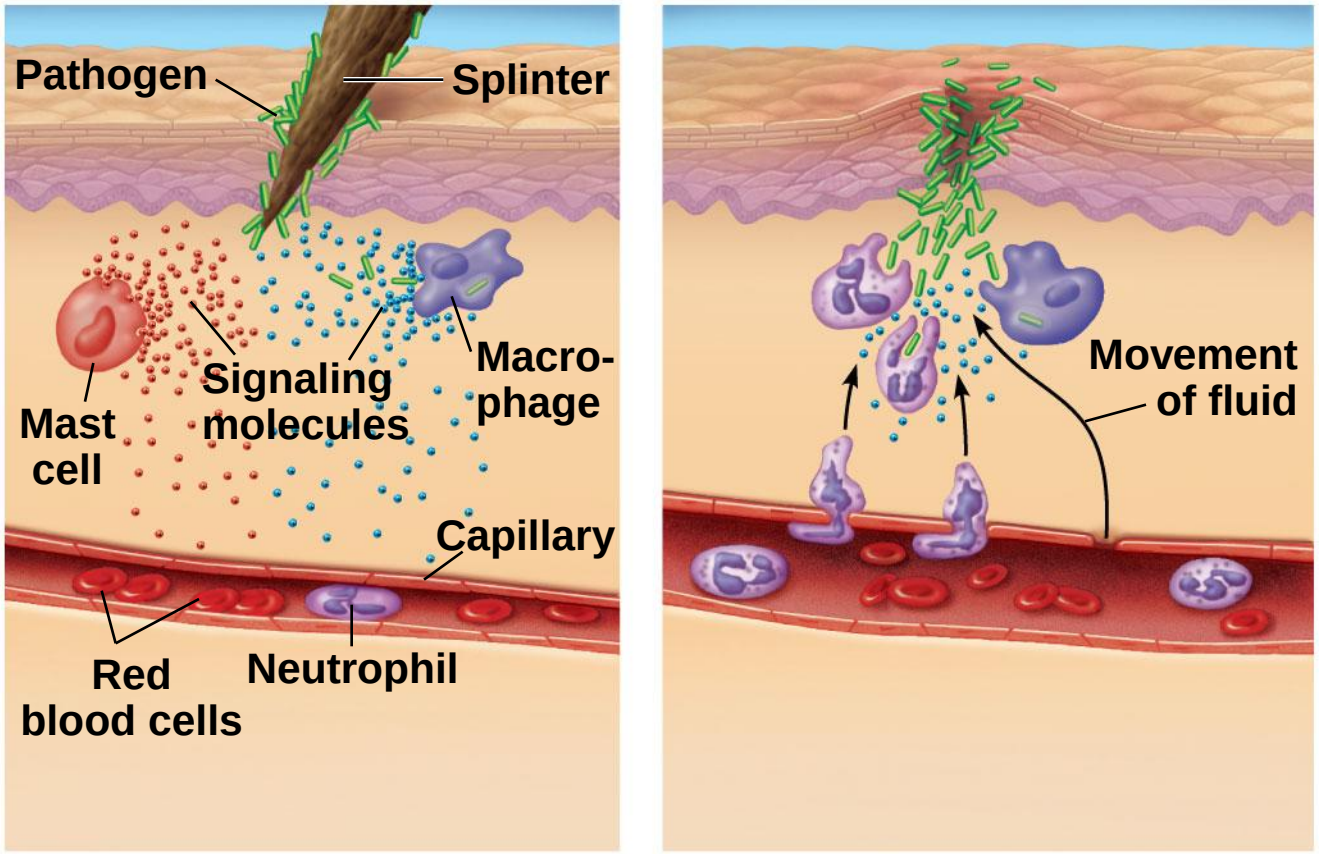
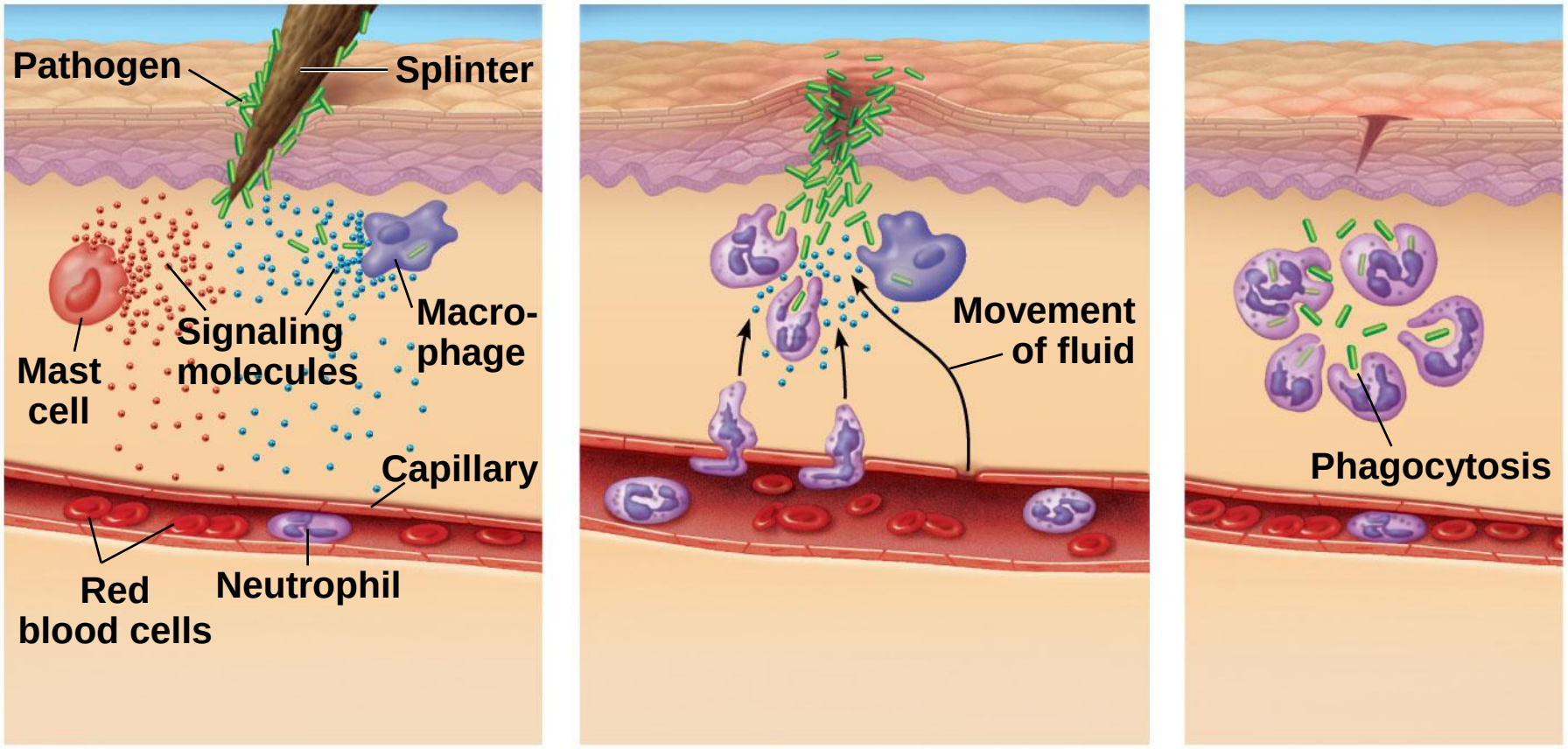


Figure 43.8-3



- 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

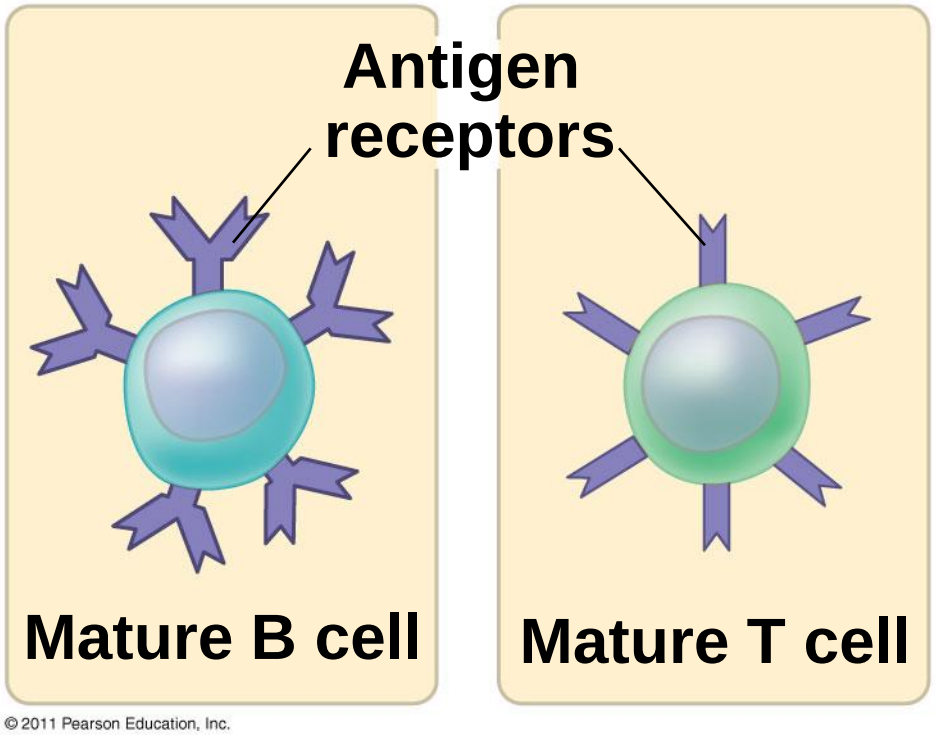
- Some pathogens avoid destruction by modifying their surface to prevent recognition or by resisting breakdown following phagocytosis
- Tuberculosis (TB) is one such disease and kills more than a million people a year

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

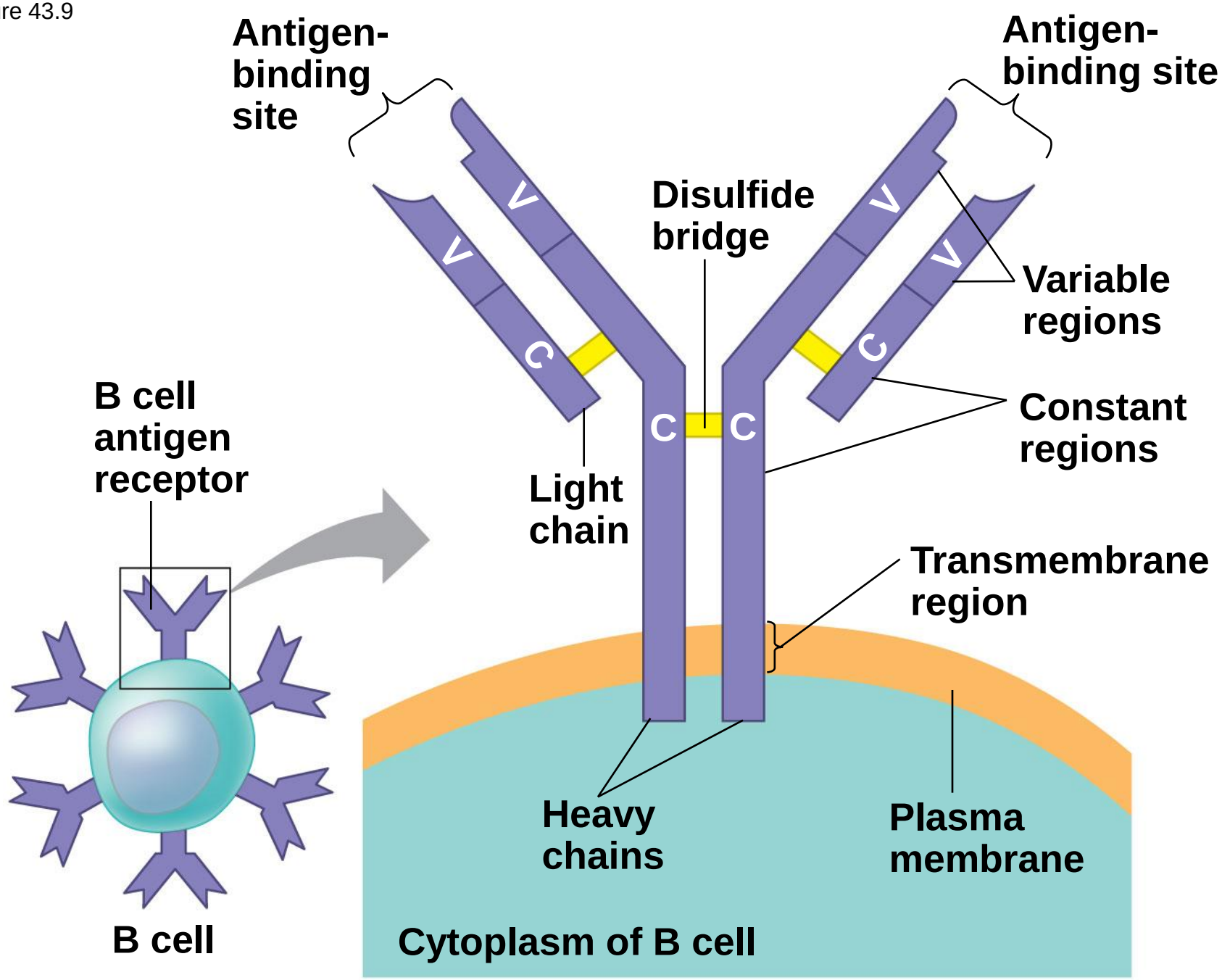


- B cells and T cells have receptor proteins that can bind to foreign molecules
- Each individual lymphocyte is specialized to recognize a specific type of molecule

Antigen Recognition by B Cells and Antibodies

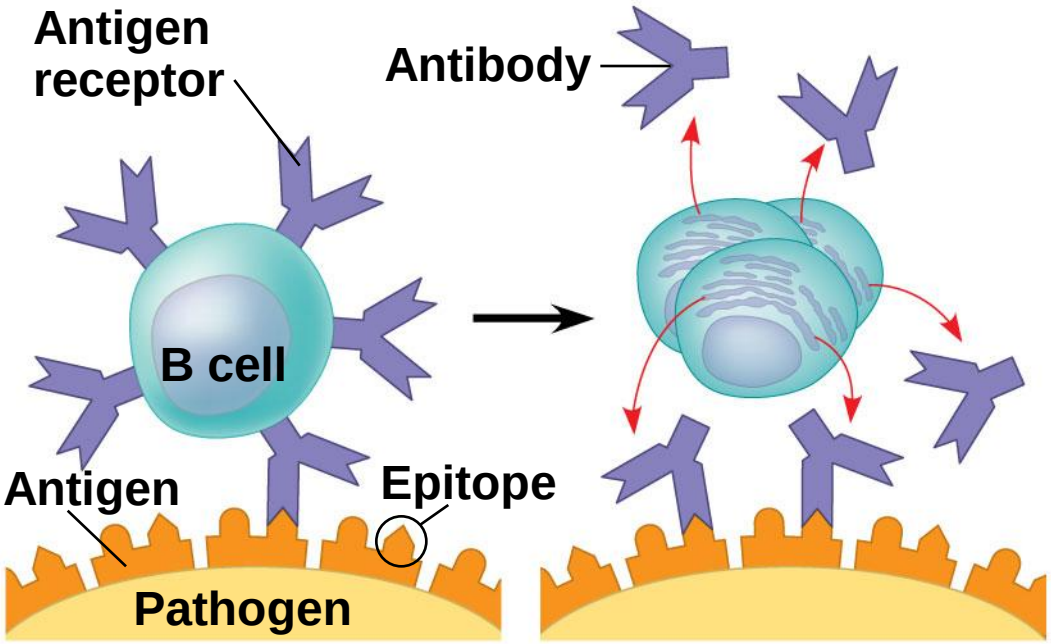
- Each B cell antigen receptor is a Y-shaped molecule with two identical **heavy chains** and two identical **light chains**
- The constant regions of the chains vary little among B cells, whereas the variable regions differ greatly
- The variable regions provide antigen specificity

