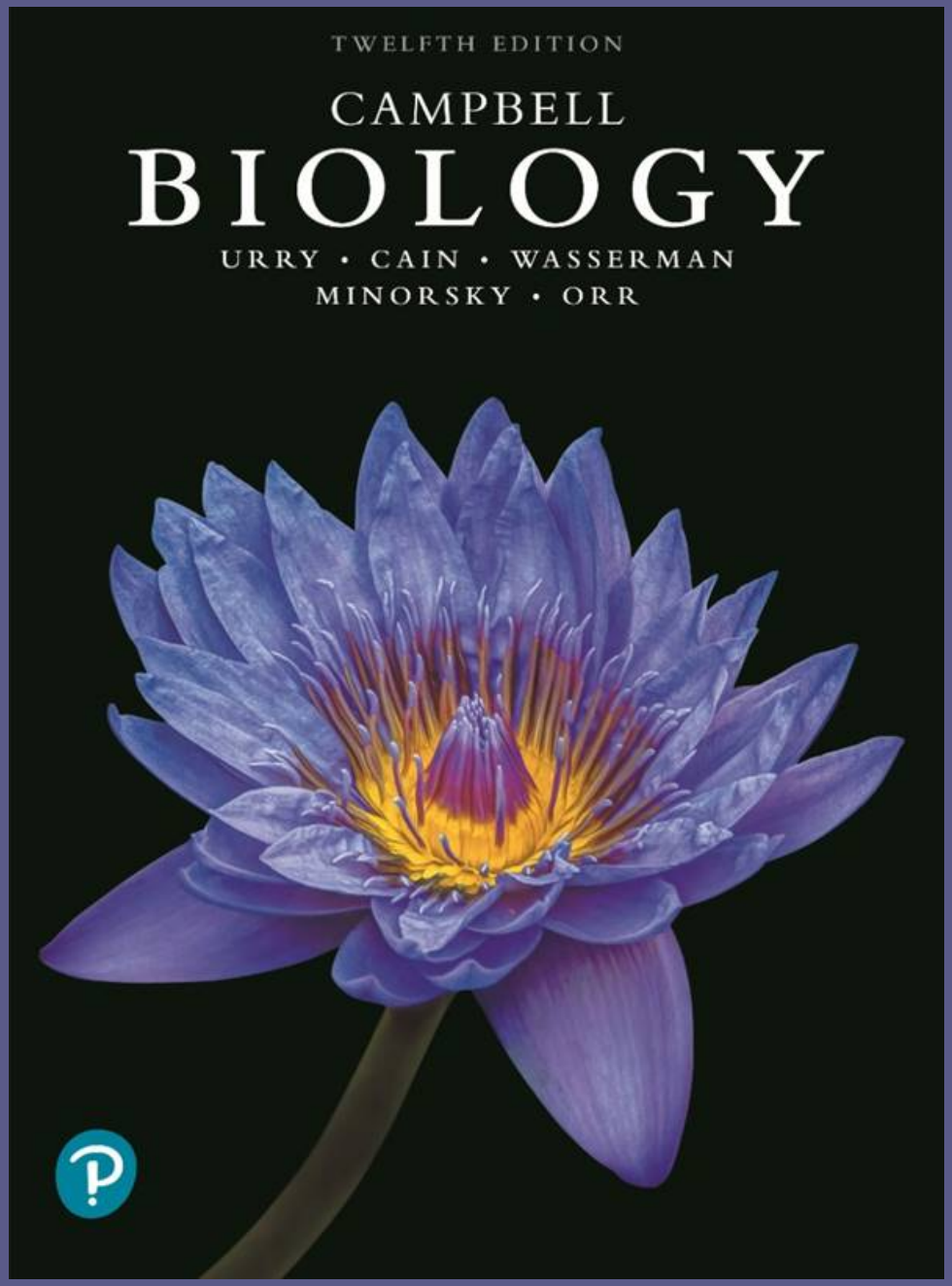


Chapter 43

The Immune System

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

Figure 43.1a

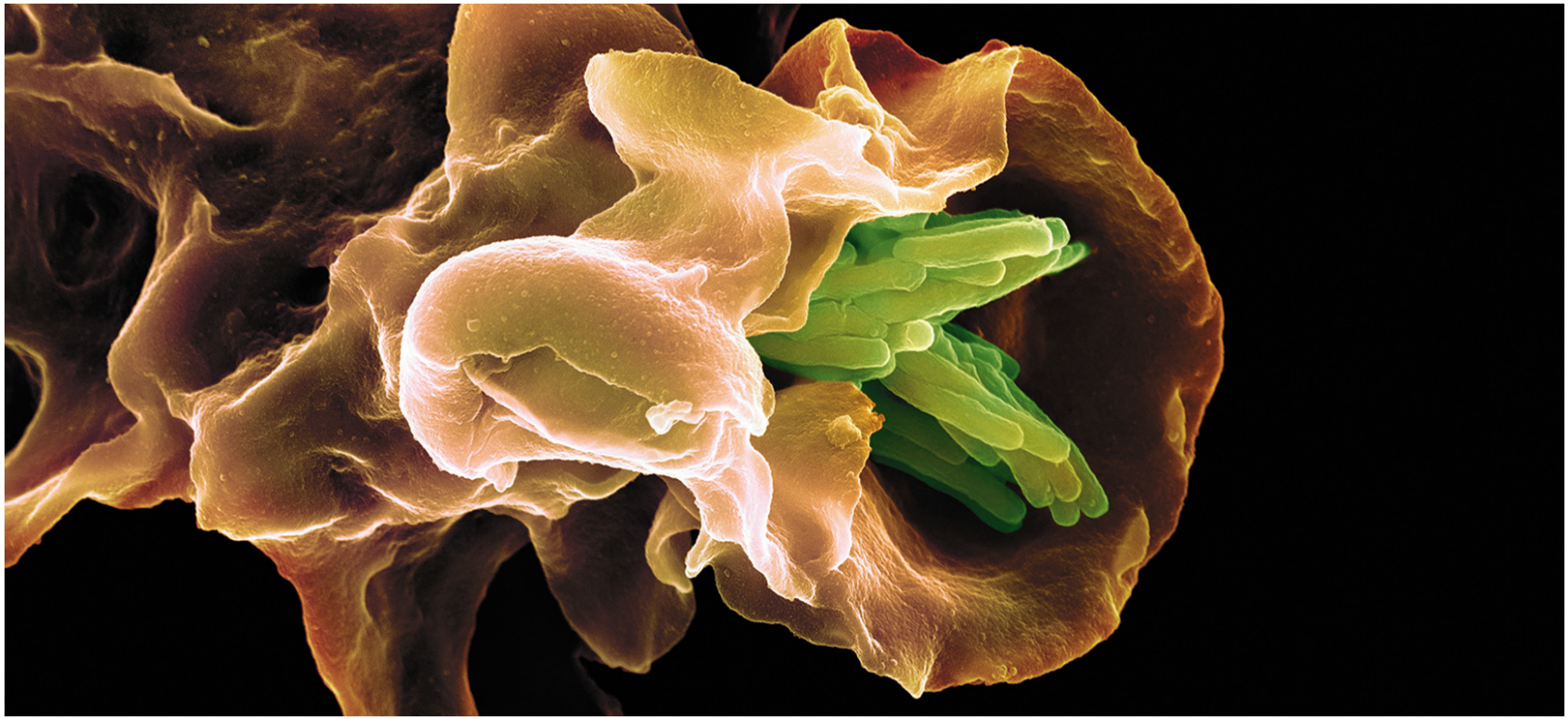
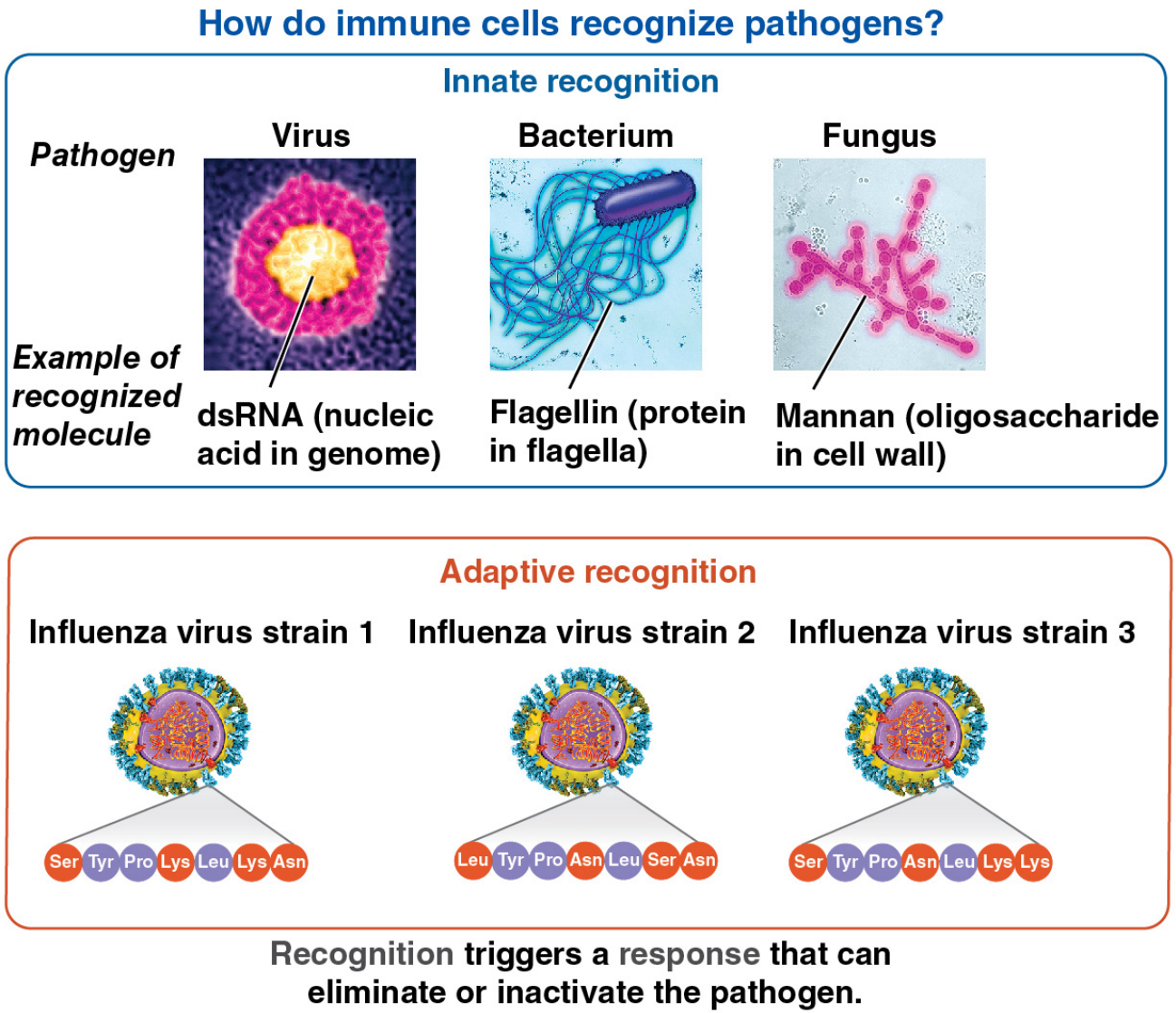


Figure 43.1b


How do immune cells recognize pathogens?
Innate recognition
Pathogen
Virus
Bacterium
Fungus
Example of recognized molecule
dsRNA (nucleic acid in genome)
Flagellin (protein in flagella)
Mannan (oligosaccharide in cell wall)
Adaptive recognition
Influenza virus strain 1
Influenza virus strain 2
Influenza virus strain 3
Ser Tyr Pro Lys Leu Lys Asn
Leu Tyr Pro Asn Leu Ser Asn
Ser Tyr Pro Asn Leu Lys Lys
Recognition triggers a response that can eliminate or inactivate the pathogen.

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

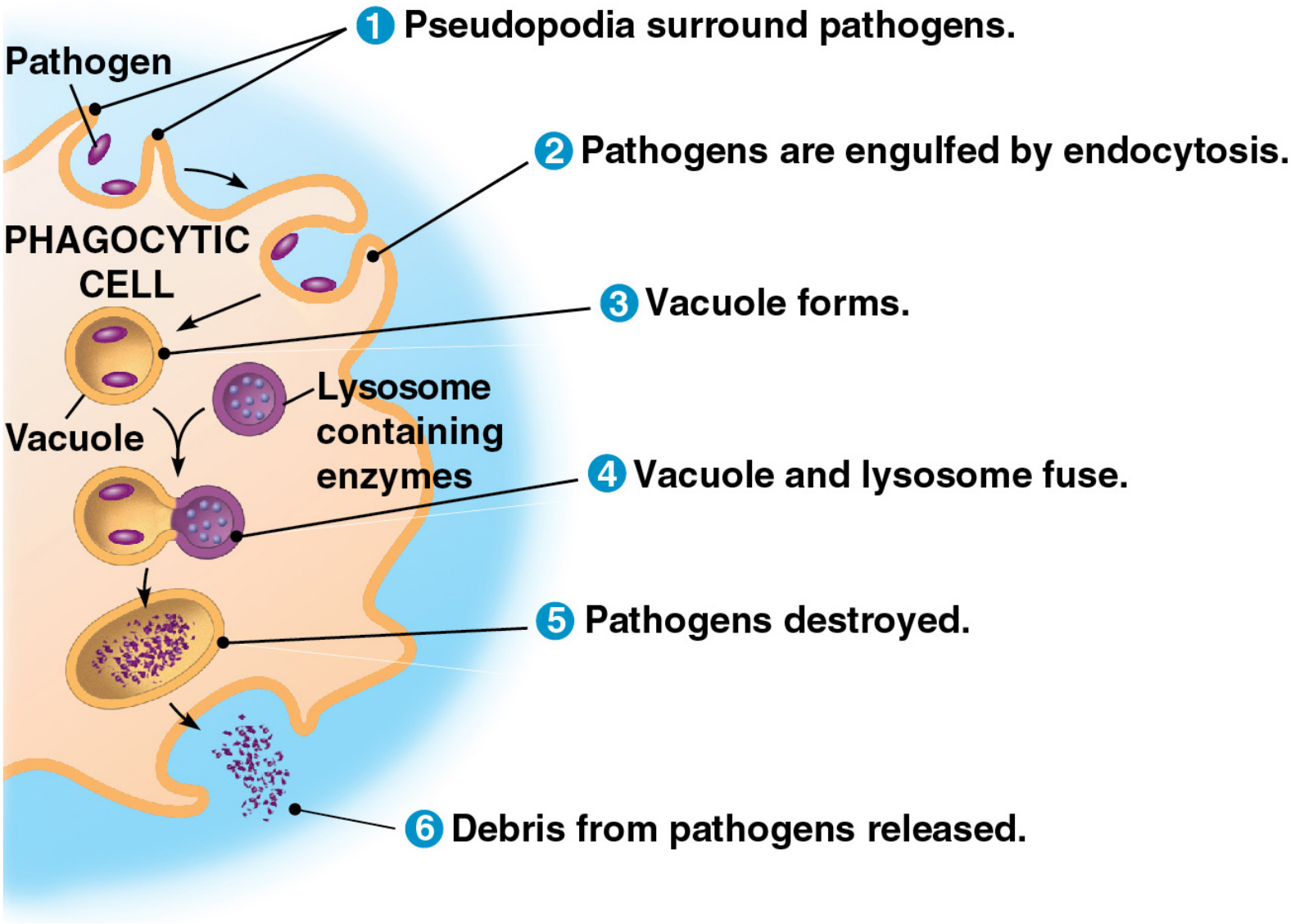
- **Pathogens** are agents that cause disease, such as bacteria, viruses, fungi, or others
- Dedicated cells of the **immune system** enable animals to avoid or limit many infections
- First lines of defense help prevent pathogens from gaining entry to the body
- Within the body, two types of molecular recognition allow detection of nonself molecules, particles, and cells