Figure 43.9

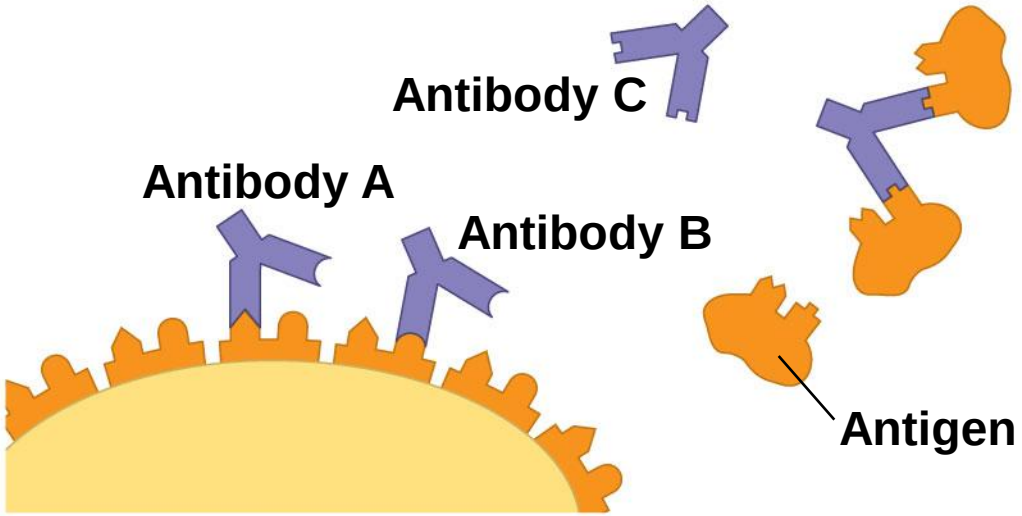


- Binding of a B cell antigen receptor to an antigen is an early step in B cell activation
- This gives rise to cells that secrete a soluble form of the protein called an **antibody** or **immunoglobulin (Ig)**
- Secreted antibodies are similar to B cell receptors but lack transmembrane regions that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

Figure 43.10

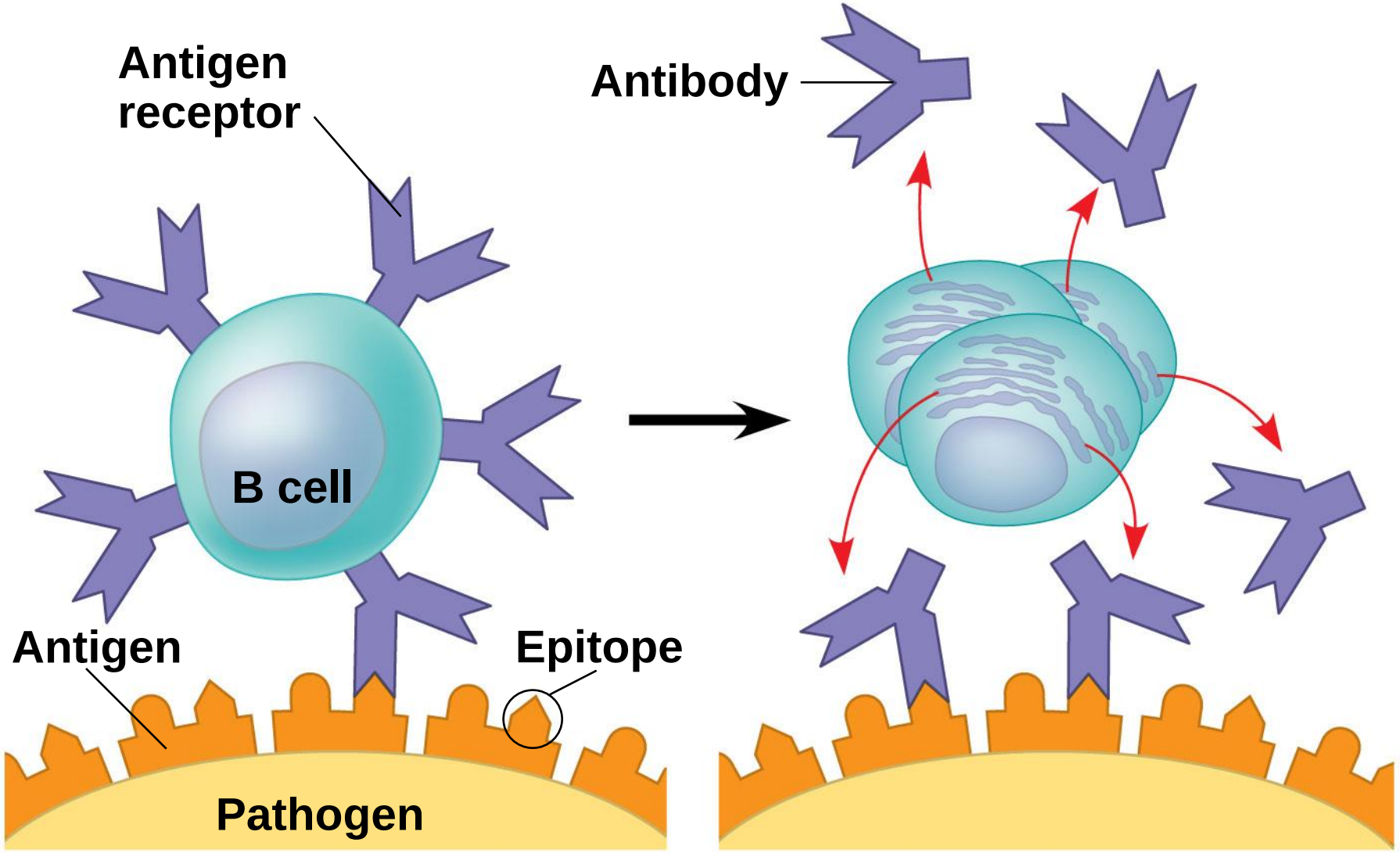


(a) B cell antigen receptors and antibodies



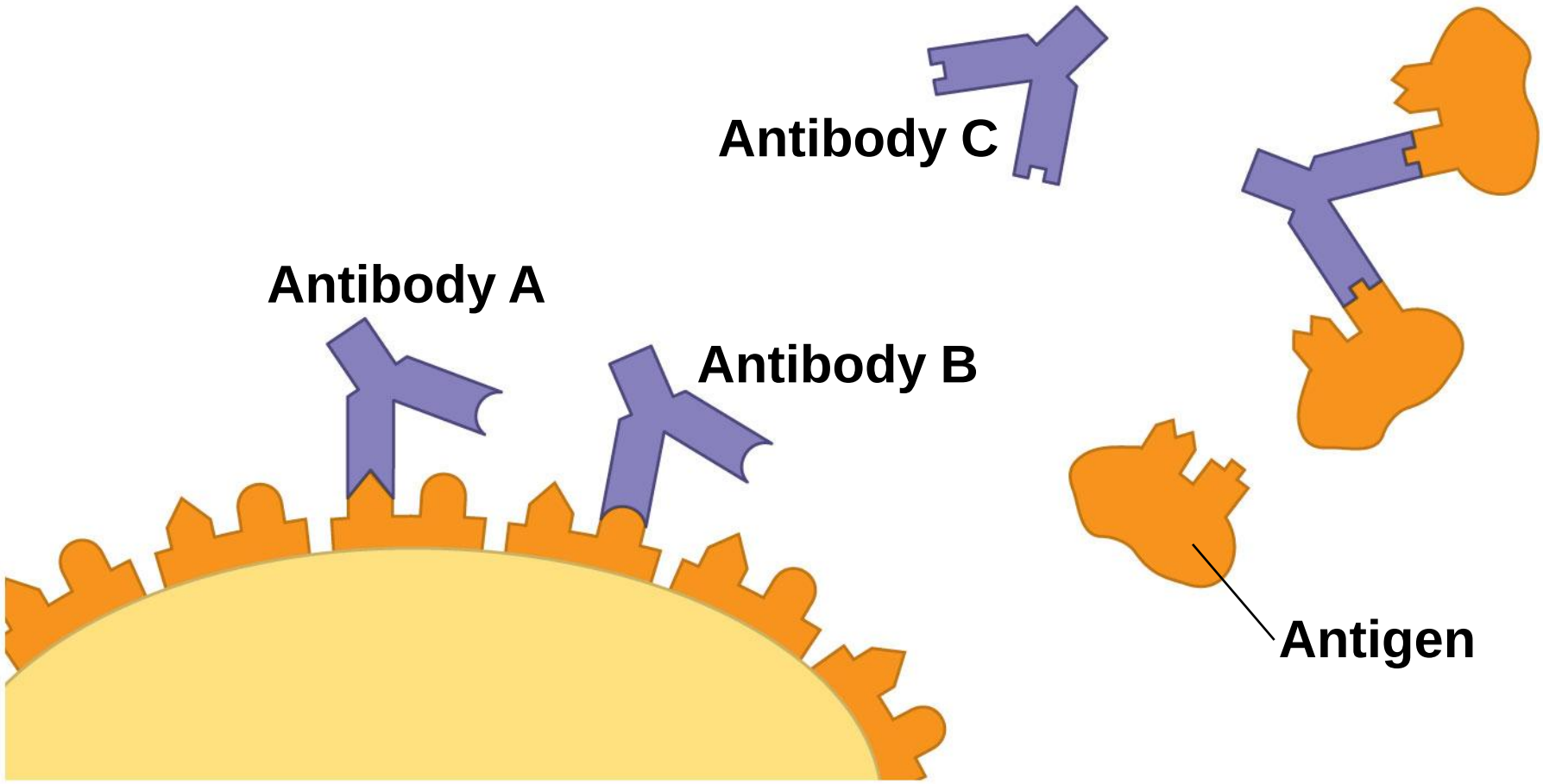
(b) Antigen receptor specificity

Figure 43.10a



(a) B cell antigen receptors and antibodies

Figure 43.10b



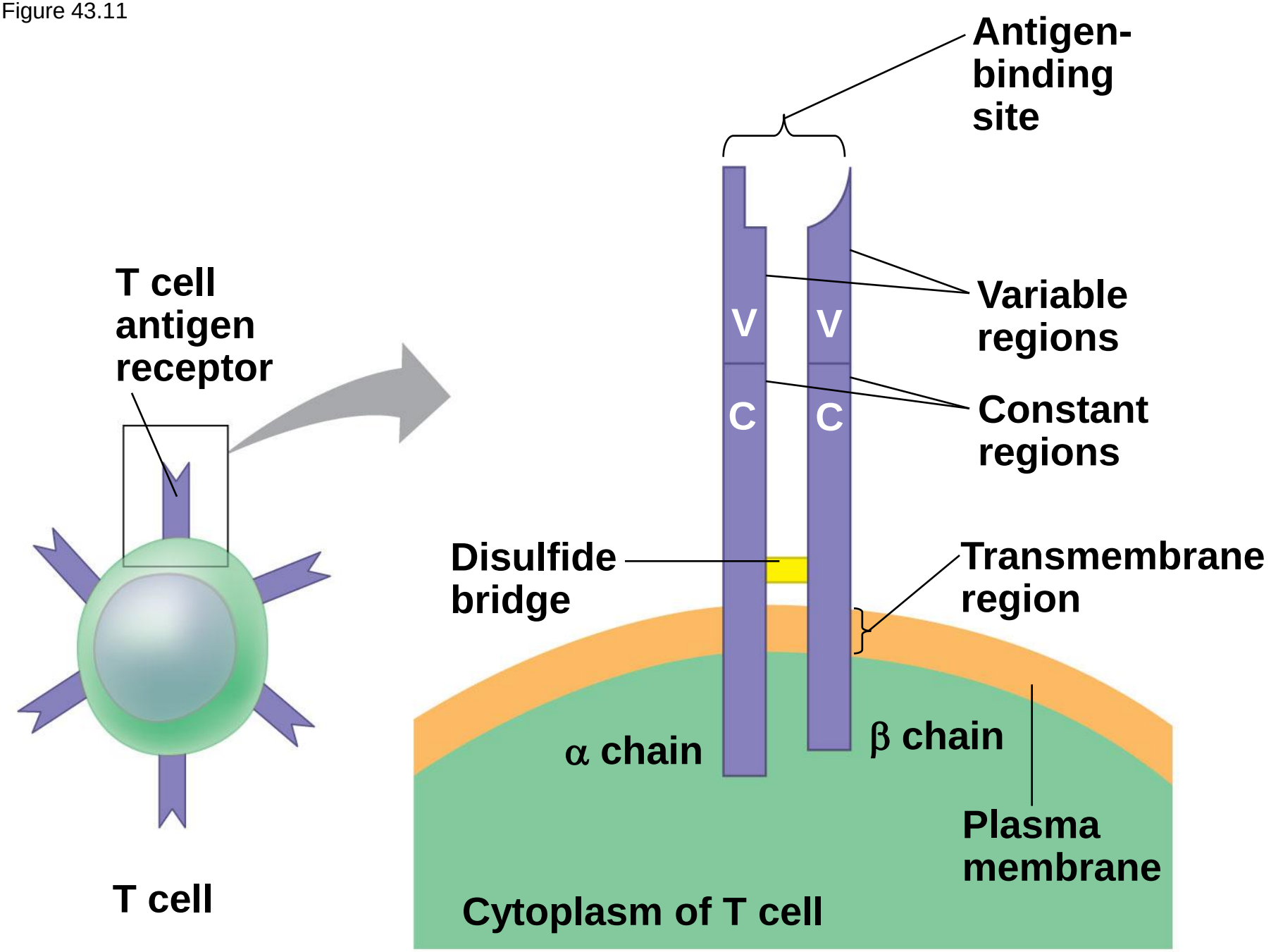
(b) Antigen receptor specificity

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

Video: T Cell Receptors

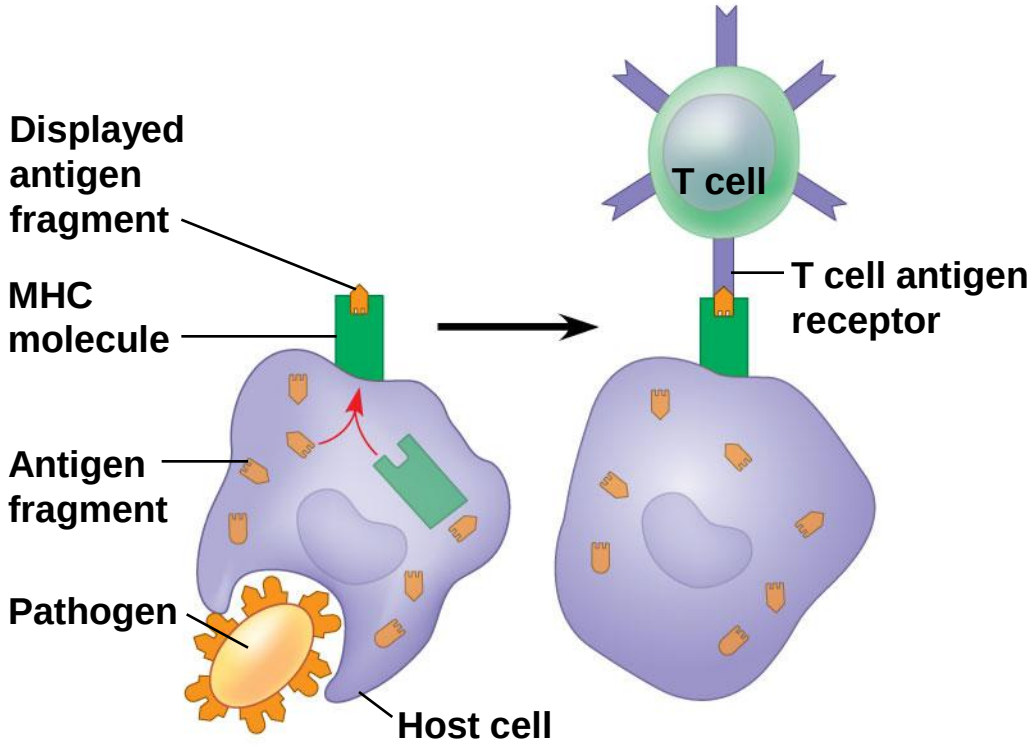
Figure 43.11



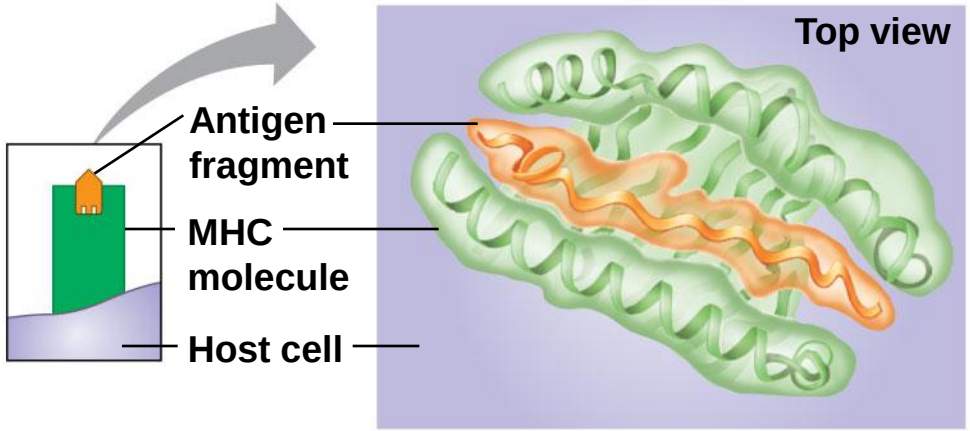
- T cells bind to antigen fragments displayed or presented on a host cell
- These antigen fragments are bound to cell-surface proteins called MHC molecules
- **MHC (major histocompatibility complex)** molecules are host proteins that display the antigen fragments on the cell surface

- 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

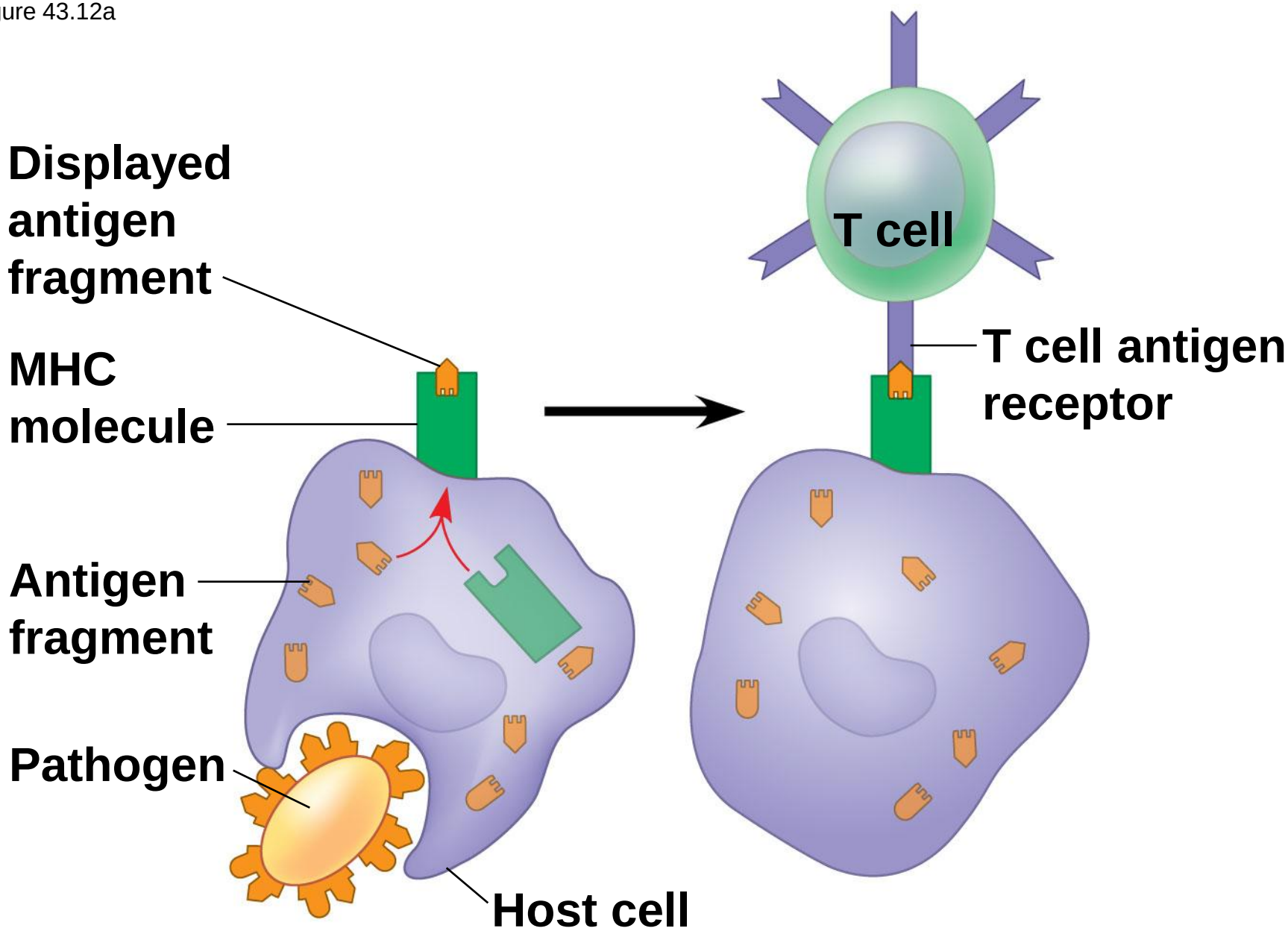


(a) Antigen recognition by a T cell



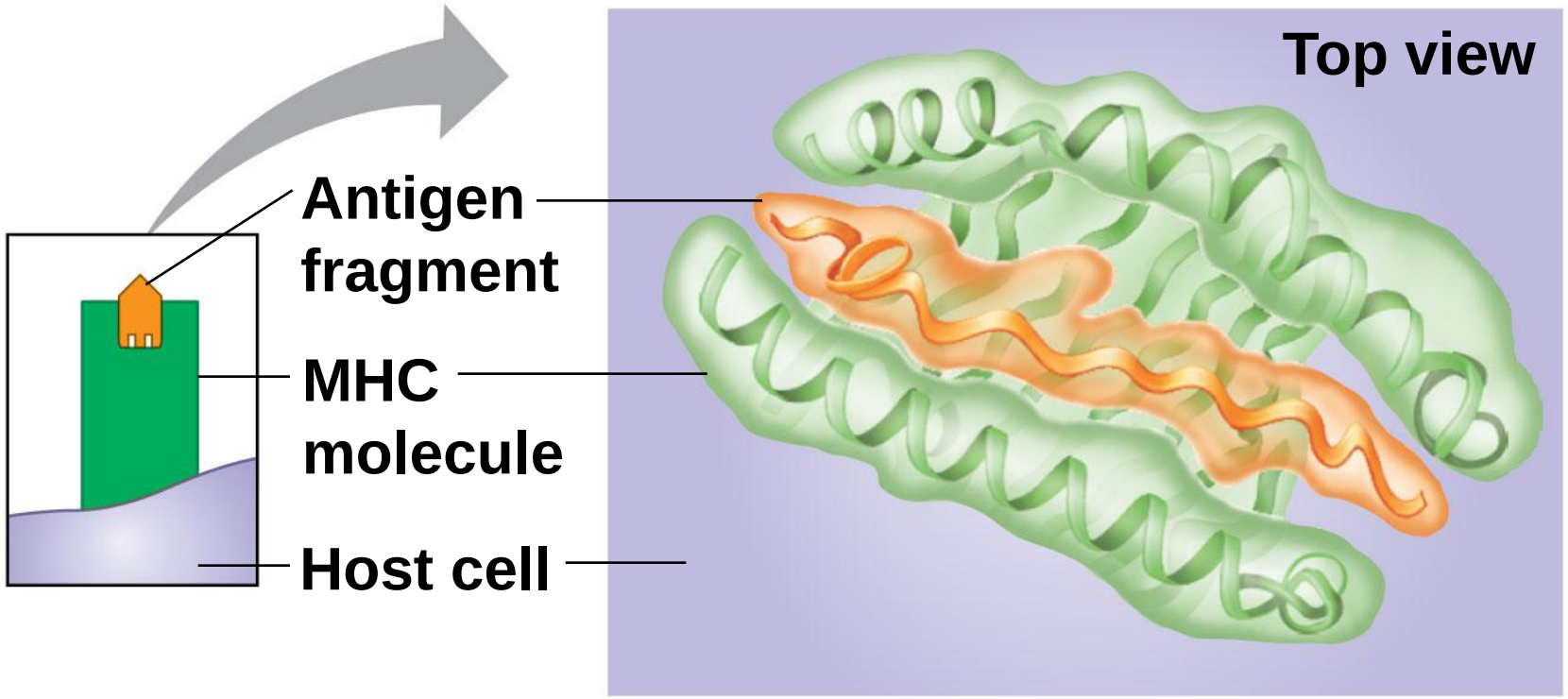
(b) A closer look at antigen presentation

Figure 43.12a



(a) Antigen recognition by a T cell

Figure 43.12b



(b) A closer look at antigen presentation

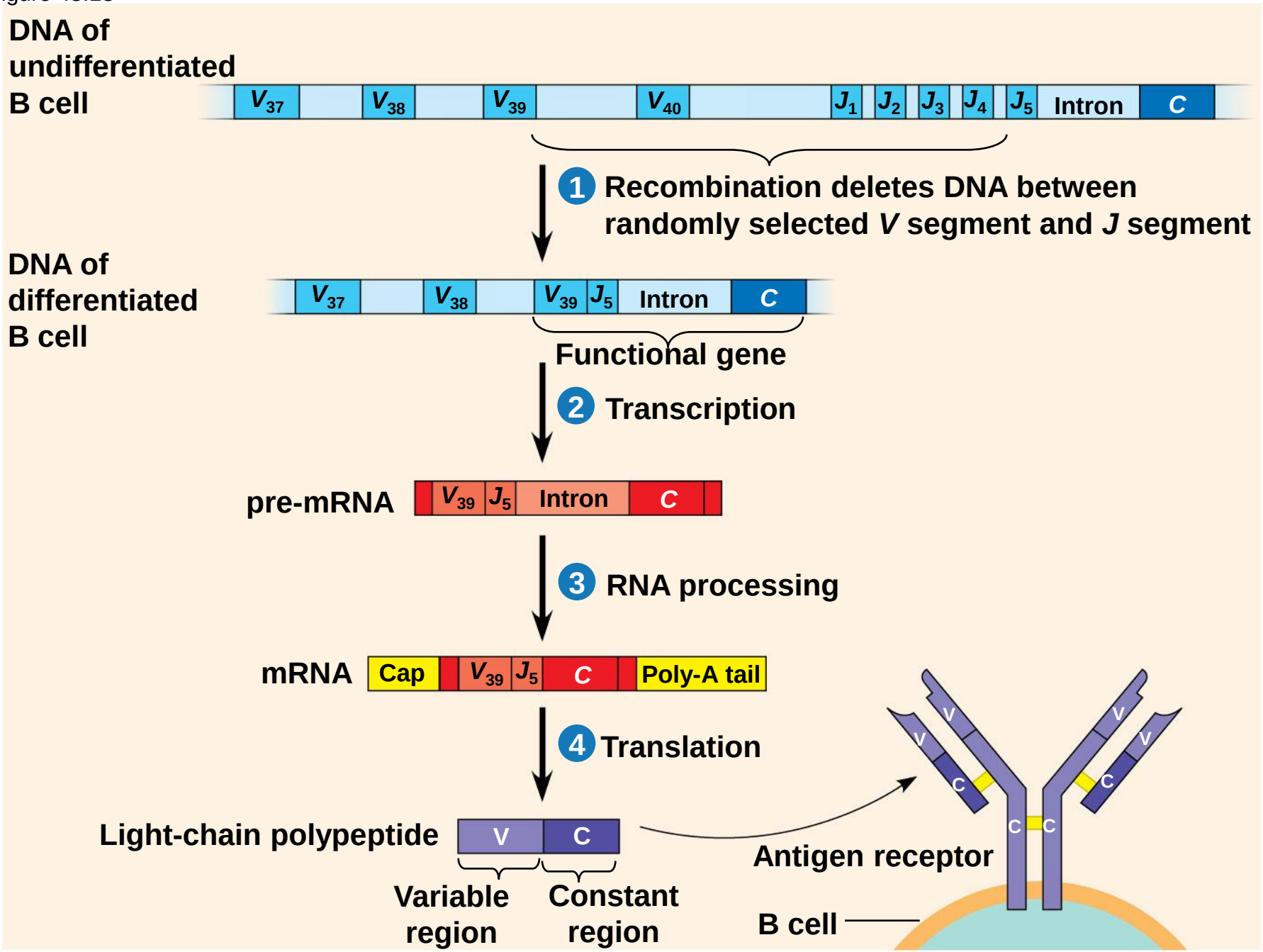
B Cell and T Cell Development

- 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

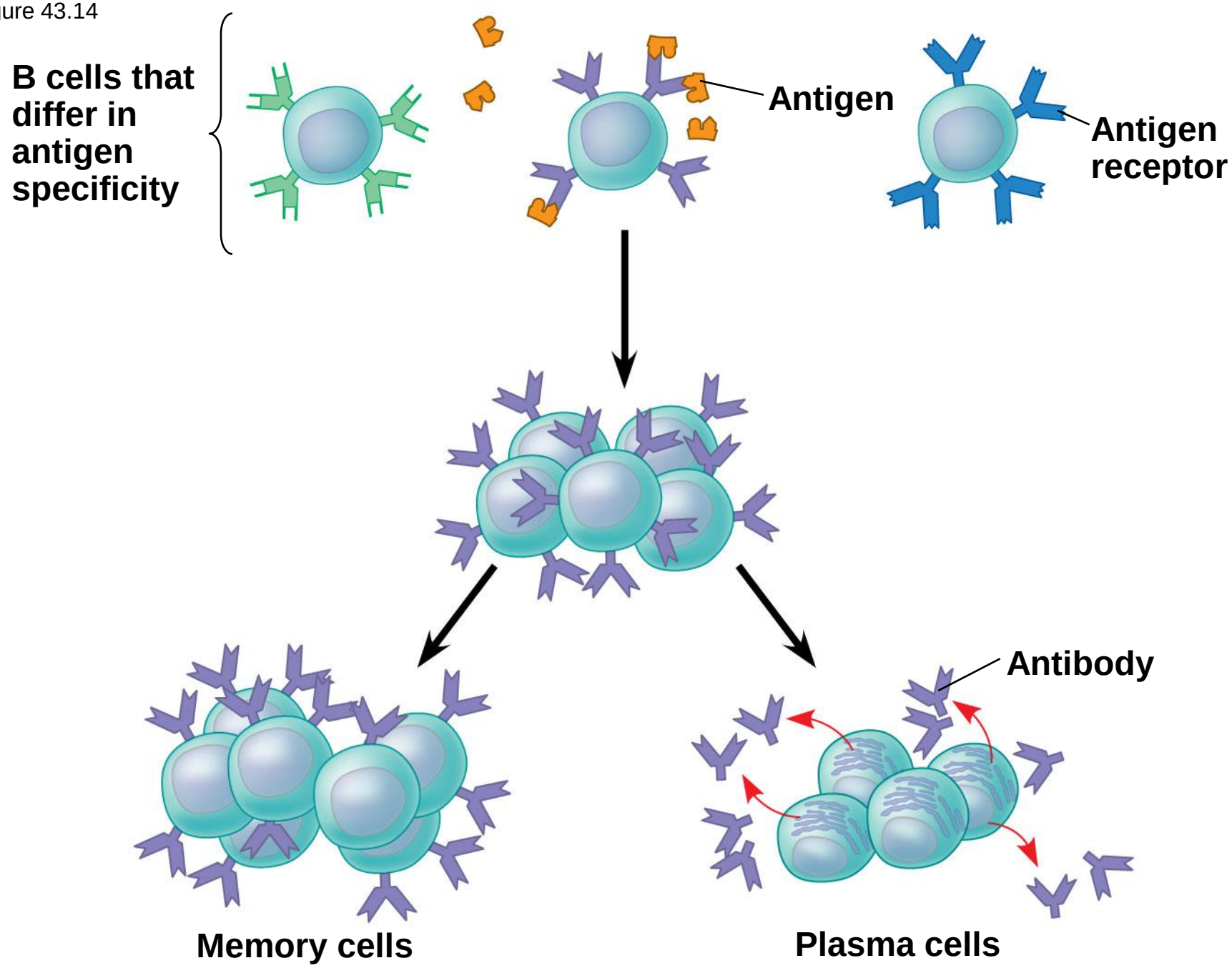
- Antigen receptors are generated by random rearrangement of DNA
- As lymphocytes mature in bone marrow or the thymus, they are tested for self-reactivity
- Some B and T cells with receptors specific for the body's own molecules are destroyed by apoptosis, or programmed cell death
- The remainder are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