- All animals have **innate immunity**, a defense active immediately upon infection
- Innate immunity includes barrier defenses
- Vertebrates also have **adaptive immunity**
- The adaptive immune response is activated after the innate response and develops more slowly

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
- Insect immune cells produce recognition proteins, each of which binds a molecule common to a large class of pathogens
- The major immune cells of insects are called *hemocytes*

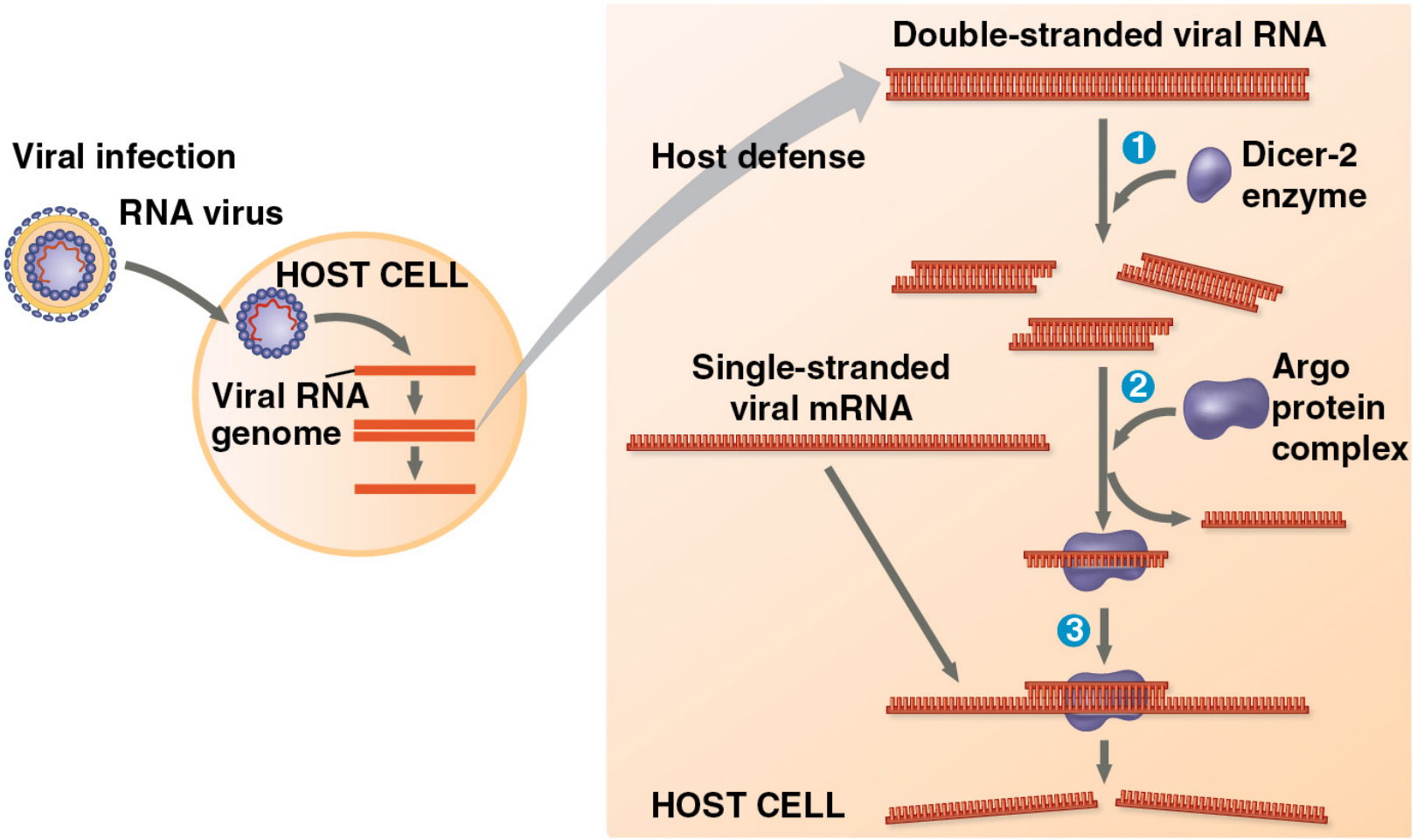
Figure 43.2


1 Pseudopodia surround pathogens.
Pathogen
2 Pathogens are engulfed by endocytosis.
PHAGOCYTIC CELL
3 Vacuole forms.
Lysosome containing enzymes
Vacuole
4 Vacuole and lysosome fuse.
5 Pathogens destroyed.
6 Debris from pathogens released.

- Some hemocytes ingest and break down microorganisms through **phagocytosis**
- Hemocytes also secrete antimicrobial peptides that inactivate or kill fungi or bacteria
- Binding of recognition proteins to fungal cell wall molecules activates a transmembrane receptor called Toll
- Toll then activates production and secretion of antimicrobial peptides that kill fungal cells

- Insects also have defenses against viruses
- Many viruses that infect insects have a genome consisting of a single strand of RNA
- This is converted into double-stranded RNA inside the host cell
- As double-stranded RNA is not produced by animals, it can trigger a specific defense against the invading virus

Figure 43.3


Viral infection
RNA virus
HOST CELL
Viral RNA genome
Host defense
Double-stranded viral RNA
1
Dicer-2 enzyme
Single-stranded viral mRNA
2
Argo protein complex
3
HOST CELL

Innate Immunity of Vertebrates

- Some innate defenses of mammals are similar to those of invertebrates
- These include barrier defenses, phagocytosis, and antimicrobial peptides
- Additional defenses unique to vertebrates are natural killer cells, interferons, and the inflammatory response

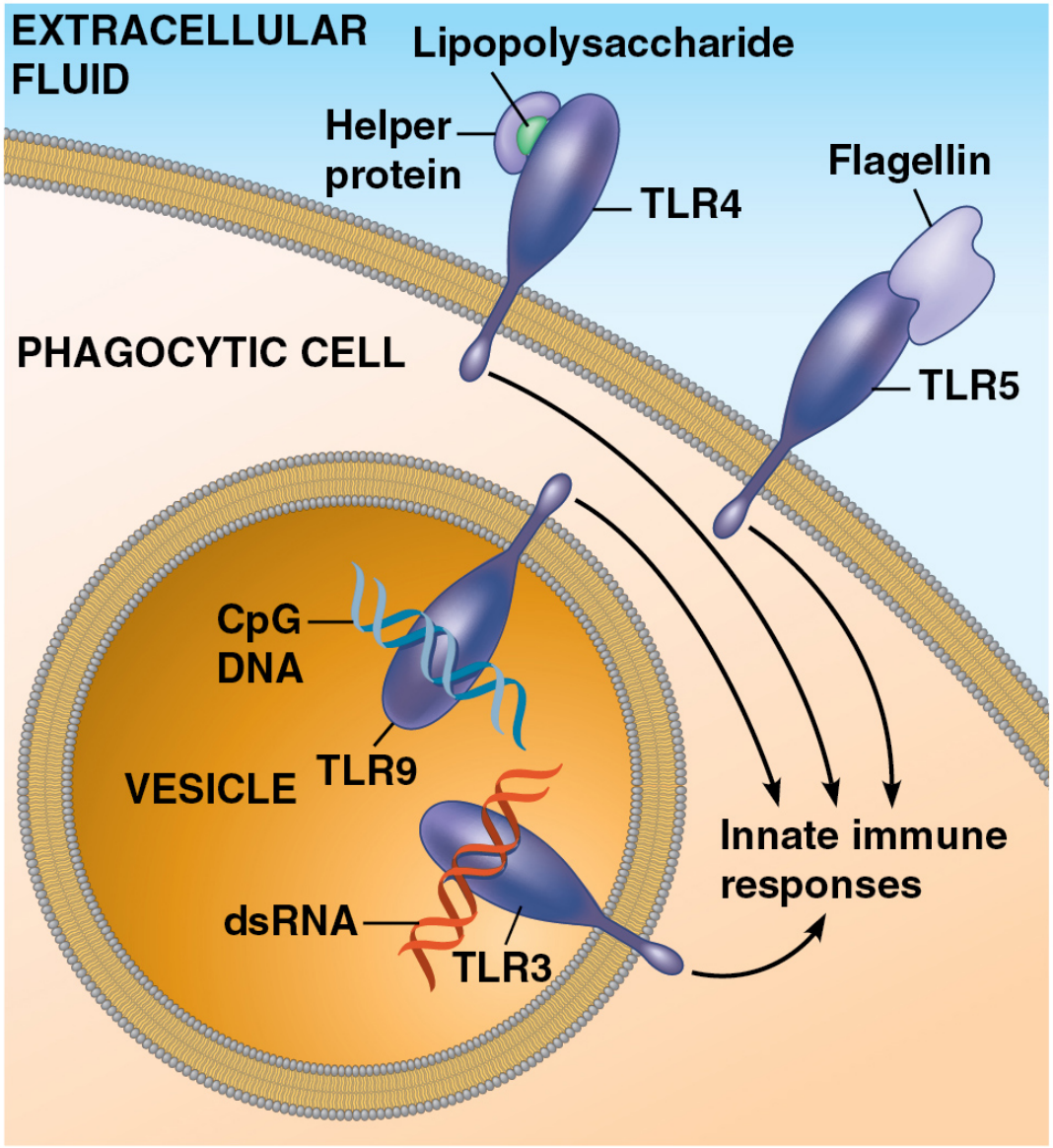
Barrier Defenses

- 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

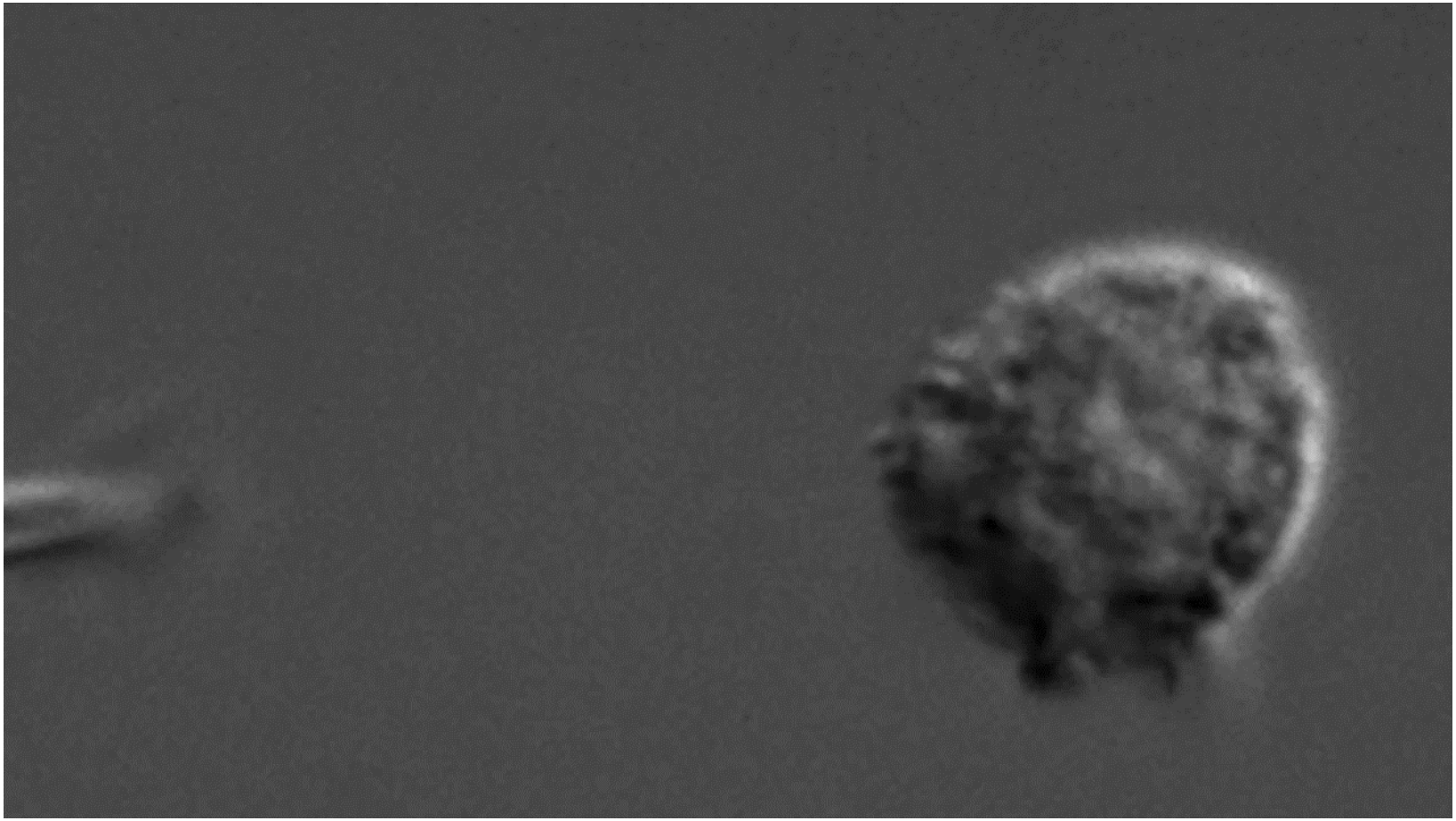
- Innate immune cells in mammals detect, devour, and destroy invading pathogens
- These cells recognize groups of pathogens using **TLRs**, or **Toll-like receptors**
- TLRs recognize fragments of molecules characteristic of a set of pathogens