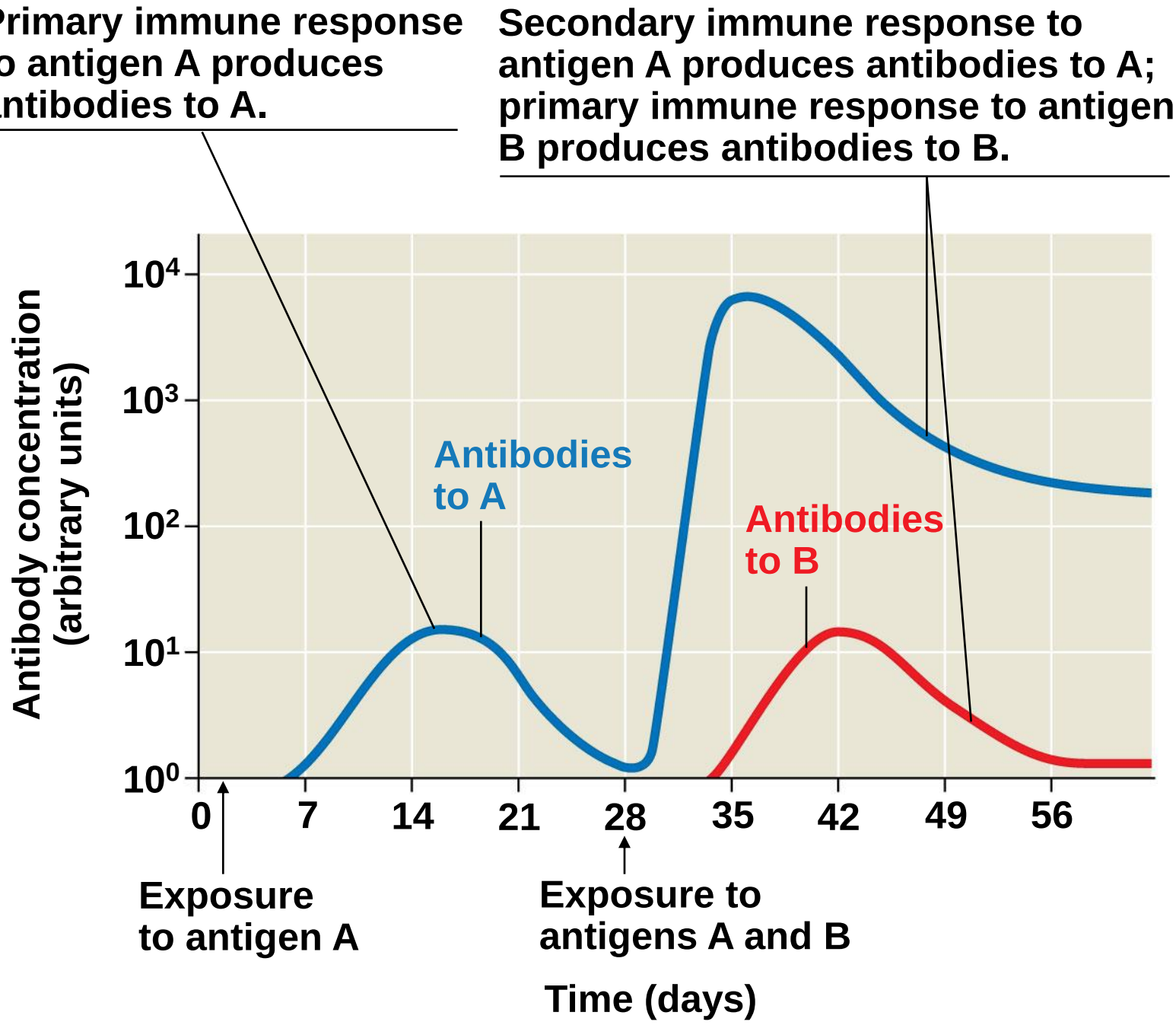


Immunological Memory

- 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

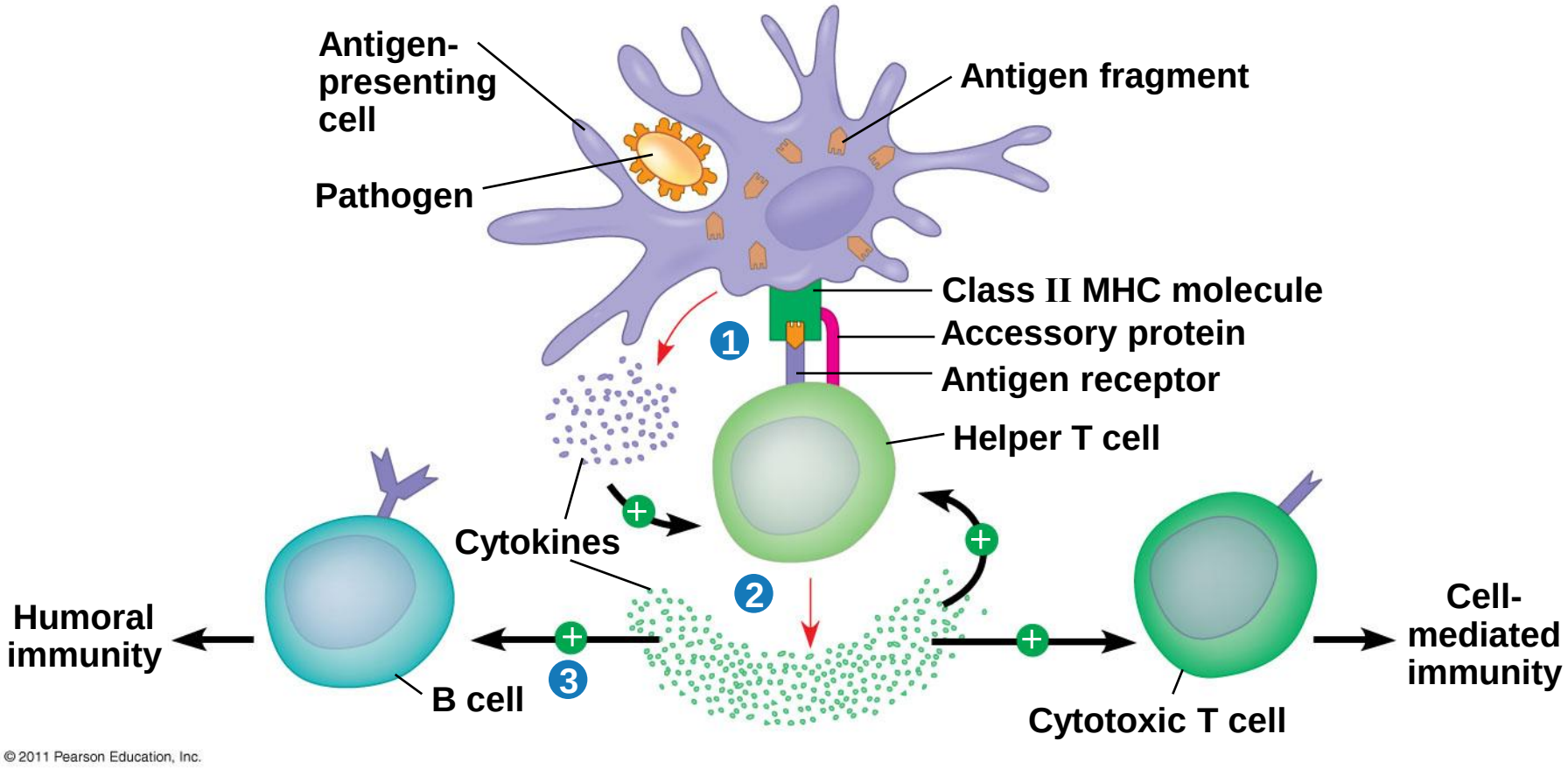
Helper T Cells: A Response to Nearly All Antigens

- 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 43.17-1

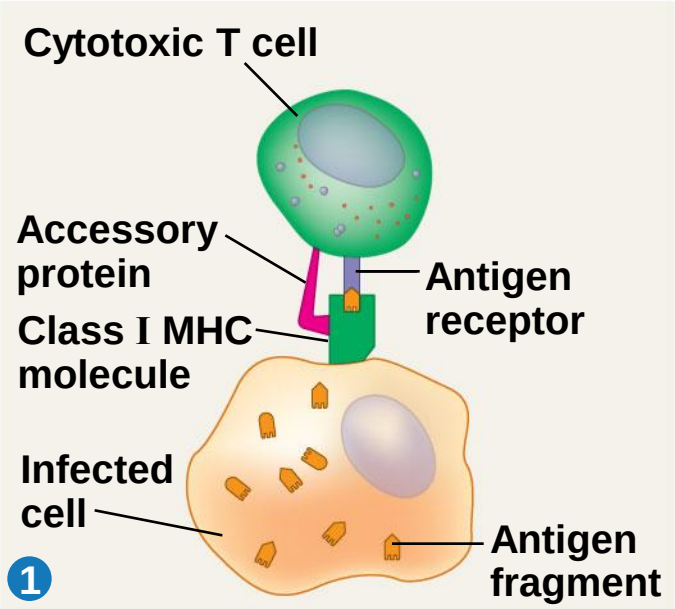


Figure 43.17-2

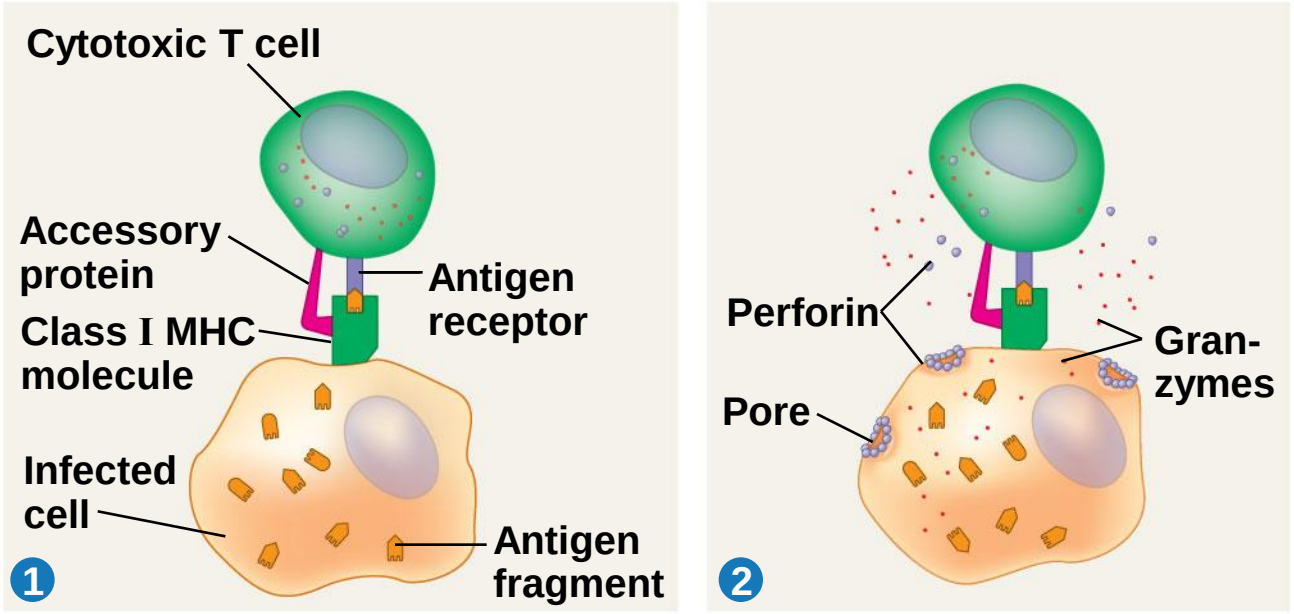
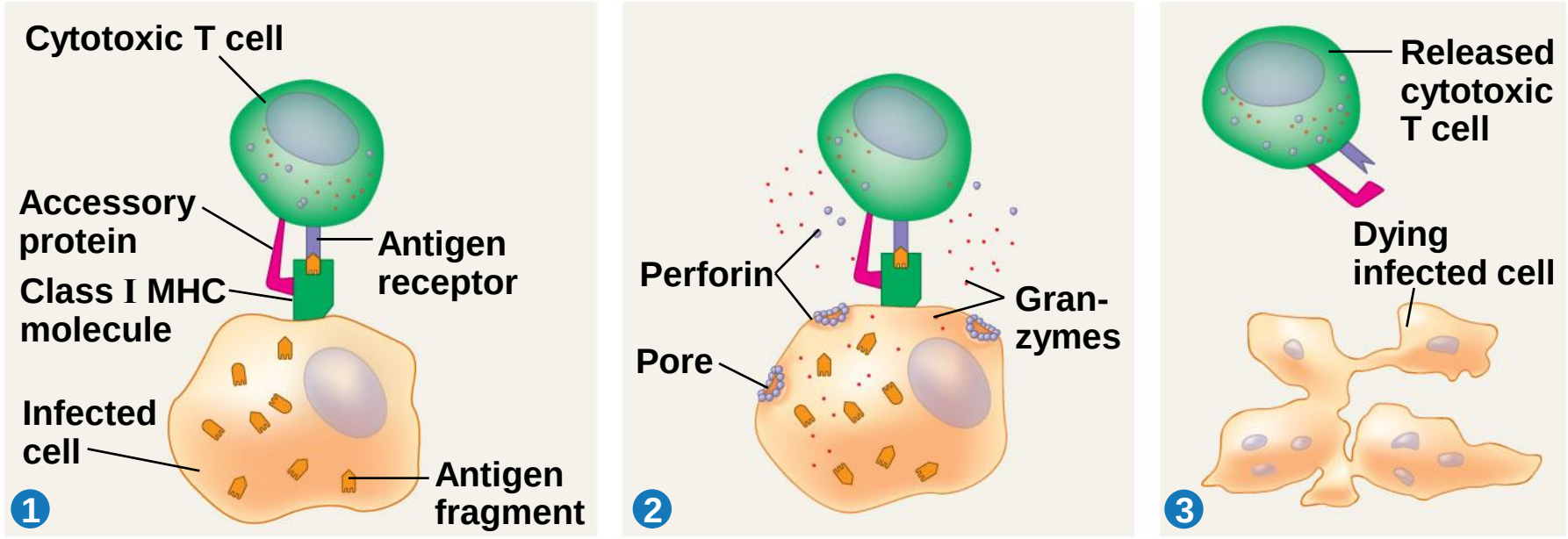


Figure 43.17-3



B Cells and Antibodies: A Response to Extracellular Pathogens

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

Activation of 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 43.18-1

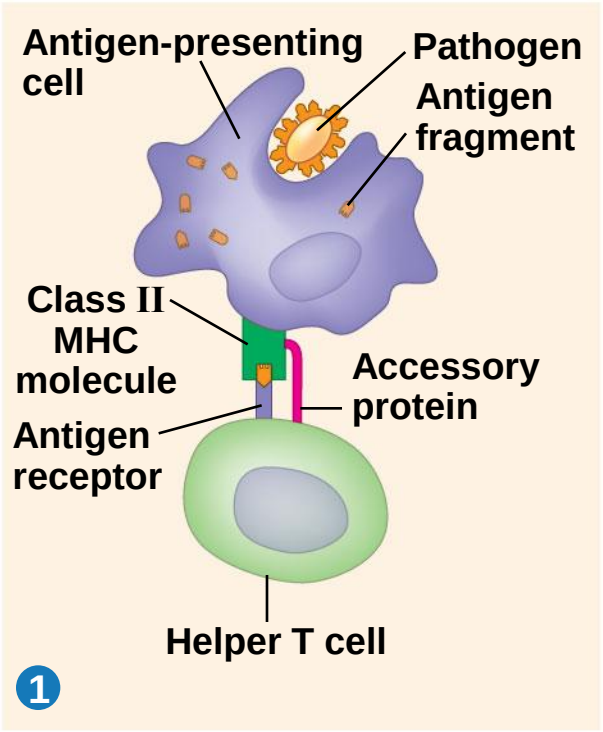


Figure 43.18-2

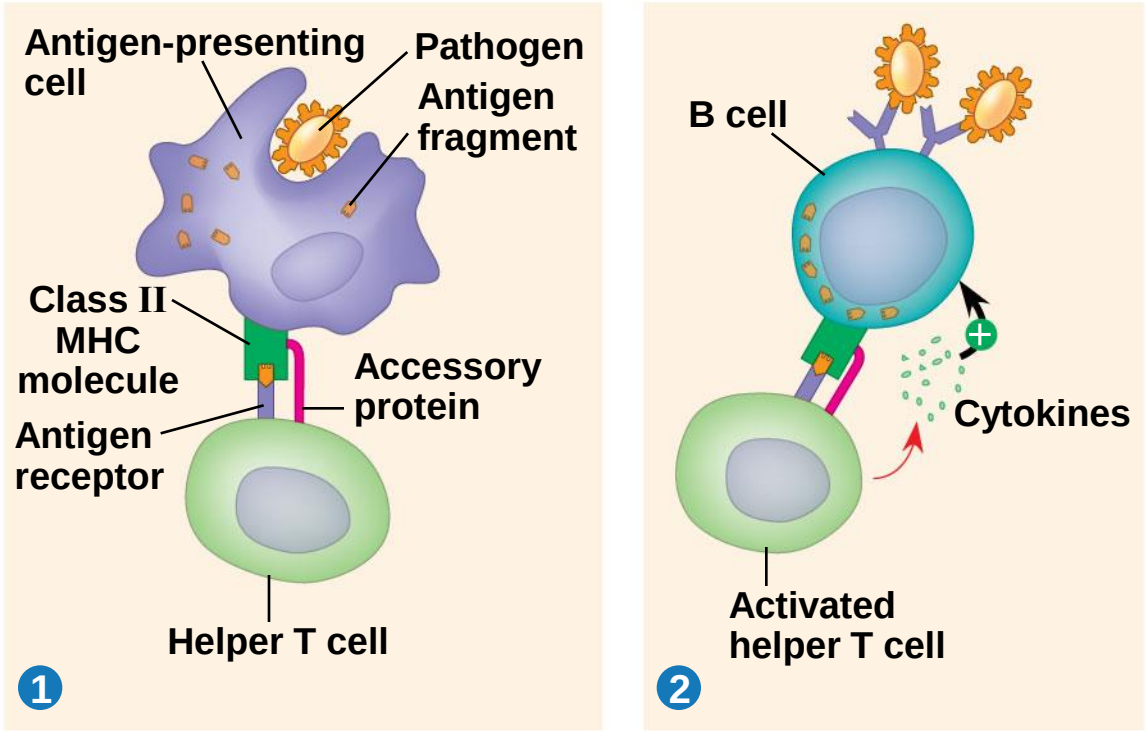
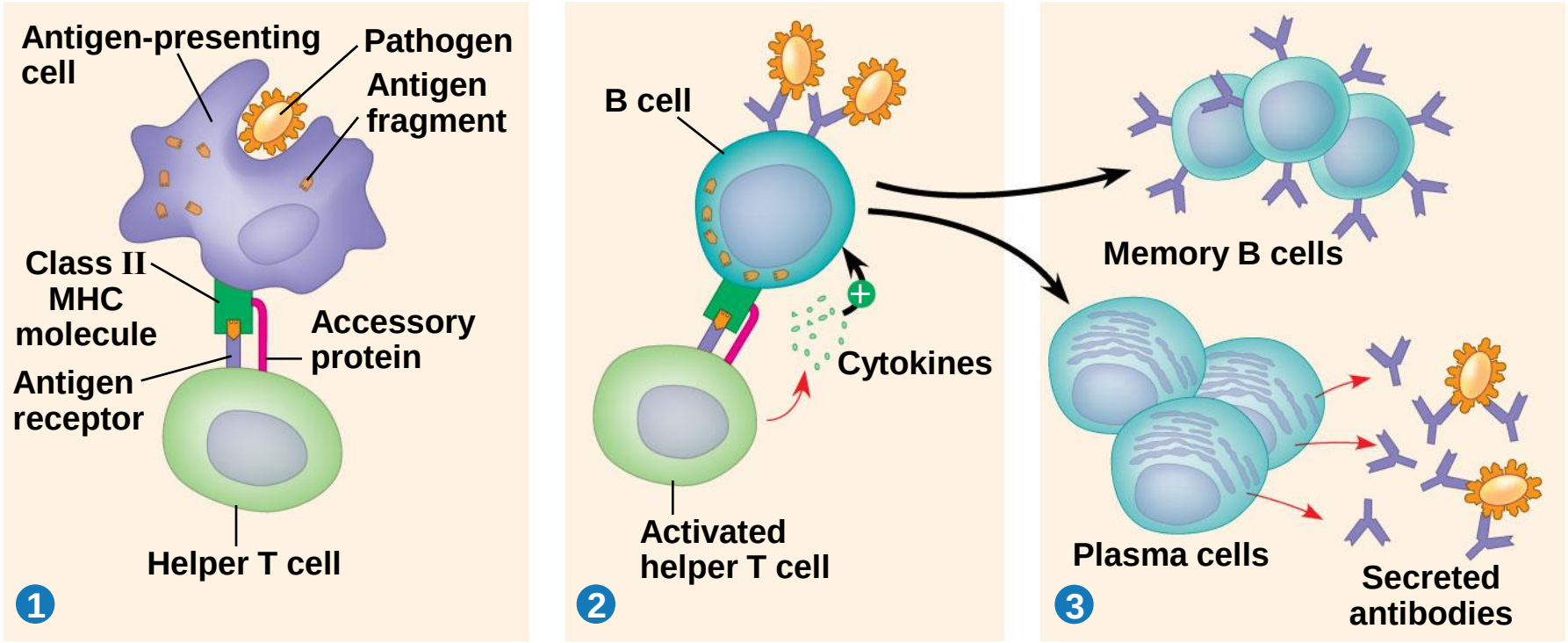


Figure 43.18-3



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 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