Figure 43.4


EXTRACELLULAR FLUID
Lipopolysaccharide
Helper protein
TLR4
Flagellin
PHAGOCYTIC CELL
TLR5
CpG DNA
TLR9
VESICLE
Innate immune responses
dsRNA
TLR3

- There are two main types of phagocytic cells, which engulf and destroy pathogens, in the mammalian body:
  - **Neutrophils** circulate in the blood
  - **Macrophages** migrate through the body or reside permanently in organs and tissues
- There are two additional types of phagocytic cells:
  - **Dendritic cells** stimulate development of adaptive immunity
  - **Eosinophils** discharge destructive enzymes against parasites

Video: Chemotaxis of a Neutrophil

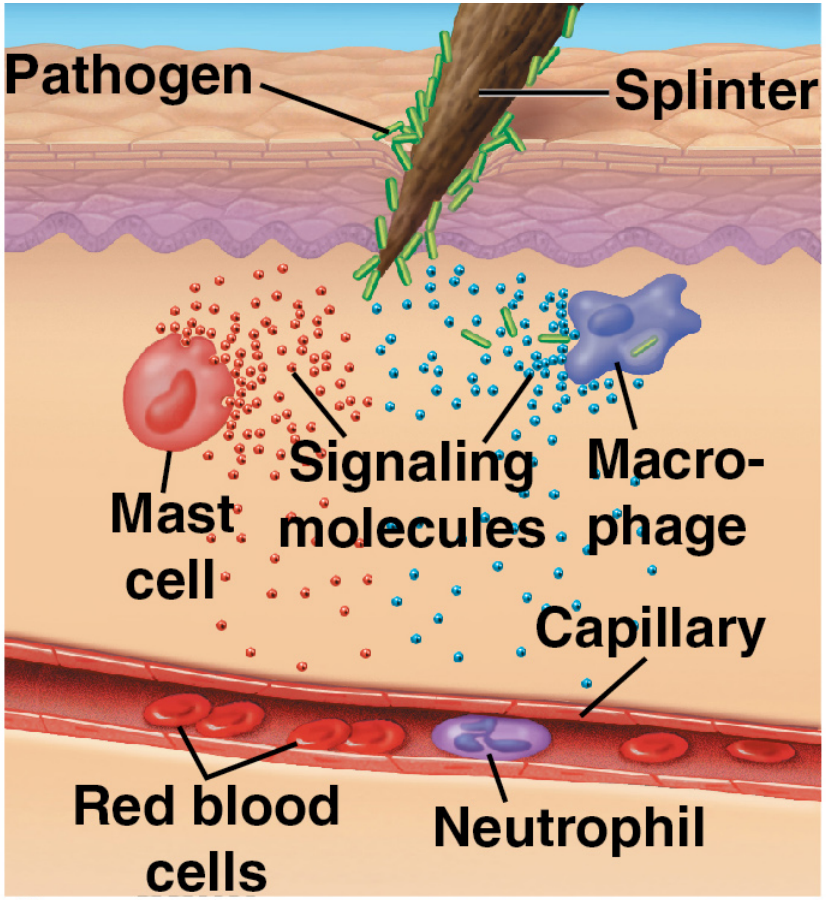


- Cellular innate defenses in vertebrates also involve **natural killer cells**
- These circulate through the body and detect abnormal cells
- They release chemicals leading to cell death, inhibiting the spread of virally infected or cancerous cells
- Many cellular innate defenses involve the lymphatic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

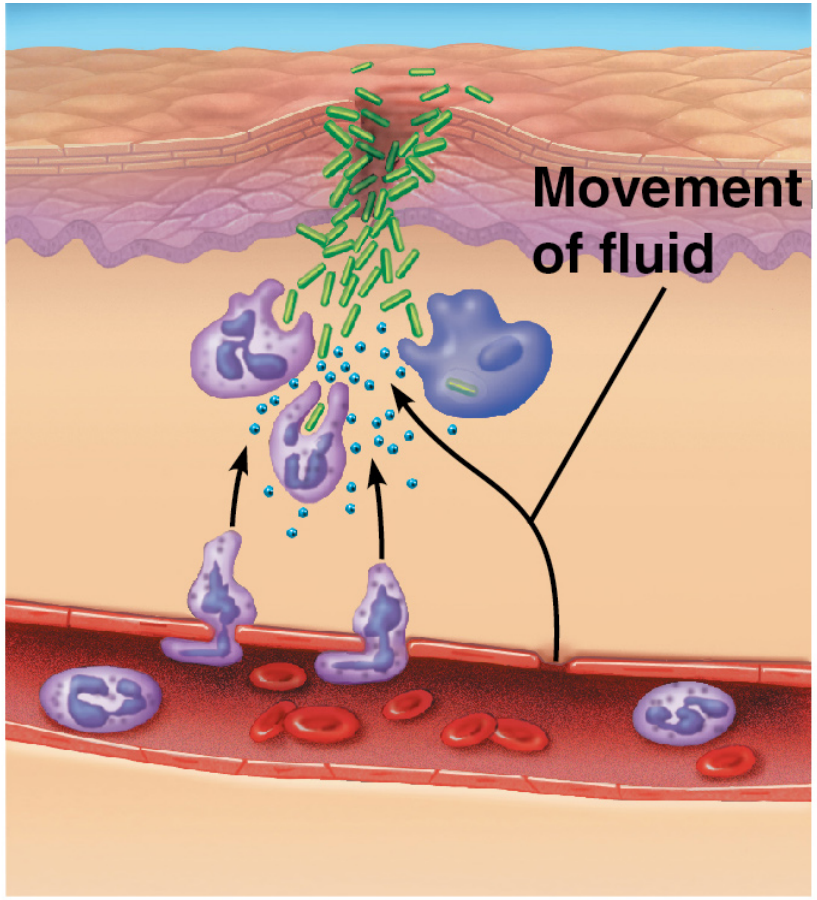
Local Inflammatory Response

- The **inflammatory response**, including heat and swelling, is brought about by molecules released upon injury or infection
- Mast cells, immune cells found in connective tissue, discharge cytokines, signaling molecules that recruit neutrophils to the site
- They also release **histamine**, which triggers blood vessels to dilate and become more permeable
- The resulting increase in blood supply produces the inflammatory response

Figure 43.5



1 Mast cells release histamines. Capillaries dilate.

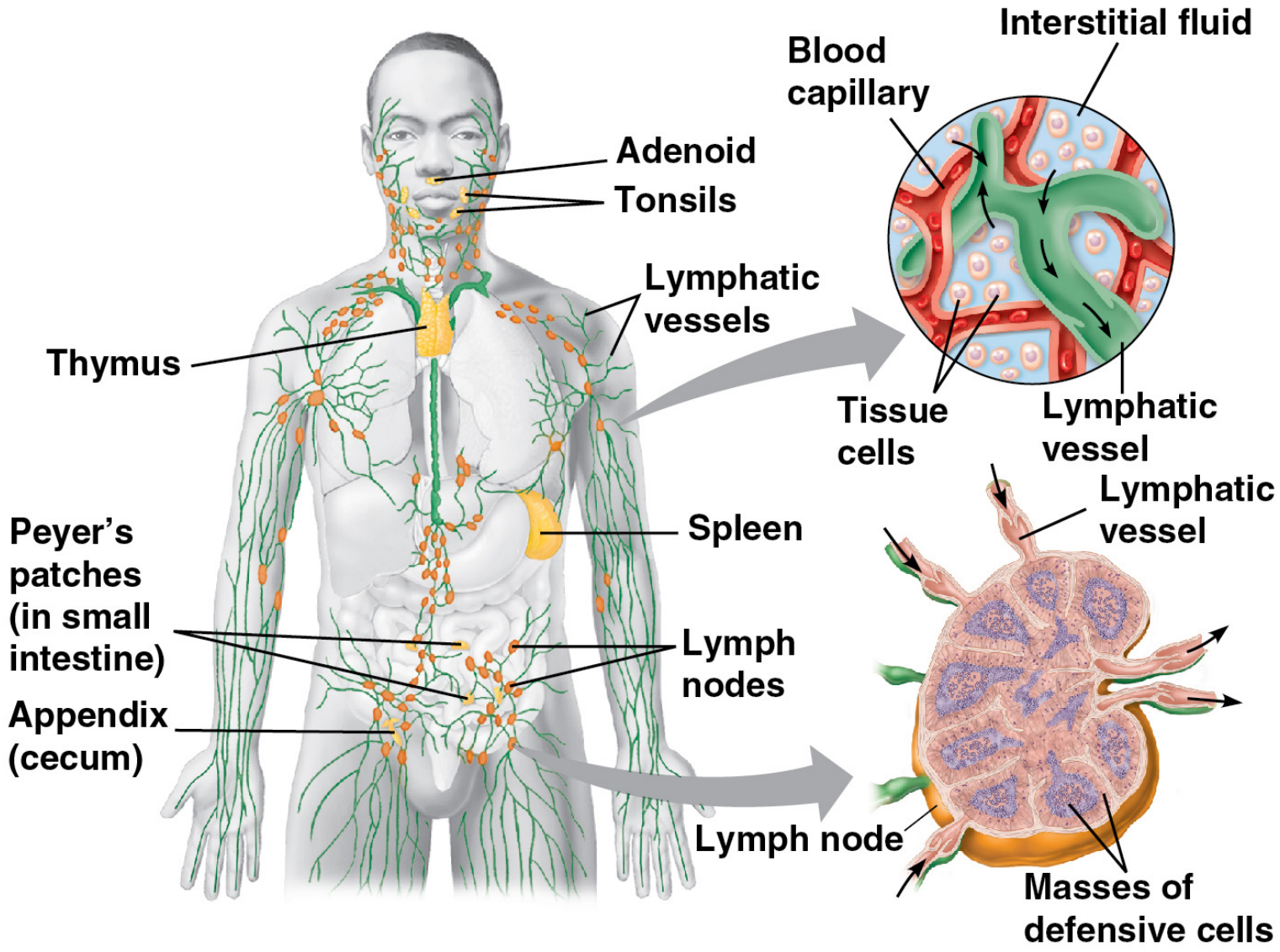


2 Neutrophils and anti-microbial peptides enter tissue.

- Cycles of signaling and response, continue the process of inflammation
- Enhanced blood flow to the site, helps deliver antimicrobial peptides
- The result is an accumulation of pus, a fluid rich in white blood cells, dead pathogens and debris from damaged tissue

- At the end of the local inflammatory response, pus and excess fluid are taken up as lymph
- This fluid is transported in the body by the lymphatic system
- Lymph nodes, throughout the body, contain macrophages, which engulf pathogens that enter the lymph
- Dendritic cells migrate to lymph nodes after interacting with pathogens, and stimulate adaptive immunity

Figure 43.6


Adenoid
Tonsils
Lymphatic vessels
Thymus
Spleen
Peyer's patches (in small intestine)
Lymph nodes
Appendix (cecum)
Lymph node
Blood capillary
Interstitial fluid
Tissue cells
Lymphatic vessel
Lymphatic vessel
Masses of defensive cells

Systemic and Chronic Inflammation

- More extensive tissue damage or infection can lead to a response that is systemic (throughout the body)
- Cells in the injured or infected tissue often secrete molecules that stimulate the release of additional neutrophils from bone marrow
- In the case of severe infection, the number of white blood cells in the bloodstream may increase severalfold within a few hours

- A systemic inflammatory response sometimes involves fever
- Substances released by macrophages activated by certain pathogens, cause the body's thermostat to reset to a higher temperature
- It is possible that this may enhance phagocytosis and accelerate tissue repair.