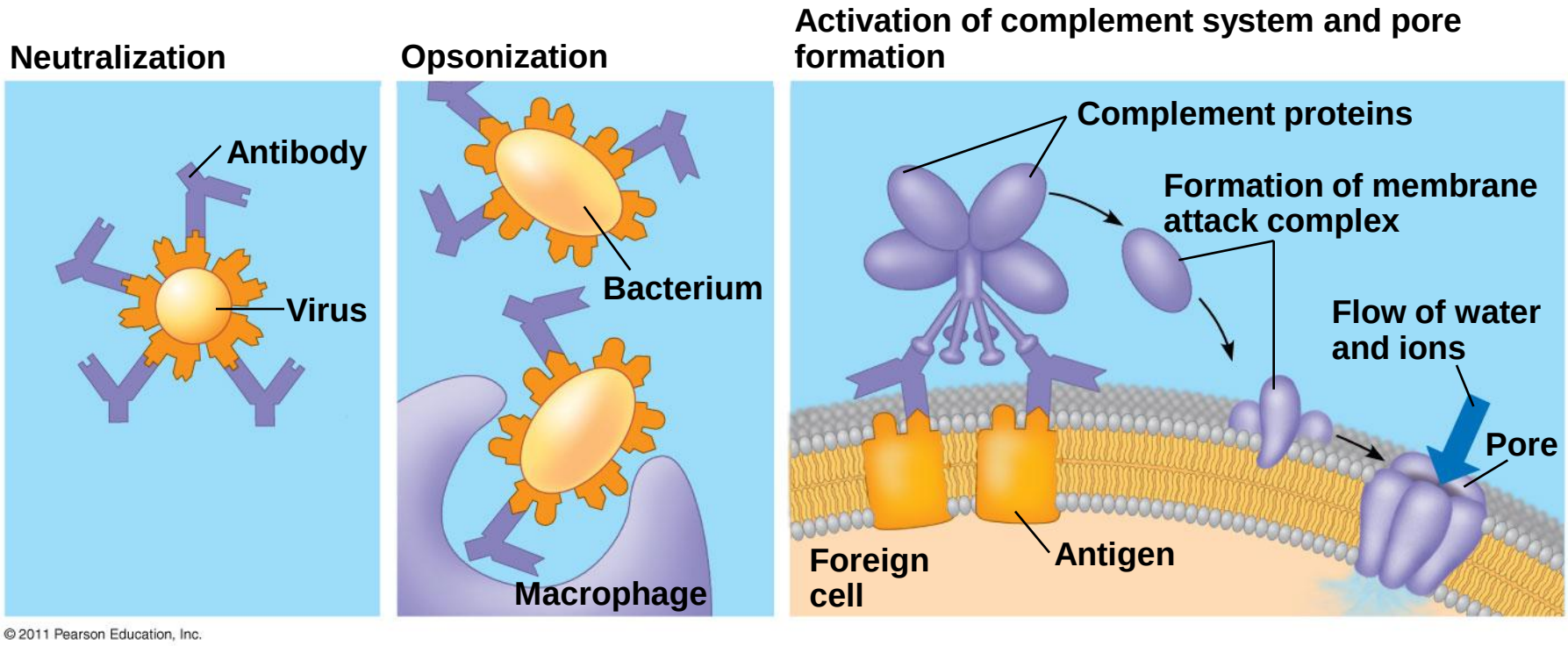


Figure 43.19a

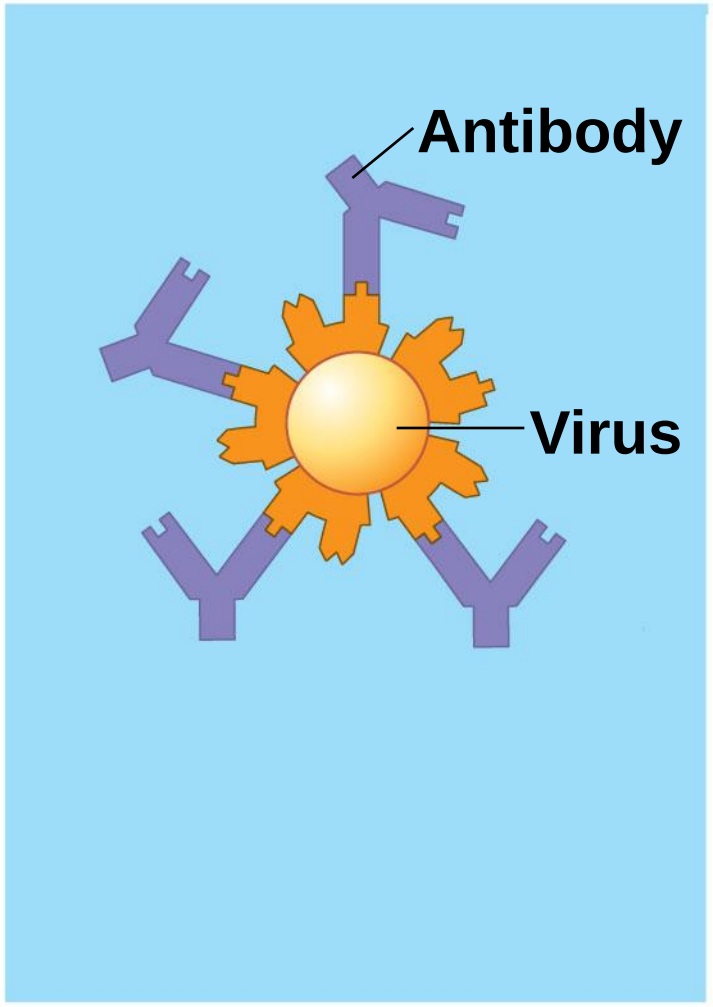


Figure 43.19b

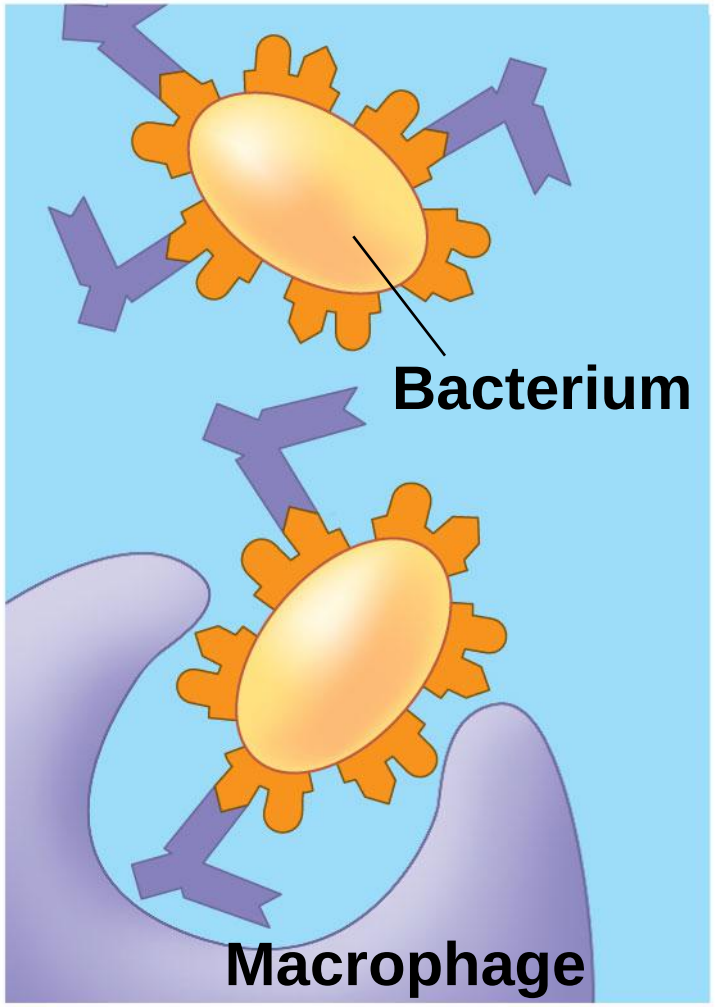
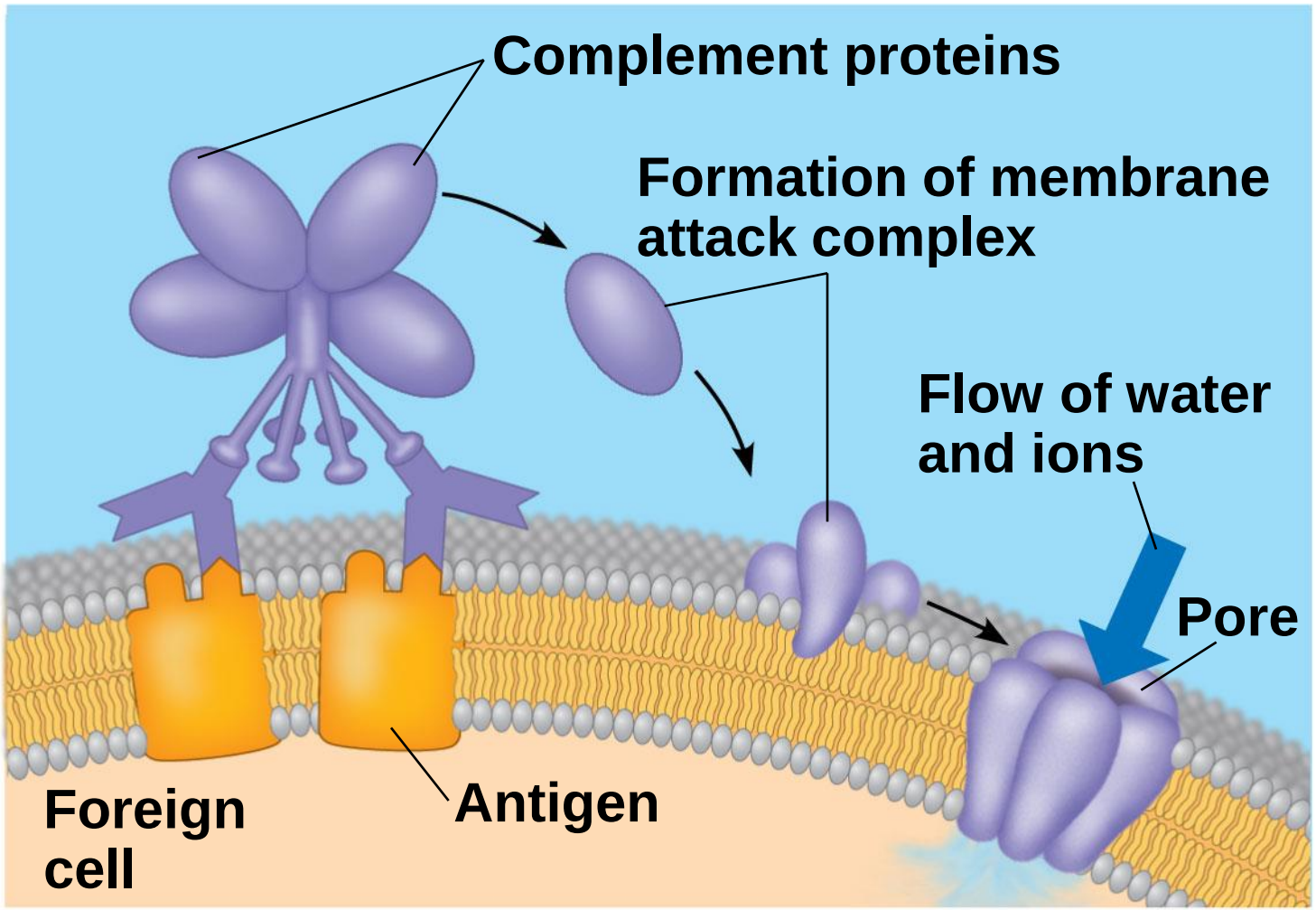


Figure 43.19c

Activation of complement system and pore formation



- 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

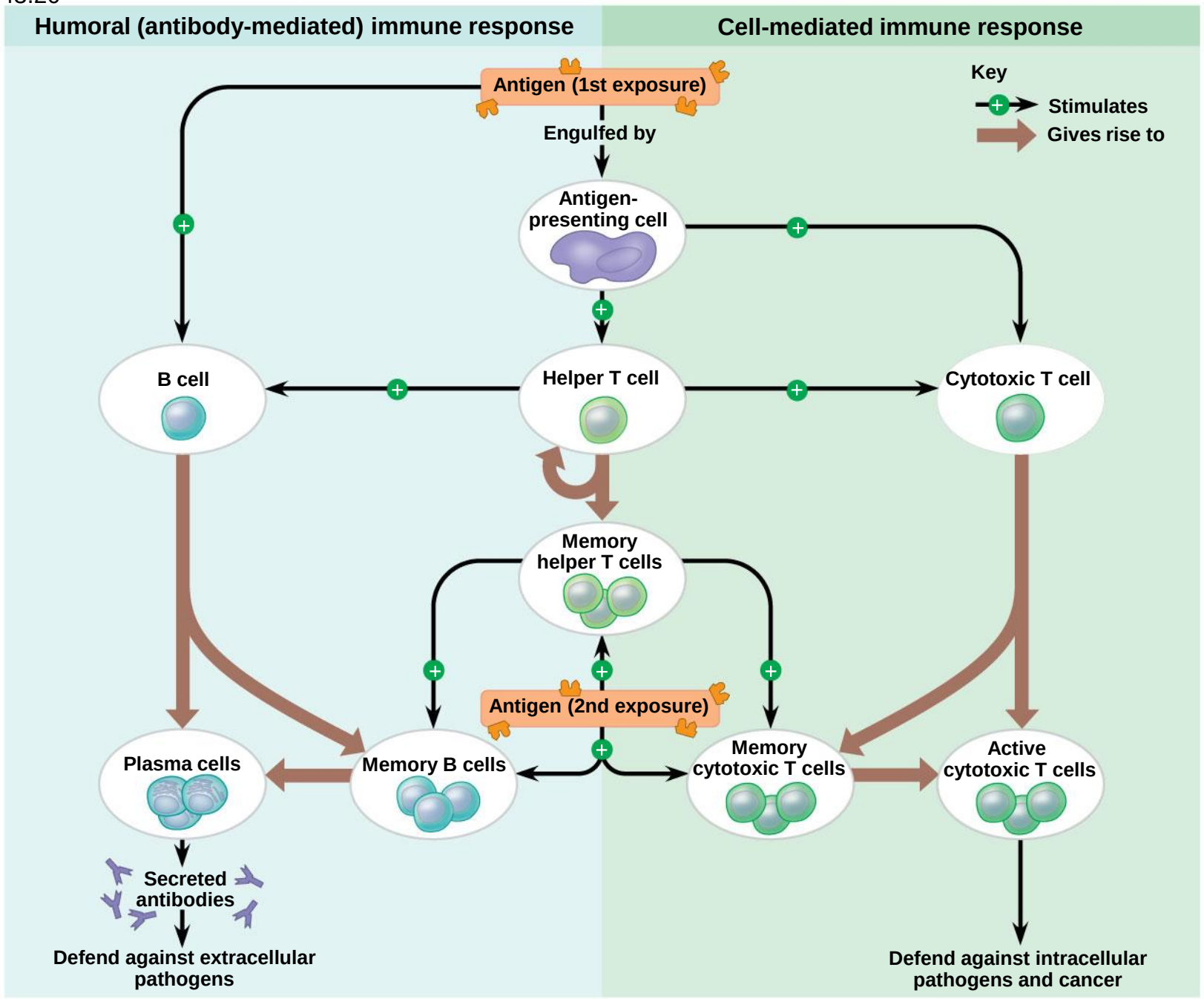


Figure 43.20a

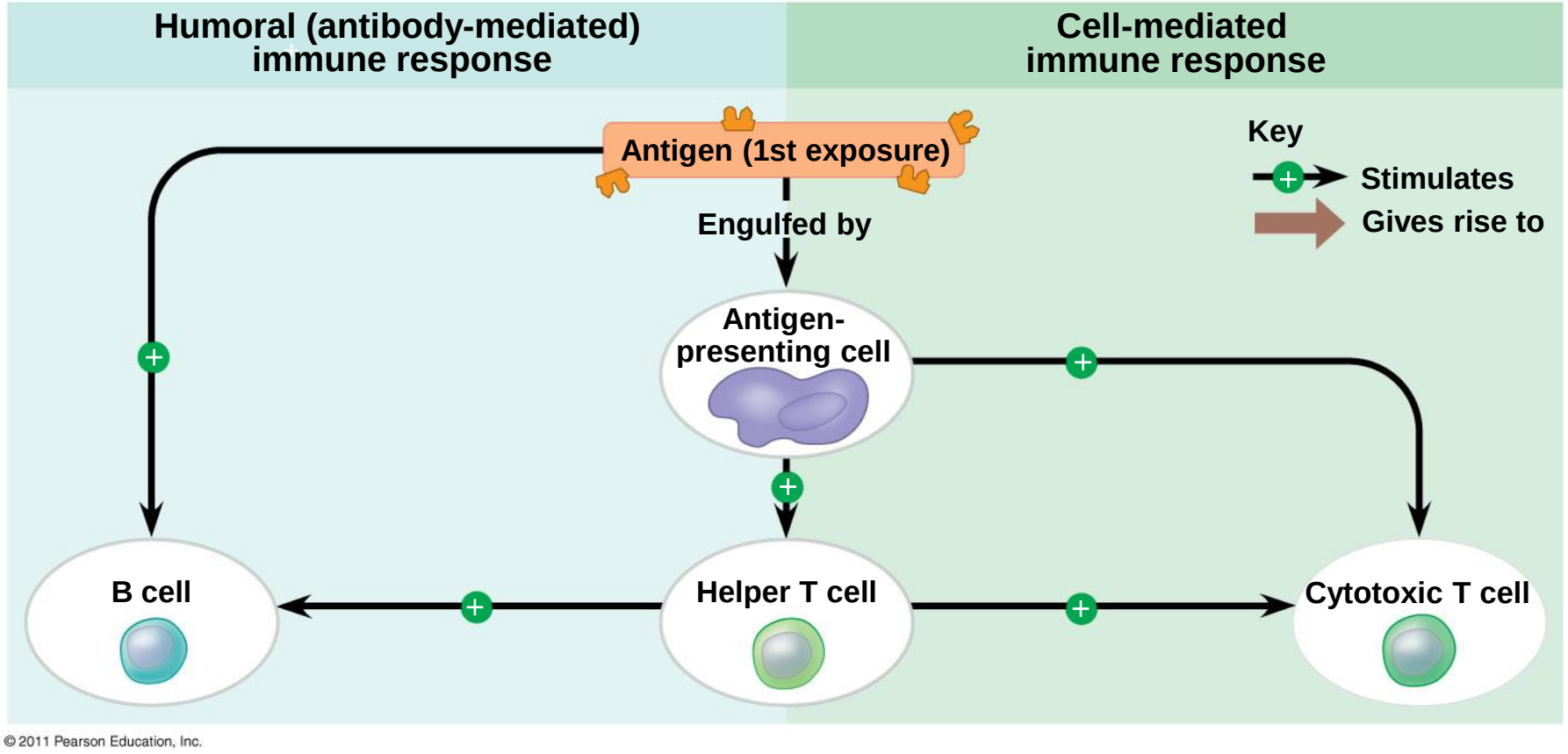
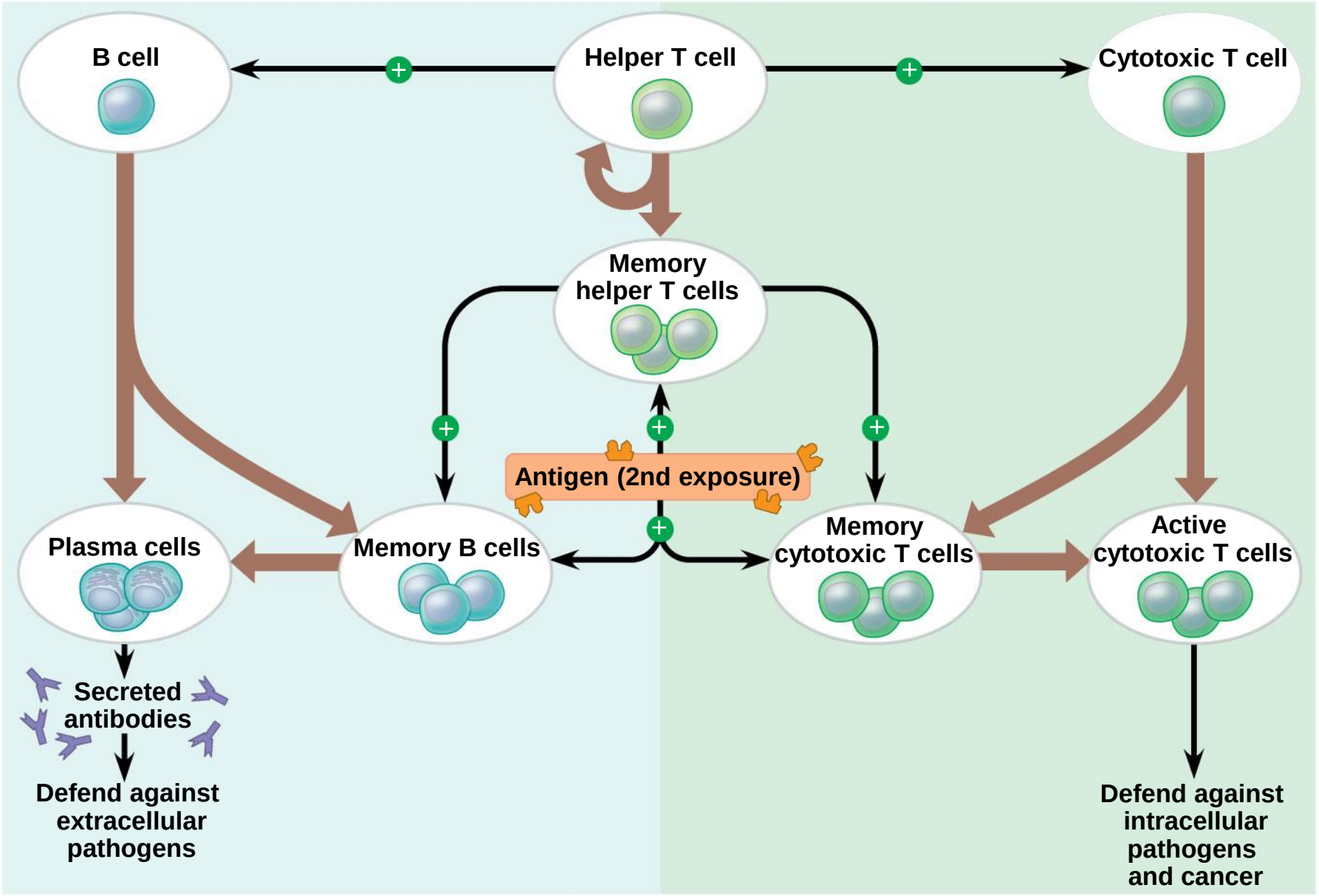