- Certain bacterial infections can induce an overwhelming system inflammatory response
- This leads to a life-threatening condition called septic shock.
- It is fatal in more than one third of cases, and occurs more often in the very old and very young
- Crohn’s disease and ulcerative colitis are debilitating disorders in which chronic (ongoing) inflammation disrupts intestinal function

Antimicrobial Peptides and Proteins

- Pathogen recognition in mammals, triggers the production and release of peptides that attack pathogens or impede their reproduction
- **Interferons** are proteins that provide innate defense by inhibiting the replication of viruses
- Some types of interferons help activate macrophages

- The **complement system** consists of about 30 proteins in blood plasma
- These are activated by substances on the surface of many pathogens
- A resulting cascade of reactions lead to lysis (bursting) of the invading cells
- The complement system also functions in the inflammatory response and in adaptive defense

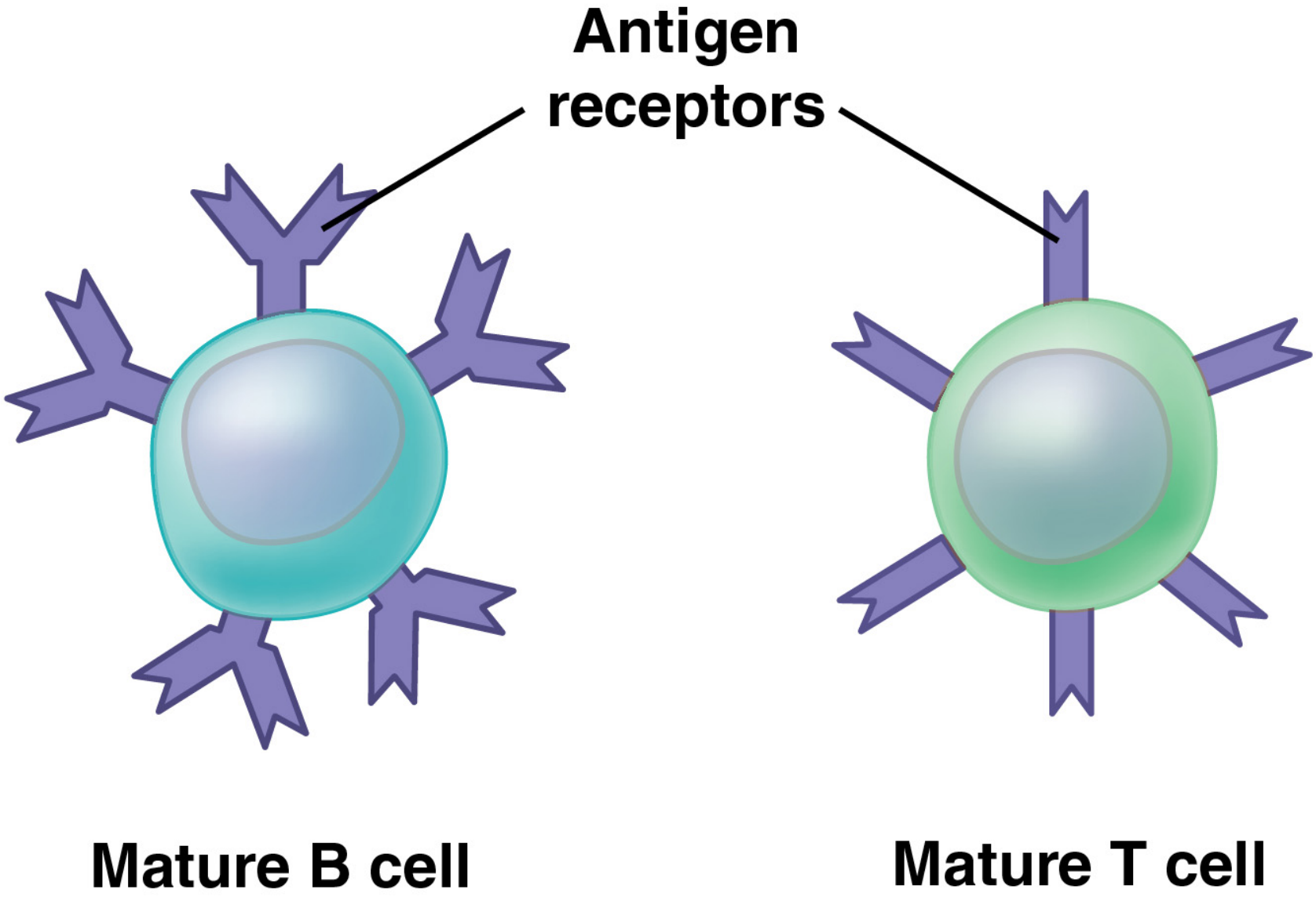
Evasion of Innate Immunity by Pathogens

- Some pathogens avoid destruction because their outer capsule interferes with molecular recognition and phagocytosis
- *Streptococcus pneumoniae* is one such bacterium, a major cause of pneumonia and meningitis in humans
- *Mycobacterium tuberculosis*, can be recognized by the host but resists breakdown
- This organism causes tuberculosis (TB), a disease that kills more than 1 million people per year

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

- Unlike innate immunity, the adaptive response is enhanced by previous exposure to the pathogen
- 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**

Figure 43.8



Antigens as the Trigger for Adaptive Immunity

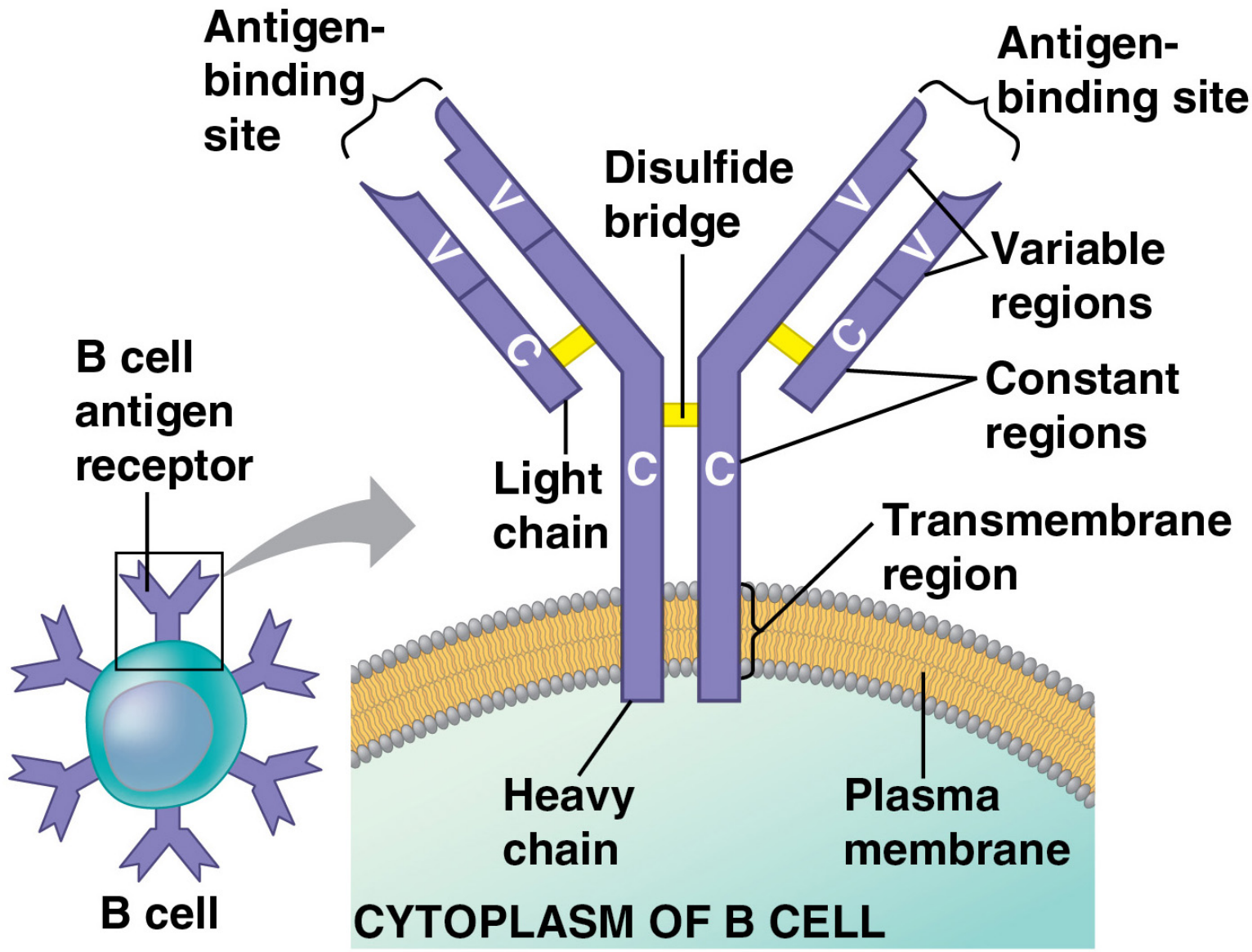
- **Antigens** are substances that can elicit a response from a B or T cell
- T or B cells bind to antigens via **antigen receptors** specific to part of one molecule of that pathogen
- The cells of the immune system produce millions of different antigen receptors
- Antigens are usually foreign, and typically large molecules, either proteins or polysaccharides
- Other antigens are toxins secreted by bacteria

- 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

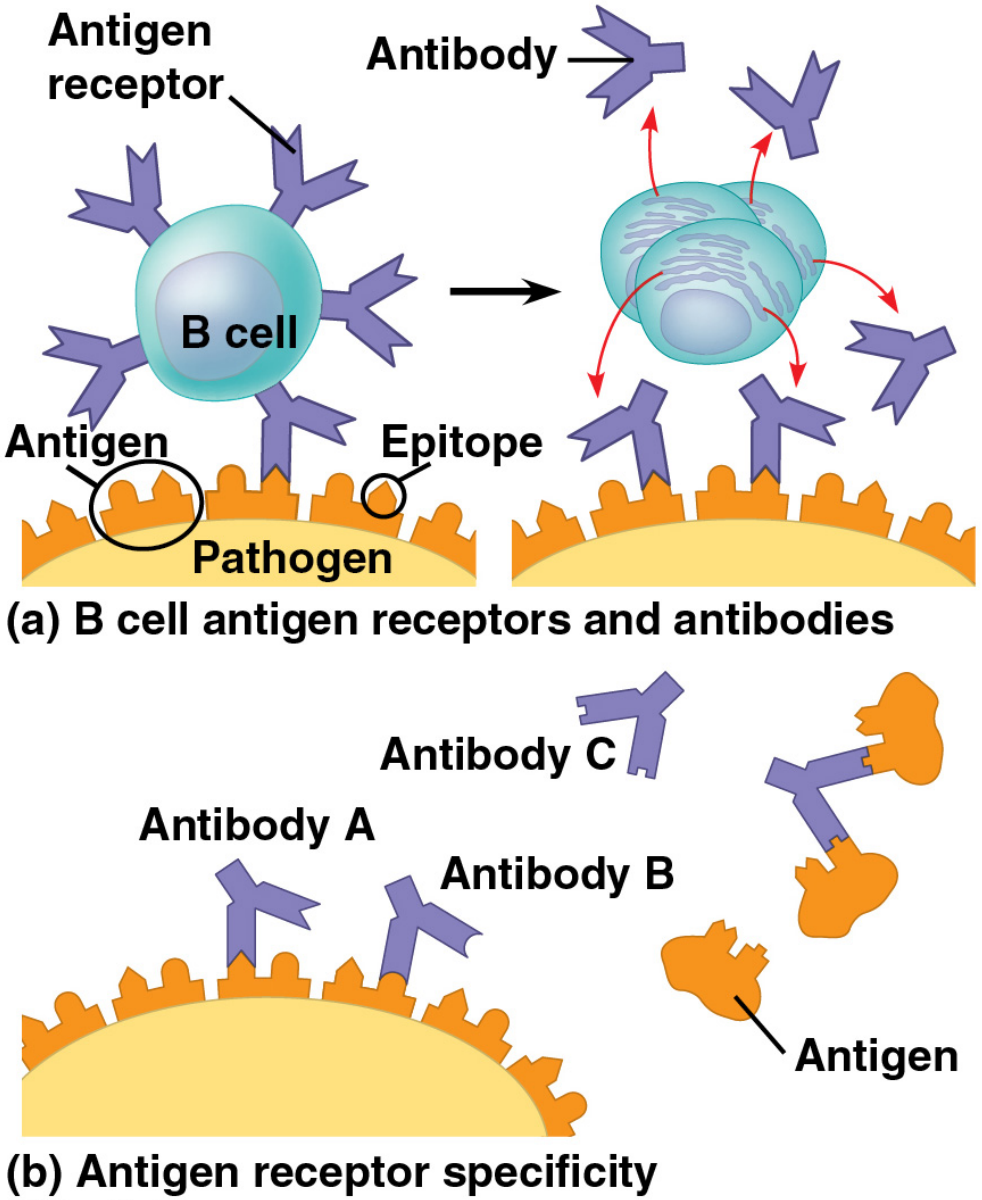
- Each B cell antigen receptor is a Y-shaped molecule with two identical **heavy chains** and two identical **light chains**
- The constant (C) regions of these chains vary little among B cells, whereas the variable (V) regions differ greatly
- The variable regions provide antigen specificity

Figure 43.9


Antigen-binding site
Antigen-binding site
Disulfide bridge
Variable regions
Constant regions
B cell antigen receptor
Light chain
Transmembrane region
Heavy chain
Plasma membrane
B cell
CYTOPLASM OF B CELL
V
V
V
V
C
C
C
C

- 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 receptor called an **antibody** or **immunoglobulin (Ig)**
- Antibodies have the same Y shape as B cell antigen receptors but are secreted, not membrane bound

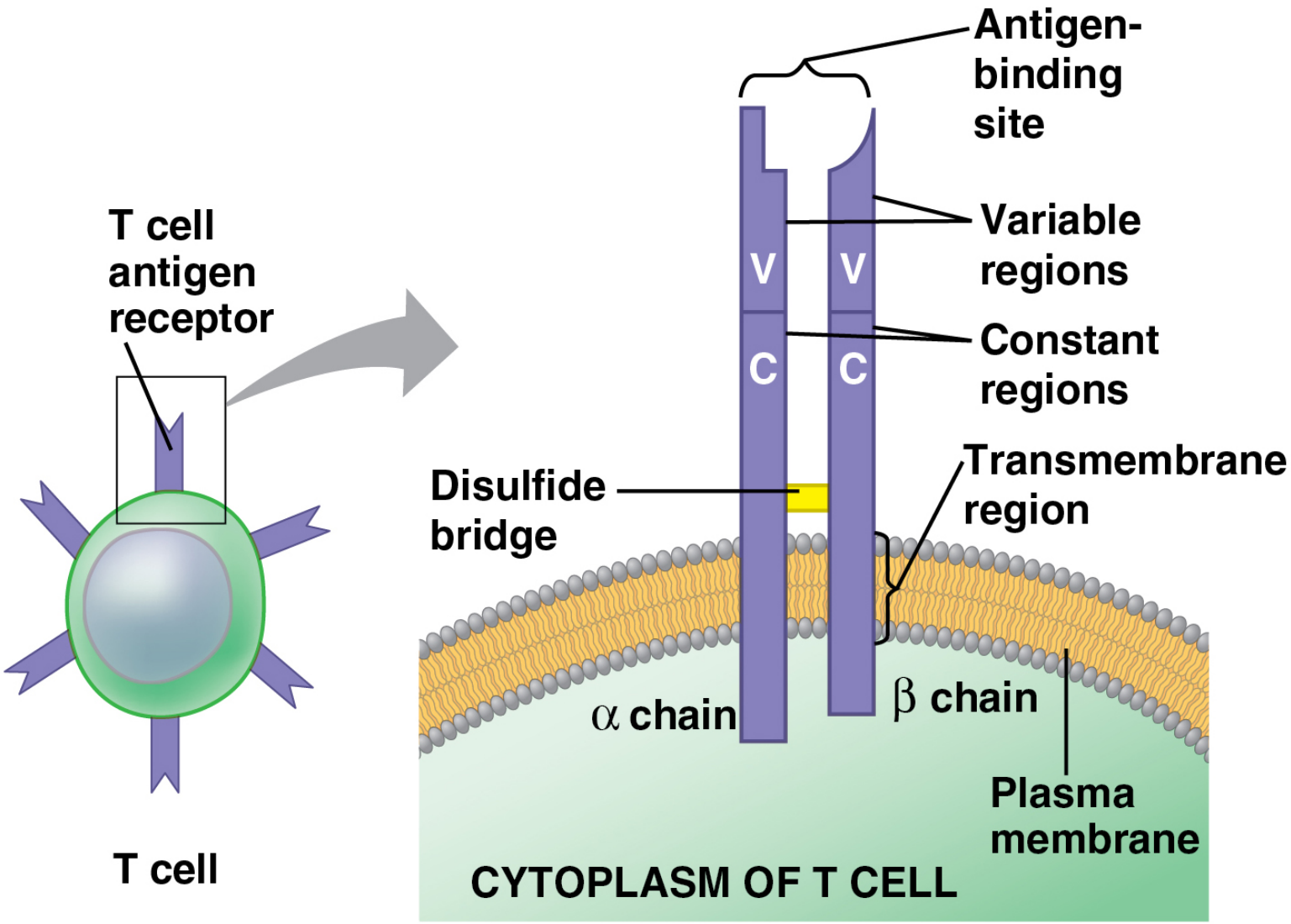
Figure 43.10


Antigen receptor
Antibody
B cell
Antigen
Epitope
Pathogen
(a) B cell antigen receptors and antibodies
Antibody C
Antibody A
Antibody B
Antigen
(b) Antigen receptor specificity

Antigen Recognition by T Cells

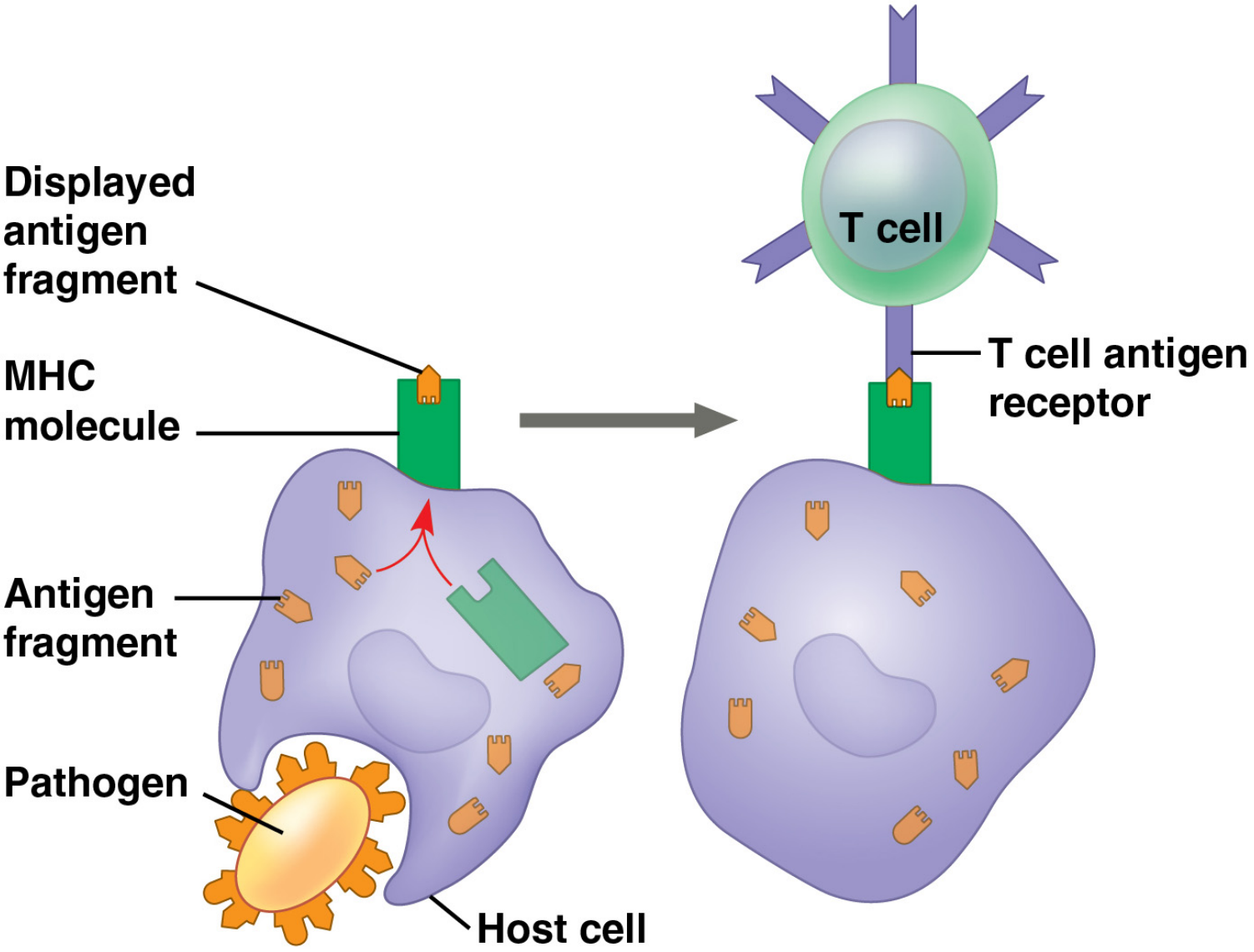
- Each T cell receptor consists of two different polypeptide chains (called α and β)
- The tips of the chain form a variable (V) region
- Here, the α and β chains together form a single antigen-binding site
- The rest is a constant (C) region

Figure 43.11


T cell antigen receptor
T cell
Antigen-binding site
Variable regions
Constant regions
Transmembrane region
Disulfide bridge
V
V
C
C
α chain
β chain
Plasma membrane
CYTOPLASM OF T CELL

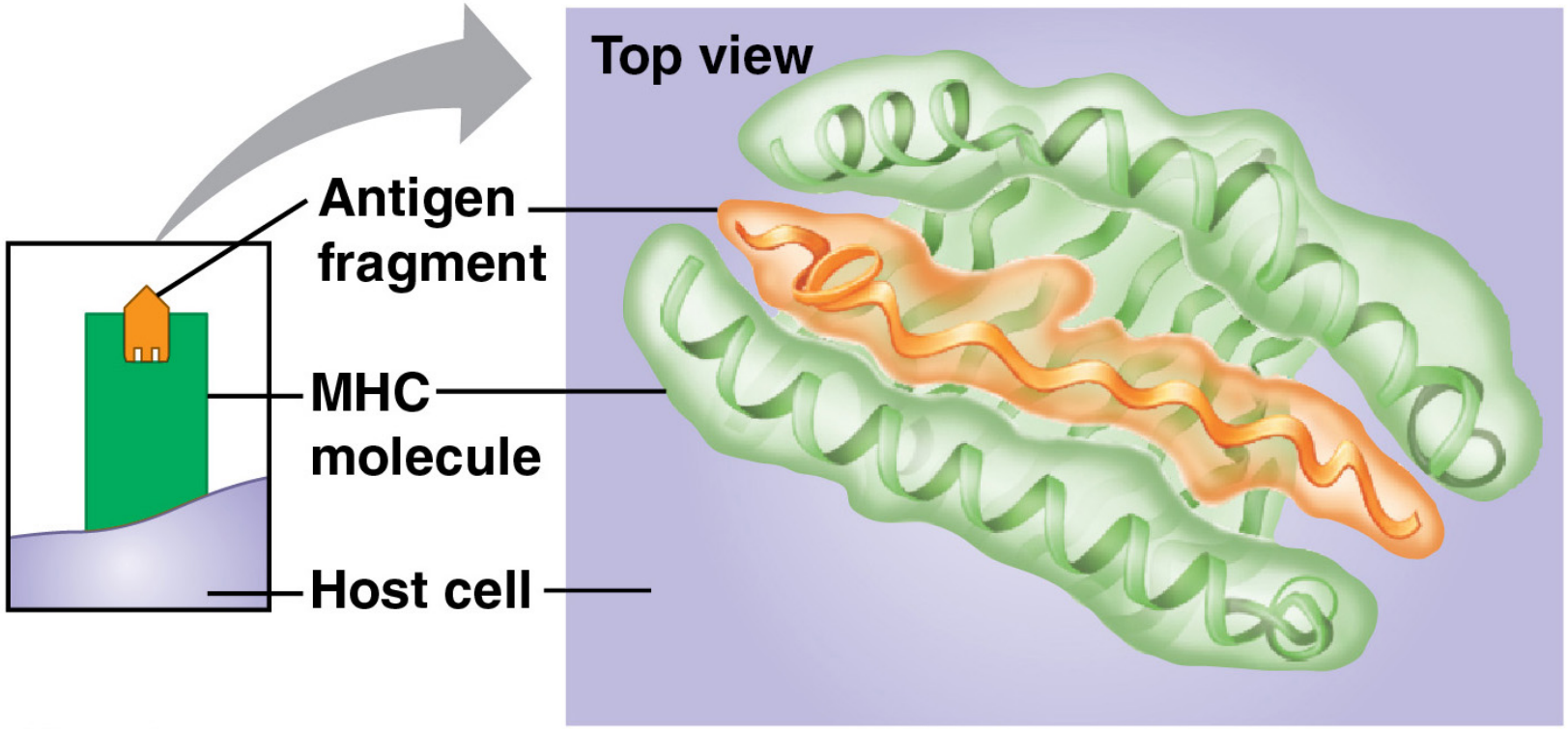
- T cells bind only to antigen fragments displayed or presented on a host cell
- These antigen fragments are bound to cell-surface proteins called **major histocompatibility complex (MHC) molecules**
- MHC molecules are host proteins that display the antigen fragments on the cell surface

Figure 43.12

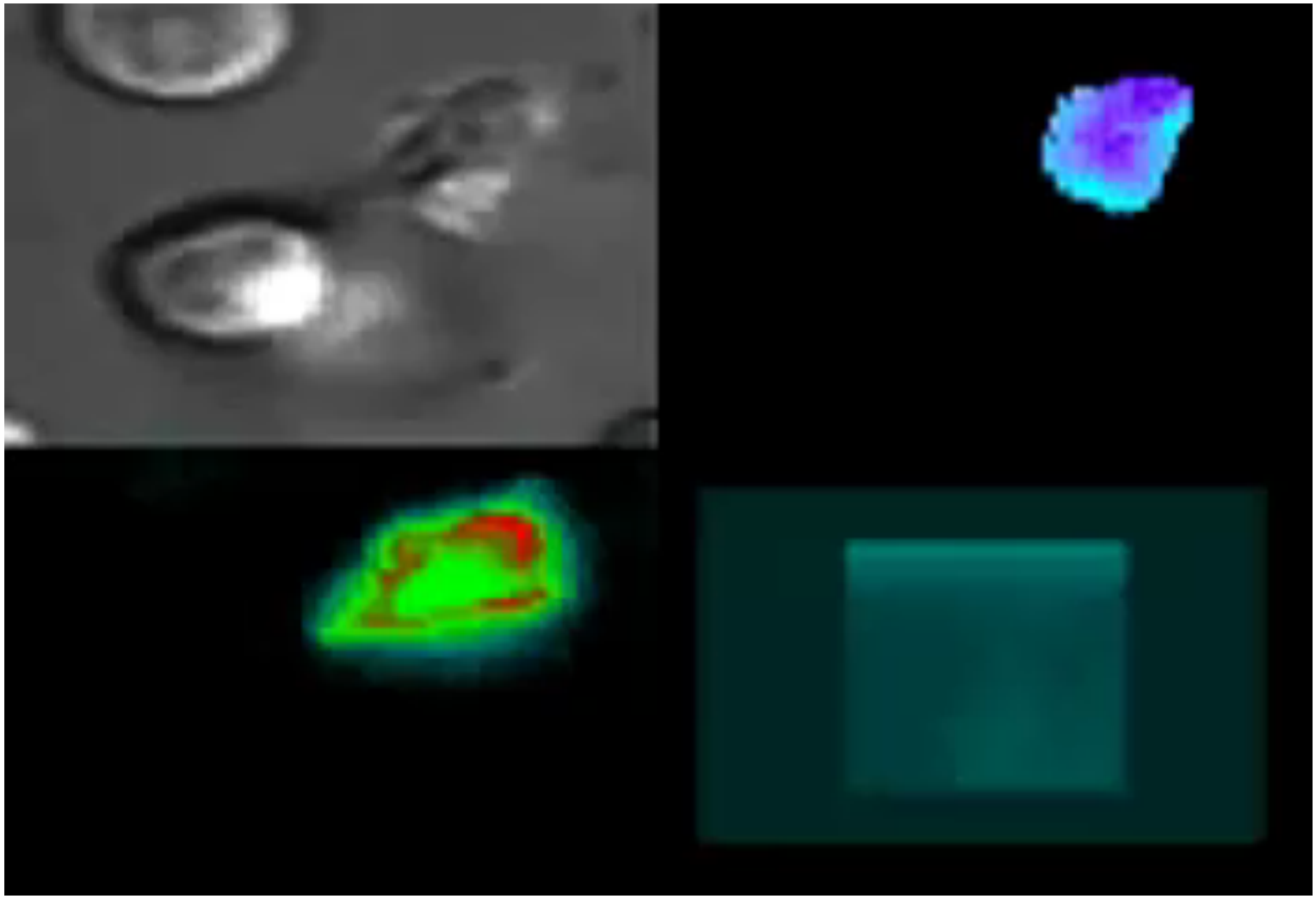

Displayed antigen fragment
MHC molecule
Antigen fragment
Pathogen
Host cell
T cell
T cell antigen receptor

- 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 43.13



Video: T Cell Receptors



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 and cells
  - B and T cells proliferate after activation
  - Immunological memory

The Basis of B Cell and T Cell Diversity

- By combining variable elements, the immune system assembles millions of different antigen receptors from a small number of parts
- An immunoglobulin (Ig) gene encodes the light chain of the B cell receptor
- Many different chains can be produced from the same gene by rearrangement of the *V*, *J*, and *C* regions