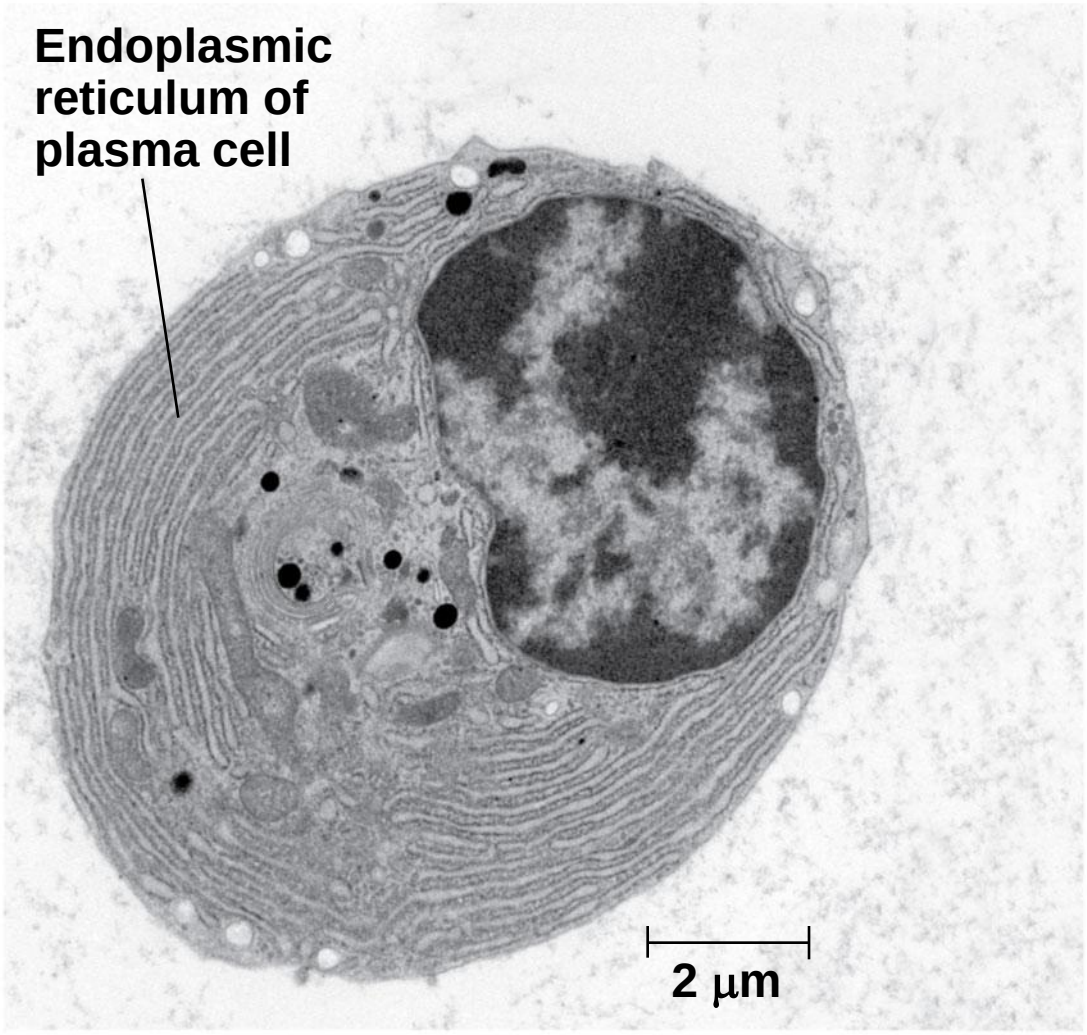
Figure 43.20b



Antibodies as Tools

- Antibody specificity and antigen-antibody binding has 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

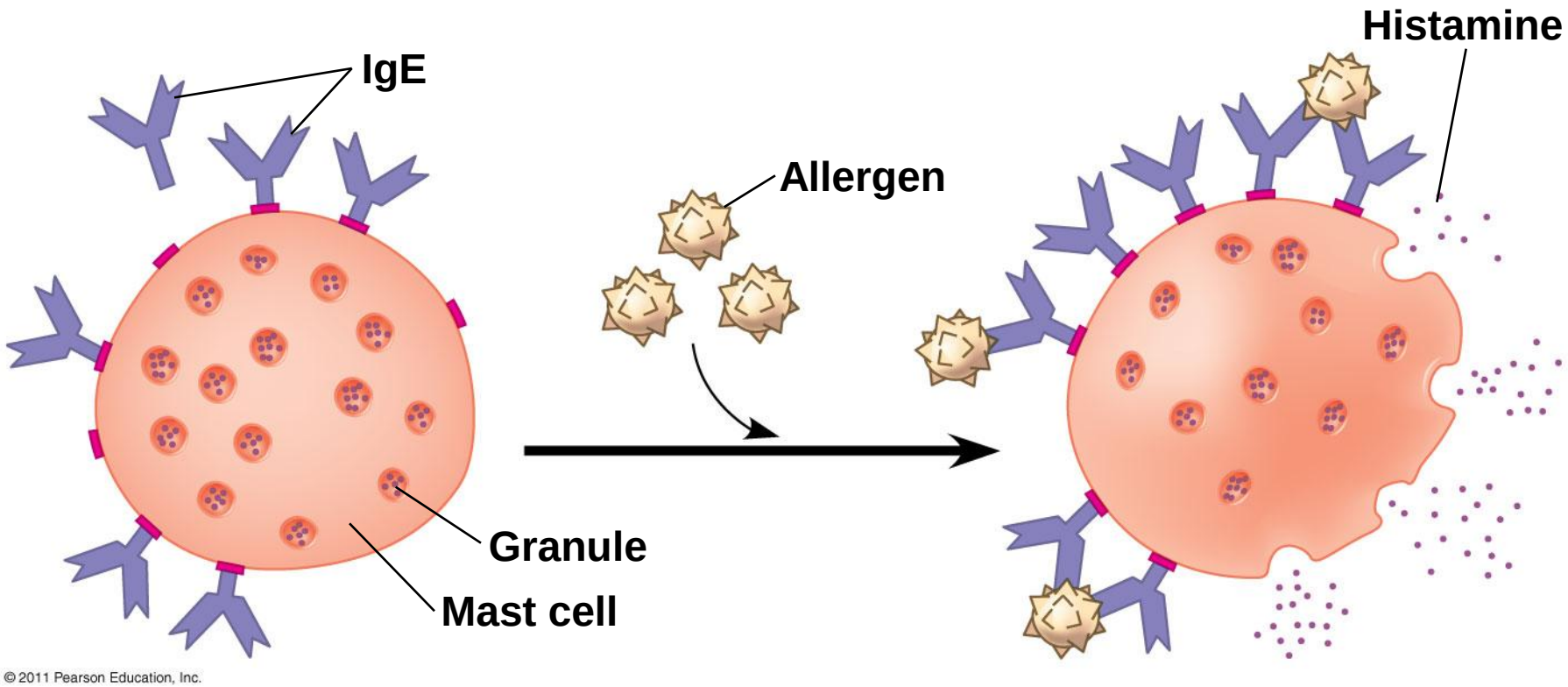
Exaggerated, Self-Directed, and Diminished Immune Responses

- 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

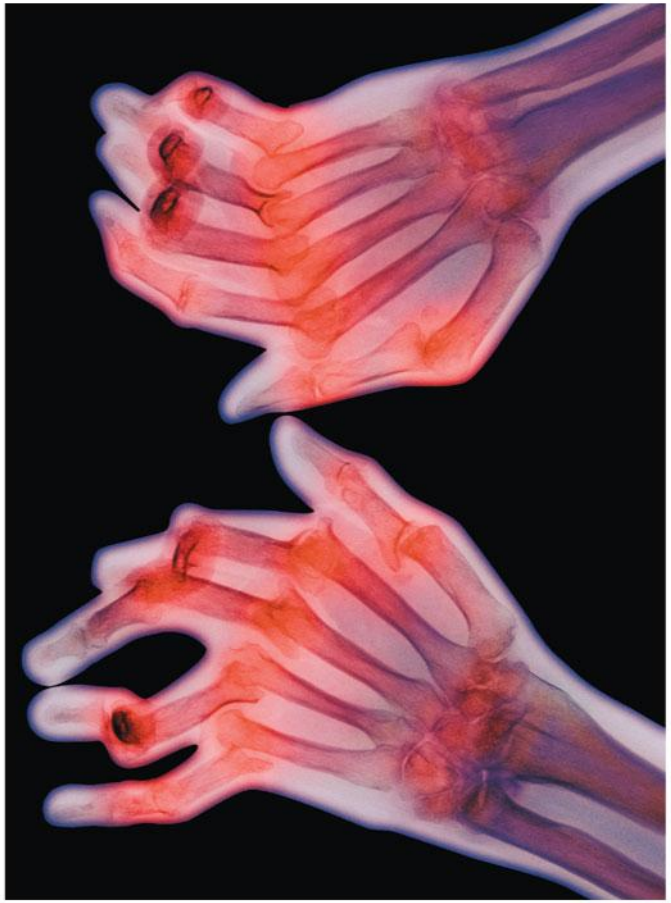


- The next time the allergen enters the body, it binds to mast cell–associated IgE molecules
- Mast cells release histamine and other mediators that cause vascular changes leading to typical allergy symptoms
- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction, within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

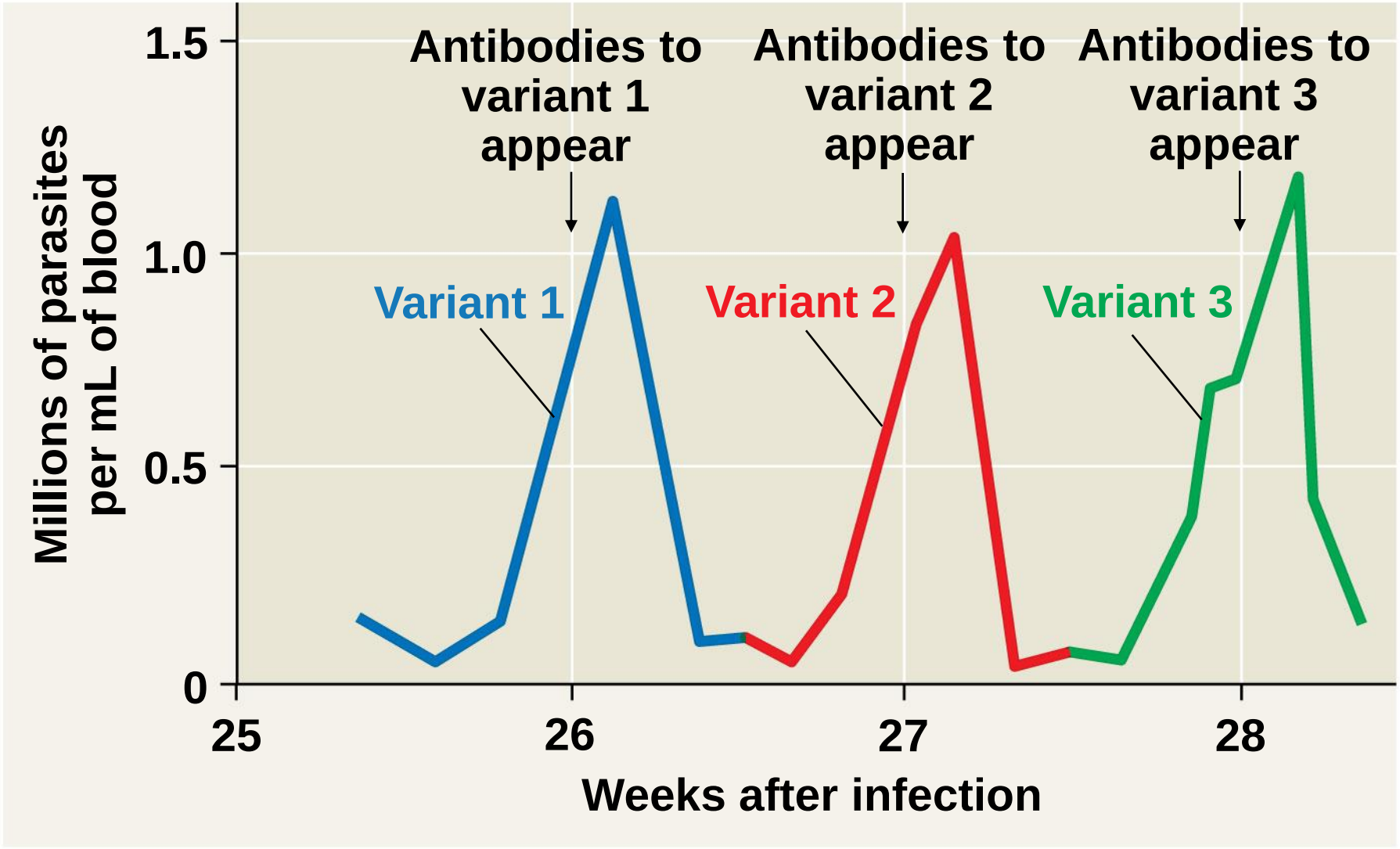
Evolutionary Adaptations of Pathogens That Underlie Immune System Avoidance

- 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

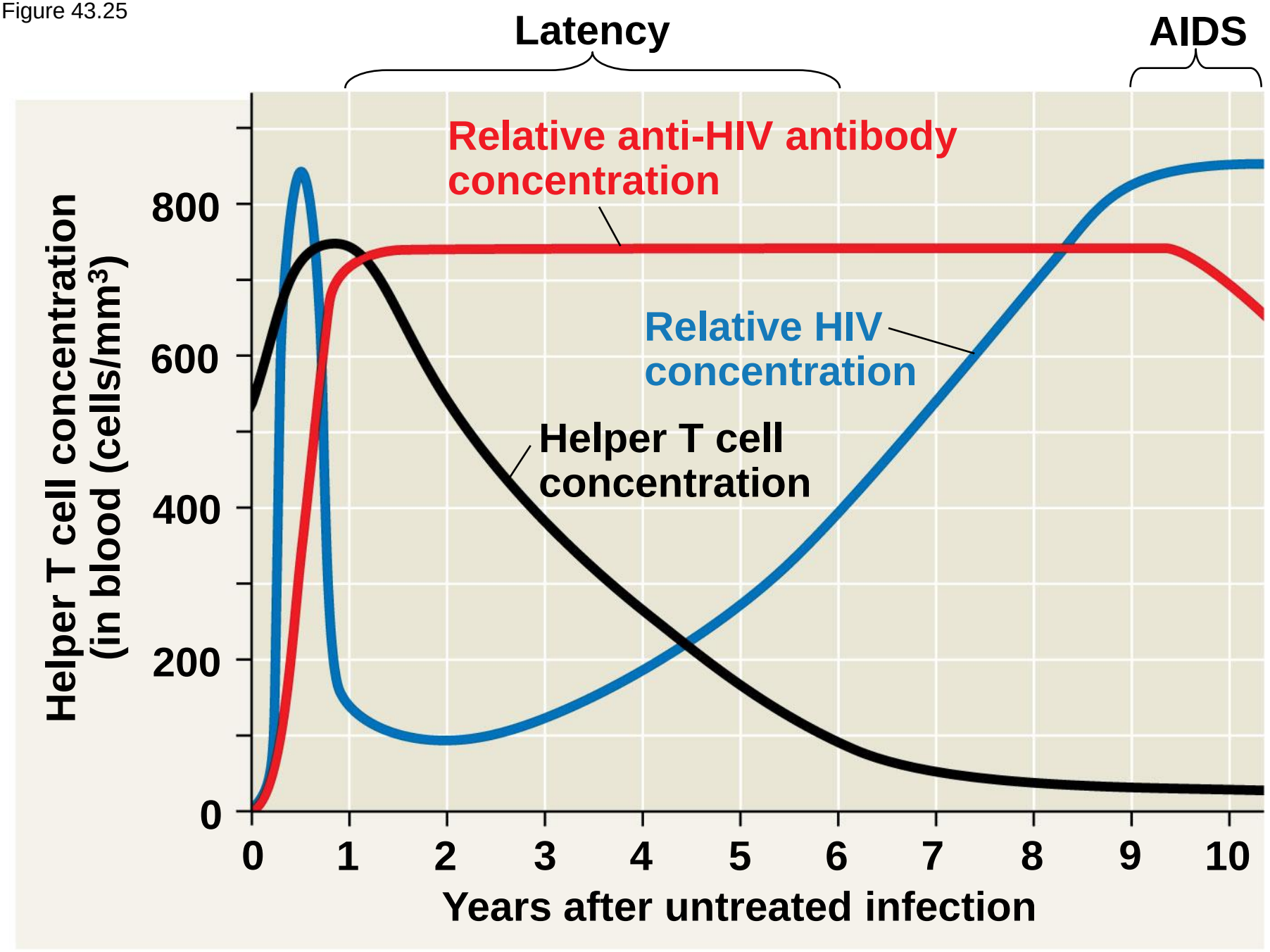
- Some viruses may remain in a host in an inactive state called latency
- Herpes simplex viruses can be present in a human host without causing symptoms