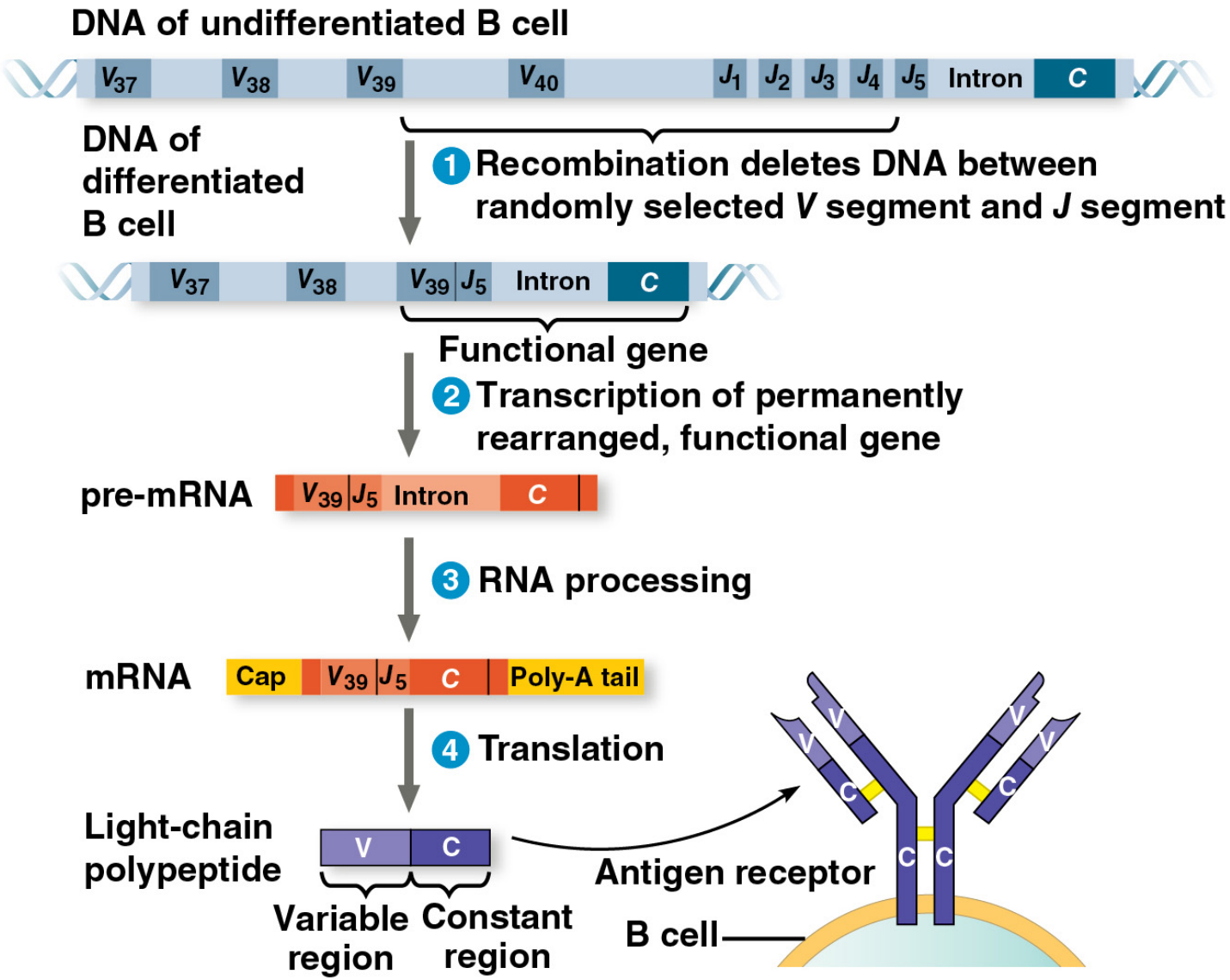
- The capacity to generate diversity is built into the structure of Ig genes
- The light chain is encoded by three segments:
  - A variable (V) segment
  - A joining (J) segment
  - A constant (C) segment
- The V and J segments together encode the variable region of the receptor while the C segment encodes the constant region

- The light chain gene contains a single C segment
- It has 40 different V segments and 5 different J segments
- The pieces can be combined in 200 different ways
- The number of heavy chain combinations is greater, resulting in more diversity

Antigen Receptor Gene Rearrangement

- Assembling a functional Ig gene requires rearrangement of the DNA
- And enzyme complex called recombinase acts randomly to connect different *V* and *J* segments in each B cell
- Light and heavy chain genes both undergo these rearrangements
- In any given cell there is only one allele of a light-chain gene and only one allele of a heavy-chain gene

Figure 43.14


DNA of undifferentiated B cell
V37
V38
V39
V40
J1
J2
J3
J4
J5
Intron
C
DNA of differentiated B cell
1 Recombination deletes DNA between randomly selected V segment and J segment
V37
V38
V39
J5
Intron
C
Functional gene
2 Transcription of permanently rearranged, functional gene
pre-mRNA
V39
J5
Intron
C
3 RNA processing
mRNA
Cap
V39
J5
C
Poly-A tail
4 Translation
Light-chain polypeptide
V
C
Variable region
Constant region
Antigen receptor
B cell

- The Ig gene rearrangements are permanent and passed on to daughter cells when the lymphocyte divides
- The rearranged genes are transcribed and translated to produce unique antigen receptors
- There are millions of different arrangements possible among humans
- Mutations introduced during VJ recombination contribute even more diversity

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, leaving only lymphocytes that react to foreign molecules

Proliferation of B Cells and T Cells

- In the body there are few lymphocytes with antigen receptors specific 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 bearing the receptor

- 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 **effector cells** that act immediately against the antigen
- Effector cells are plasma cells that secrete antibodies
- The remaining cells in the clone become long-lived **memory cells** that can give rise to effector cells if the same antigen is encountered again

Figure 43.15

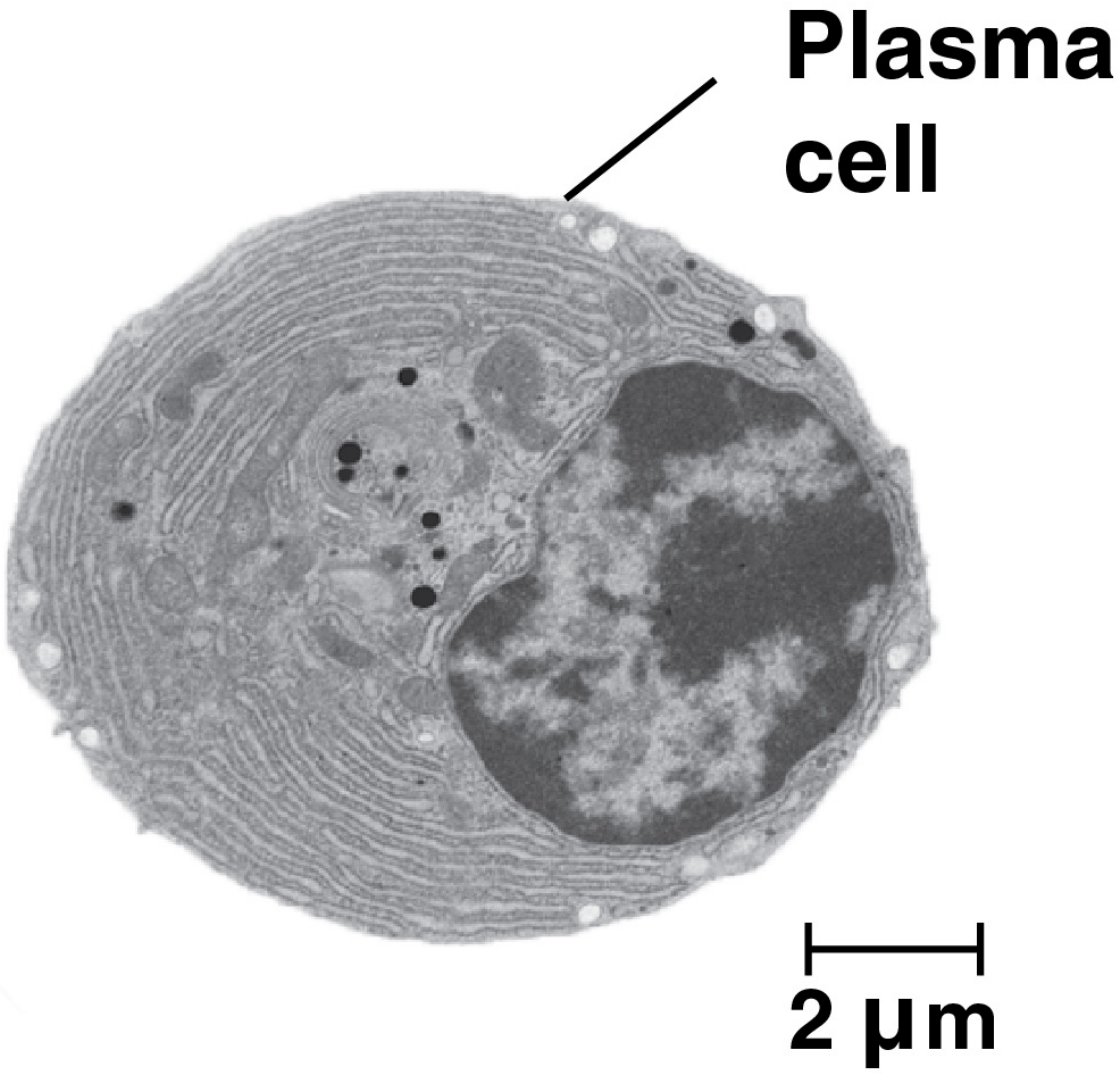
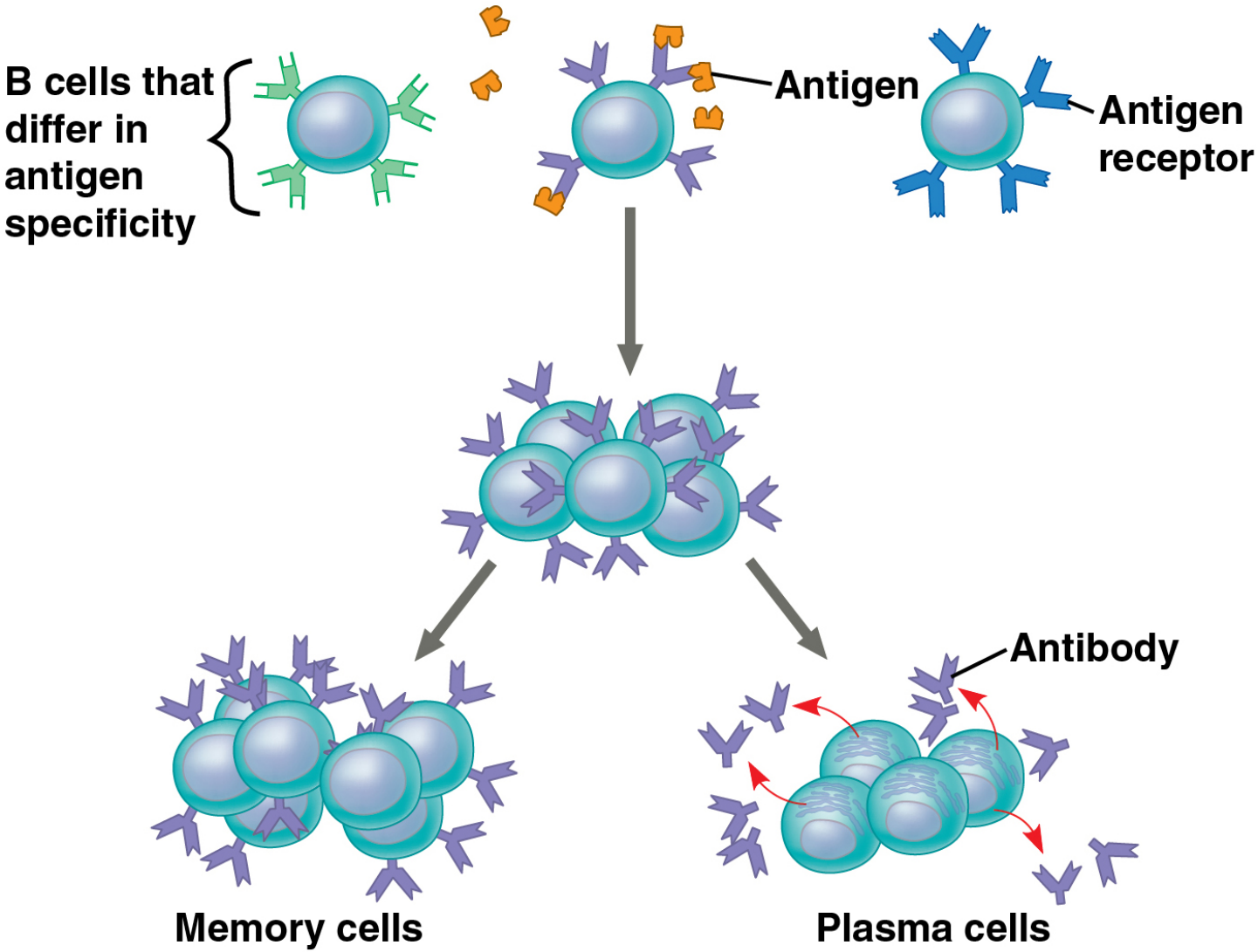


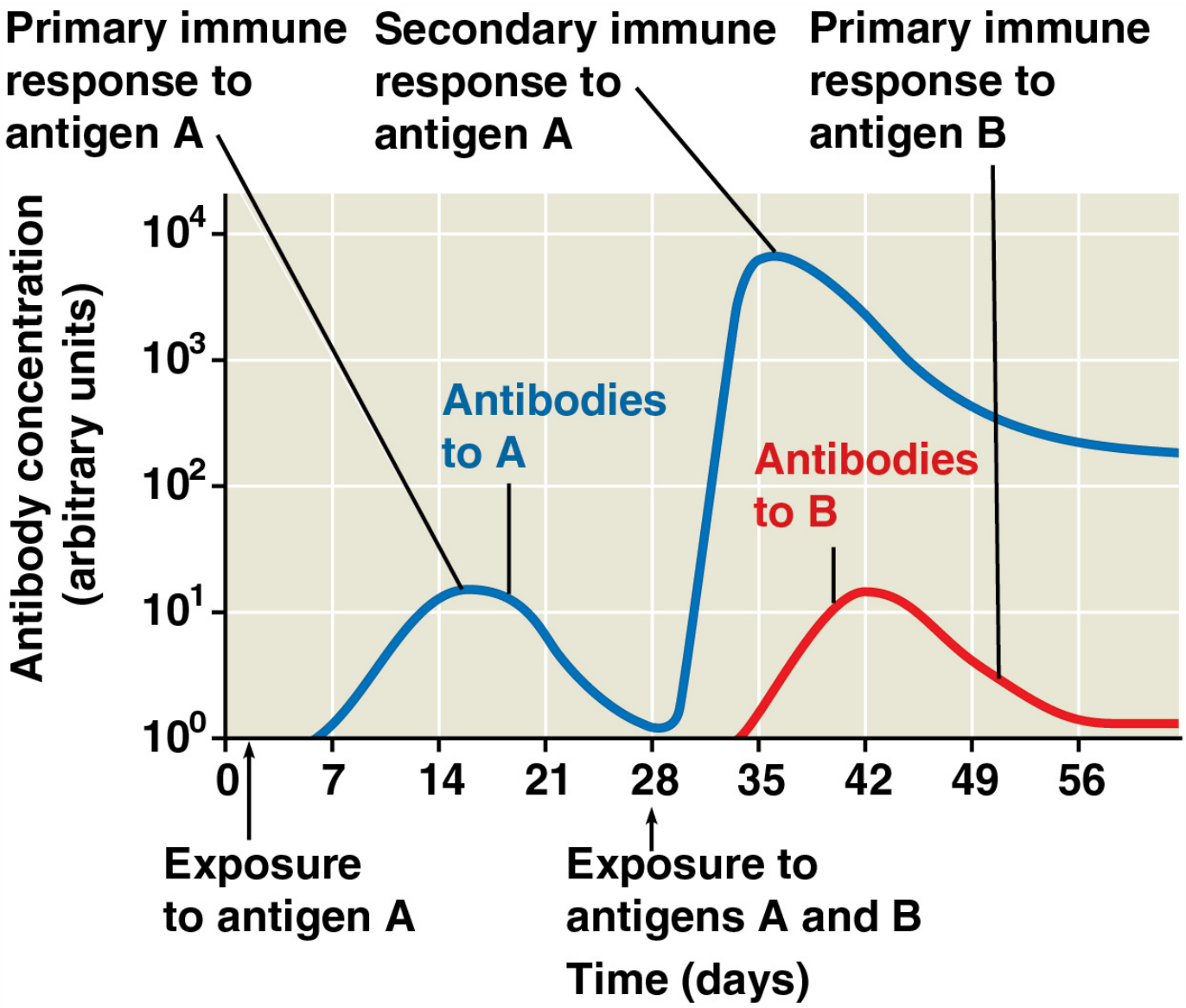
Figure 43.16


B cells that differ in antigen specificity
Antigen
Antigen receptor
Antibody
Memory cells
Plasma 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**
- A clone of lymphocytes is formed that are specific to the pathogen
- In the **secondary immune response**, memory cells facilitate a faster, greater, and more prolonged response from a reservoir of T and B memory cells

Figure 43.17


Primary immune response to antigen A
Secondary immune response to antigen A
Primary immune response to antigen B
Antibody concentration (arbitrary units)
10^4
10^3
10^2
10^1
10^0
Antibodies to A
Antibodies to B
0
7
14
21
28
35
42
49
56
Exposure to antigen A
Exposure to antigens A and B
Time (days)

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

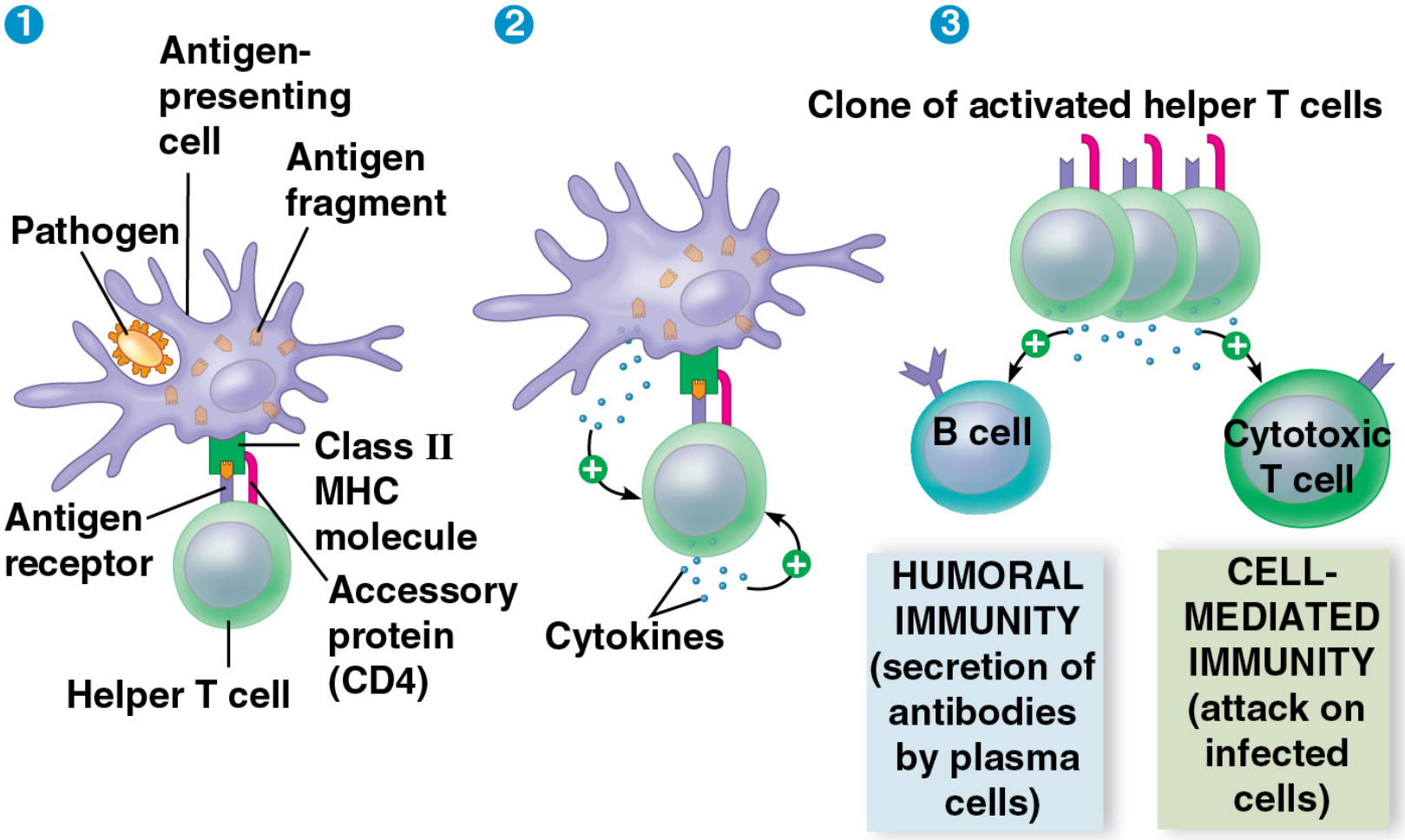
- The defenses provided by B and T lymphocytes can be divided into the humoral immune response and the cell-mediated immune response
- In the **humoral immune response**, antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph
- In the **cell-mediated immune response**, specialized T cells destroy infected host cells

Helper T Cells: Activating Adaptive Immunity

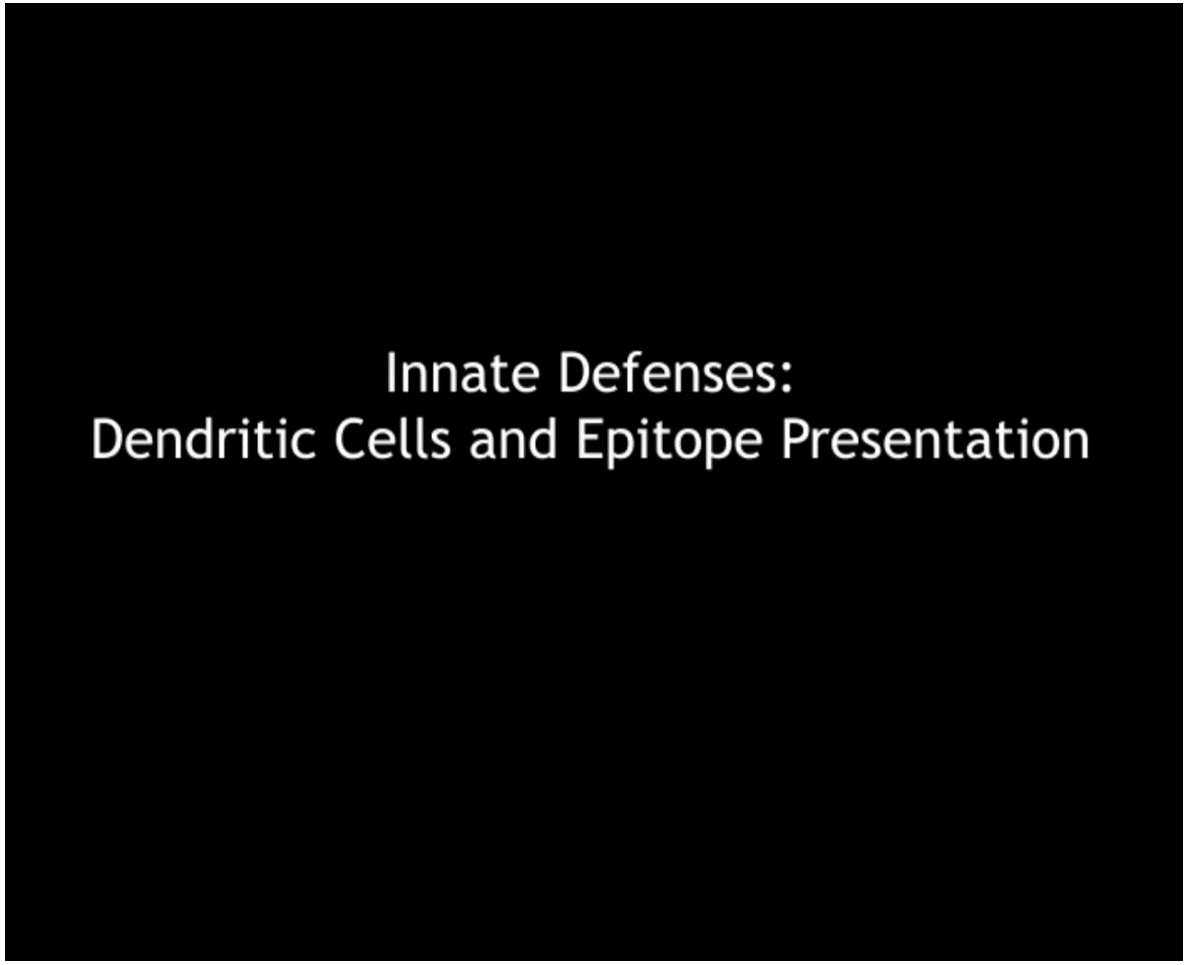
- A type of T cell called a **helper T cell** activates both the humoral and cell-mediated immune responses
- This requires the presence of a foreign molecule that can bind the antigen receptor on the helper T cell
- And, the antigen must be displayed on the surface of an **antigen-presenting cell**
- Antigen-presenting cells have class I and II MHC molecules on their surfaces

- Class II MHC molecules provide a molecular signature by 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 cytokine signals are exchanged between the two cells
- The helper T cell is stimulated to produce its own set of cytokines

Figure 43.18


1
Antigen-presenting cell
Antigen fragment
Pathogen
Class II MHC molecule
Antigen receptor
Accessory protein (CD4)
Helper T cell
2
Cytokines
3
Clone of activated helper T cells
B cell
Cytotoxic T cell
HUMORAL IMMUNITY (secretion of antibodies by plasma cells)
CELL-MEDIATED IMMUNITY (attack on infected cells)