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

Figure 43.26

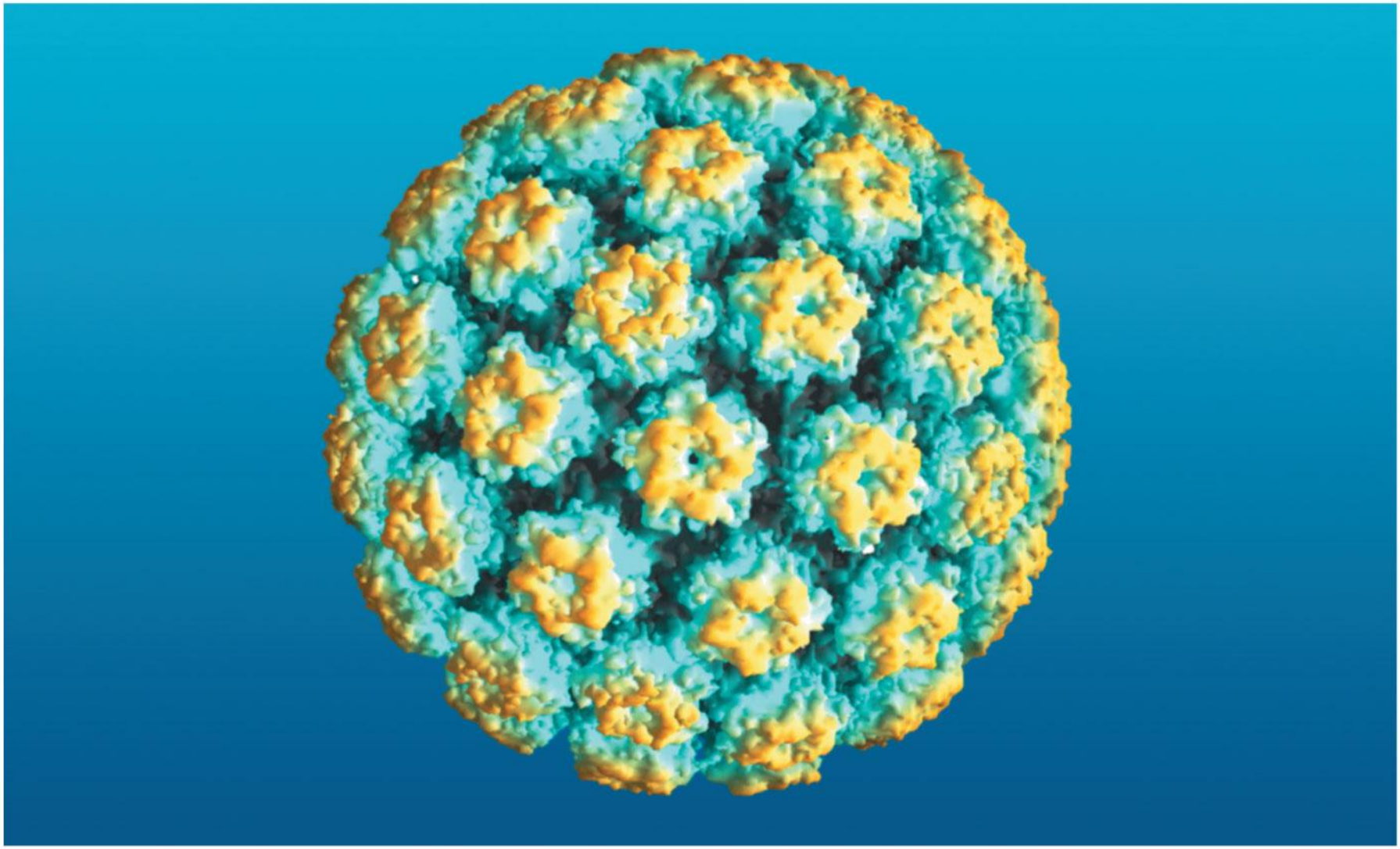


Figure 43.UN02

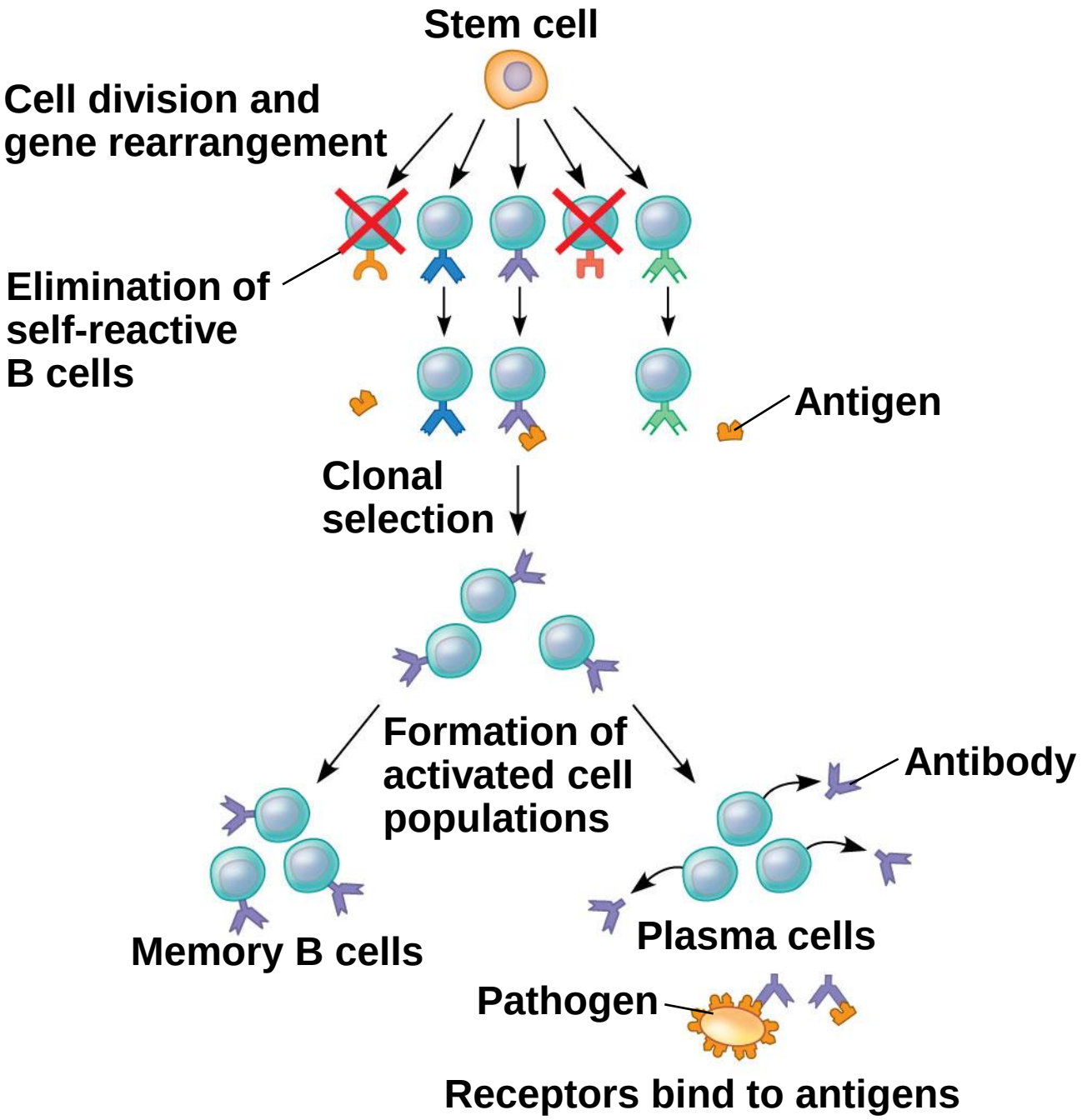
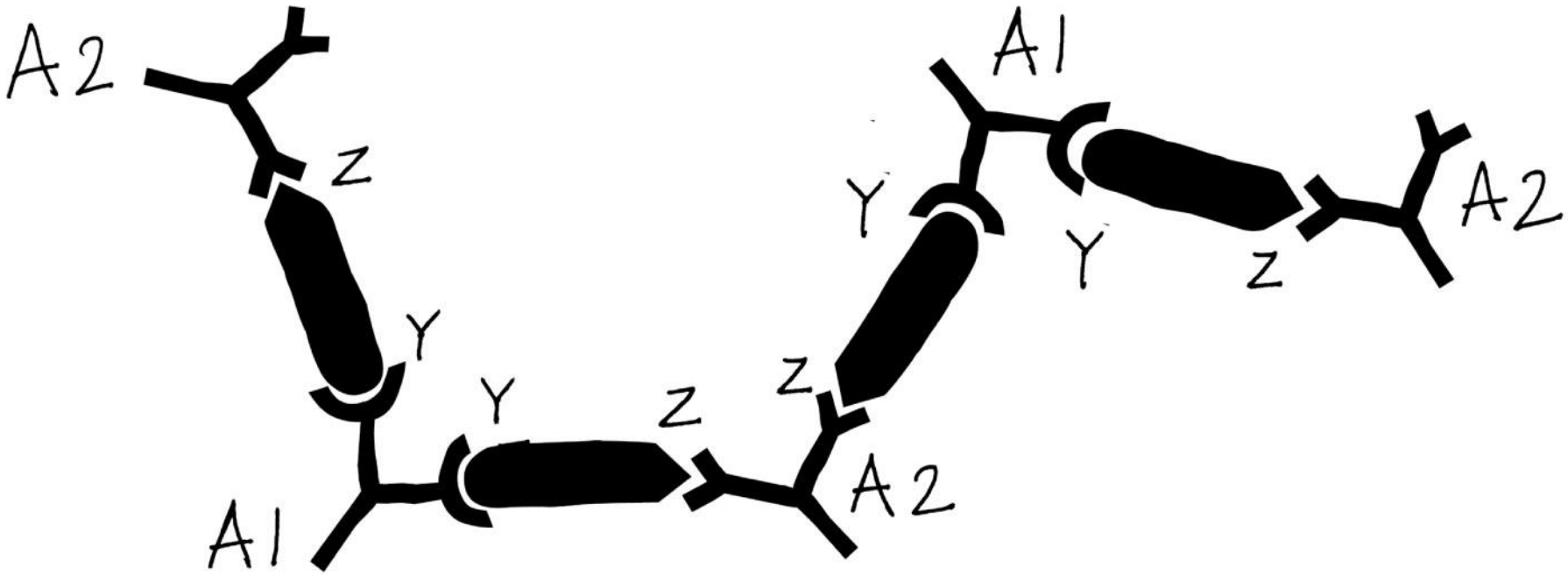


Figure 43.UN03



Antibodies Table

Fig. 43-20

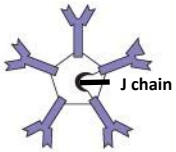
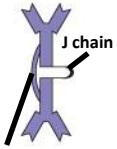
Class of Immunoglobulin (Antibody)	Distribution	Function
IgM (pentamer) 	First Ig class produced after initial exposure to antigen; then its concentration in the blood declines	Promotes neutralization and cross-linking of antigens; very effective in complement system activation
IgG (monomer) 	Most abundant Ig class in blood; also present in tissue fluids	Promotes opsonization, neutralization, and cross-linking of antigens; less effective in activation of complement system than IgM Only Ig class that crosses placenta, thus conferring passive immunity on fetus
IgA (dimer) 	Present in secretions such as tears, saliva, mucus, and breast milk	Provides localized defense of mucous membranes by cross-linking and neutralization of antigens Presence in breast milk confers passive immunity on nursing infant
IgE (monomer) 	Present in blood at low concentrations	Triggers release from mast cells and basophils of histamine and other chemicals that cause allergic reactions
IgD (monomer) 	Present primarily on surface of B cells that have not been exposed to antigens	Acts as antigen receptor in the antigen-stimulated proliferation and differentiation of B cells (clonal selection)

Fig. 43-20a

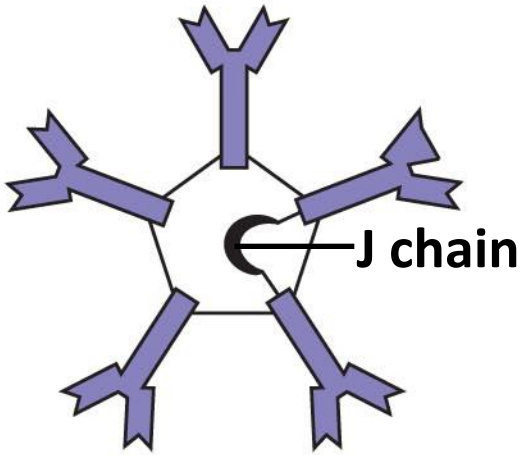
Class of Immuno-globulin (Antibody)	Distribution	Function
IgM (pentamer) 	First Ig class produced after initial exposure to antigen; then its concentration in the blood declines	Promotes neutraliza-tion and cross-linking of antigens; very effective in complement system activation

Fig. 43-20b

Class of Immuno-globulin (Antibody)	Distribution	Function
IgG (monomer) 	Most abundant Ig class in blood; also present in tissue fluids	Promotes opsoniza-tion, neutralization, and cross-linking of antigens; less effec-tive in activation of complement system than IgM Only Ig class that crosses placenta, thus conferring passive immunity on fetus

Fig. 43-20c

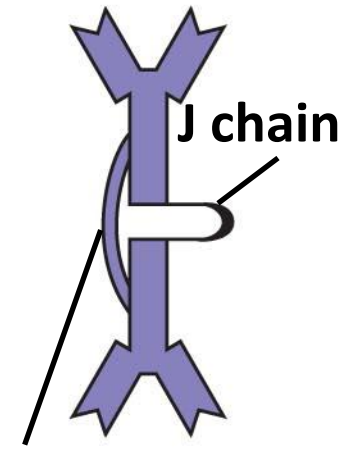
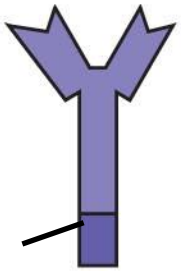
Class of Immuno-globulin (Antibody)	Distribution	Function
IgA (dimer) 	Present in secretions such as tears, saliva, mucus, and breast milk	Provides localized defense of mucous membranes by cross-linking and neutralization of antigens Presence in breast milk confers passive immunity on nursing infant

Fig. 43-20d

Class of Immuno-globulin (Antibody)	Distribution	Function
IgE (monomer) 	Present in blood at low concen-trations	Triggers release from mast cells and basophils of hista-mine and other chemicals that cause allergic reactions

Fig. 43-20e

Class of Immuno-globulin (Antibody)	Distribution	Function
IgD (monomer)  Trans-membrane region	Present primarily on surface of B cells that have not been exposed to antigens	Acts as antigen receptor in the antigen-stimulated proliferation and differentiation of B cells (clonal selection)