BioFlix® Animation: Activation of a Helper T Cell by a Dendritic Cell



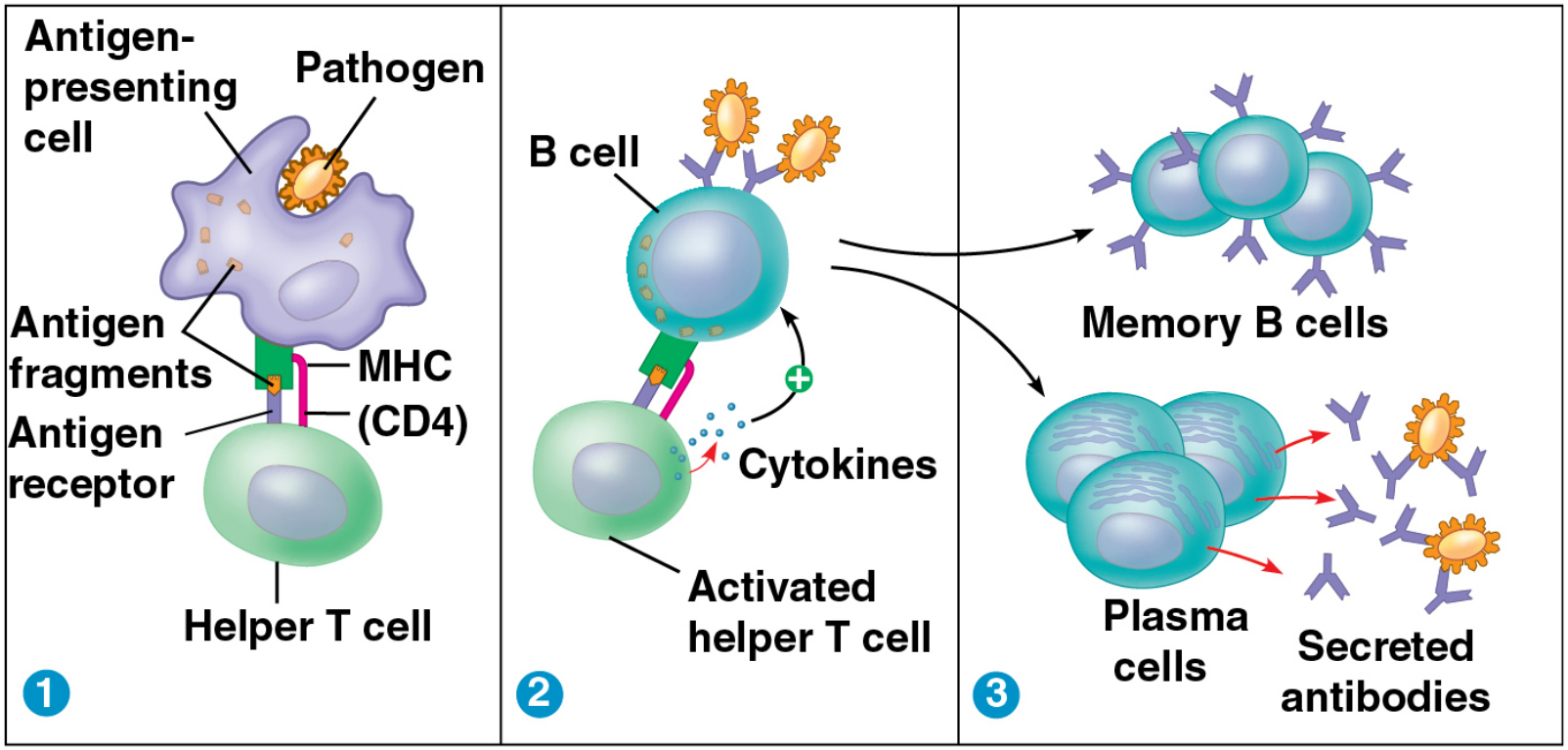
B Cells and Antibodies: A Response to Extracellular Pathogens

- The humoral response is characterized by secretion of antibodies by clonally selected B cells
- It begins with activation of the B cells

Activation of B Cells

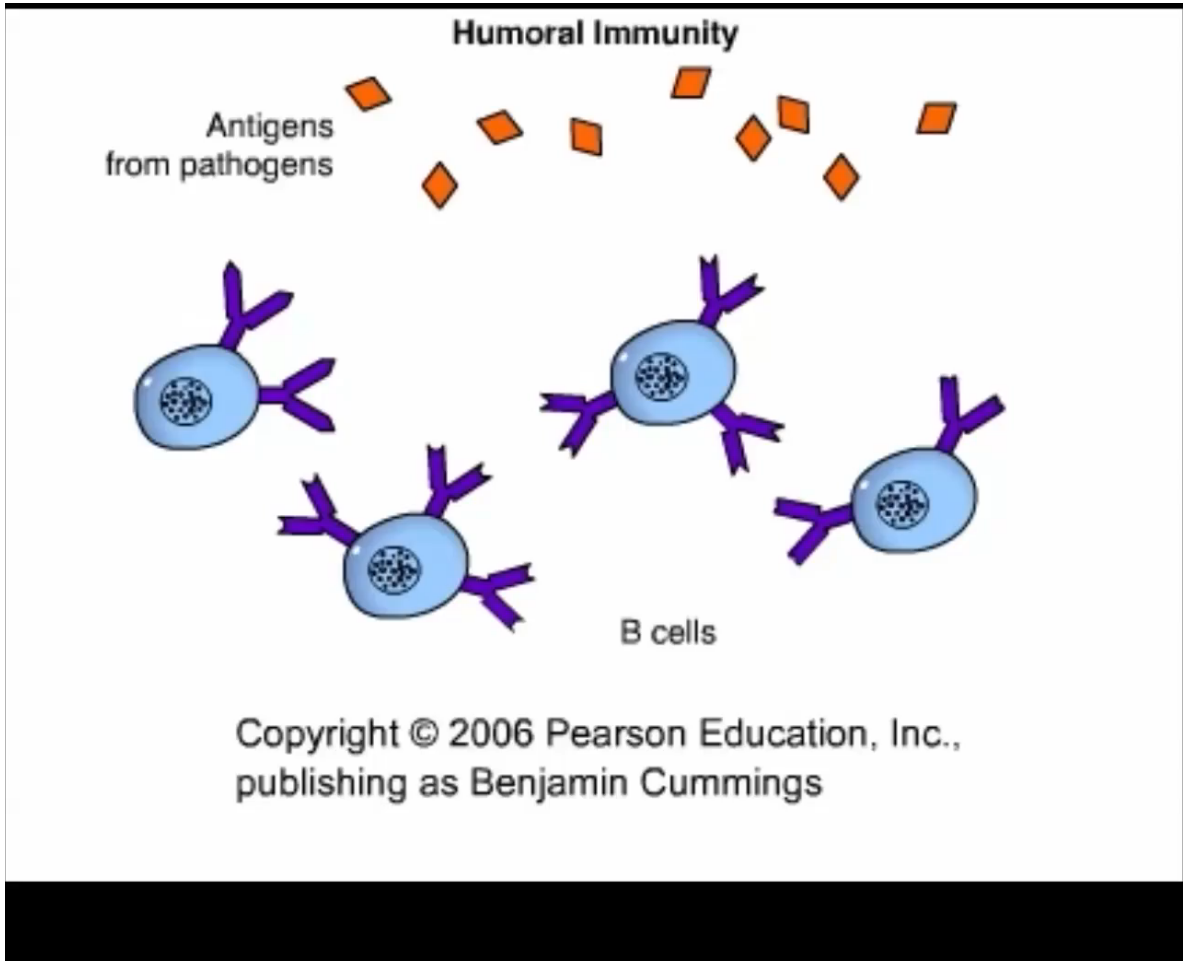
- Activation of B cells involves helper T cells and proteins on the surface of pathogens
- When an antigen binds a B cell, the cell takes in a few foreign molecules by receptor-mediated endocytosis
- The class II MHC protein of the B cell then presents an antigen fragment to a helper T cell, a process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

Figure 43.19


Antigen-presenting cell
Pathogen
Antigen fragments
MHC (CD4)
Antigen receptor
Helper T cell
1
B cell
Cytokines
Activated helper T cell
2
Memory B cells
Plasma cells
Secreted antibodies
3

- 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

Animation: Role of B Cells in Humoral Immunity

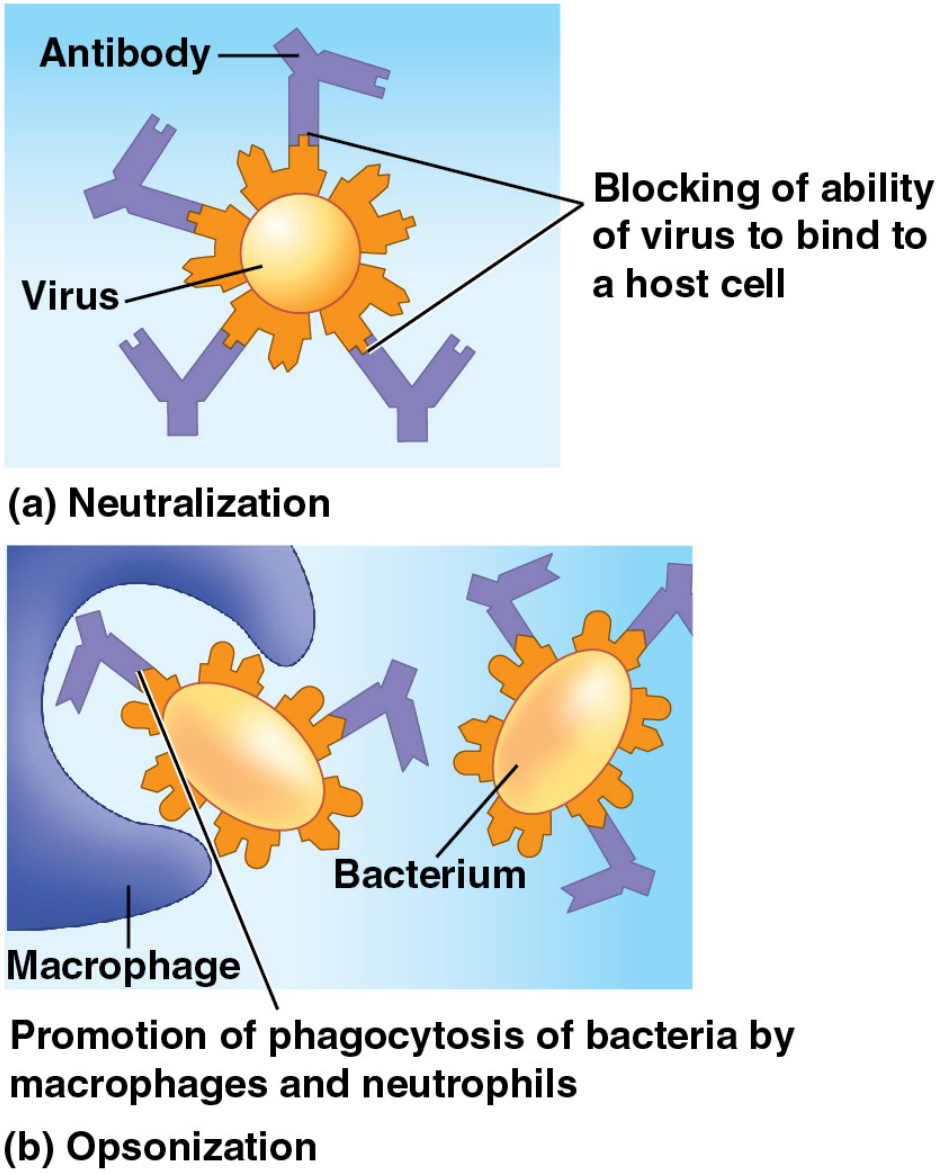


Antibody Function

- Antibodies do not kill pathogens; instead, they mark pathogens for inactivation or 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

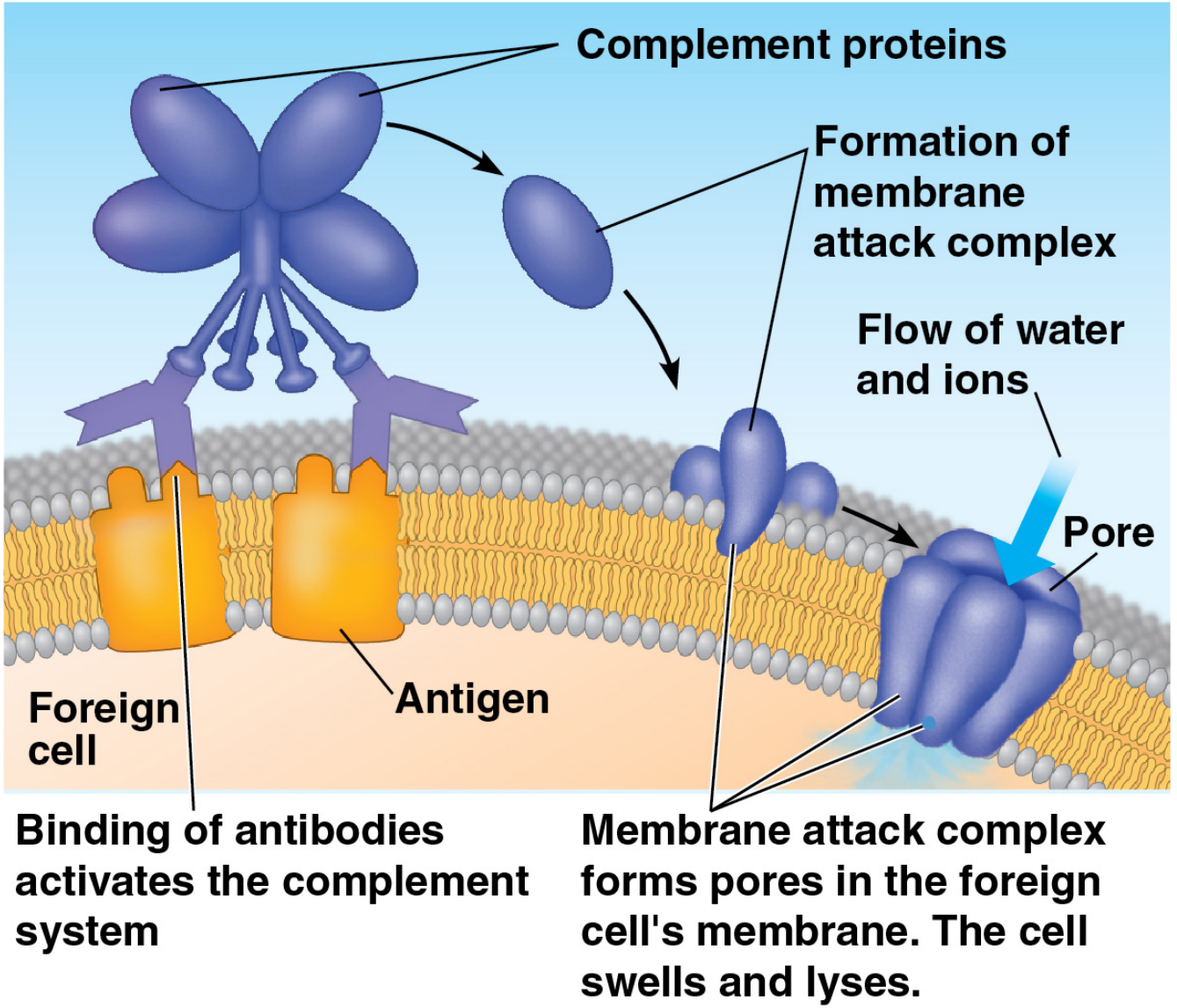
- In *opsonization*, antibodies bind to antigens on bacteria, promoting phagocytosis
- When antibodies facilitate phagocytosis, they also help fine-tune the humoral immune response
- Positive feedback between the innate and adaptive immunity contributes to a coordinated, effective response to infection

Figure 43.20


Antibody
Virus
Blocking of ability of virus to bind to a host cell
(a) Neutralization
Bacterium
Macrophage
Promotion of phagocytosis of bacteria by macrophages and neutrophils
(b) Opsonization

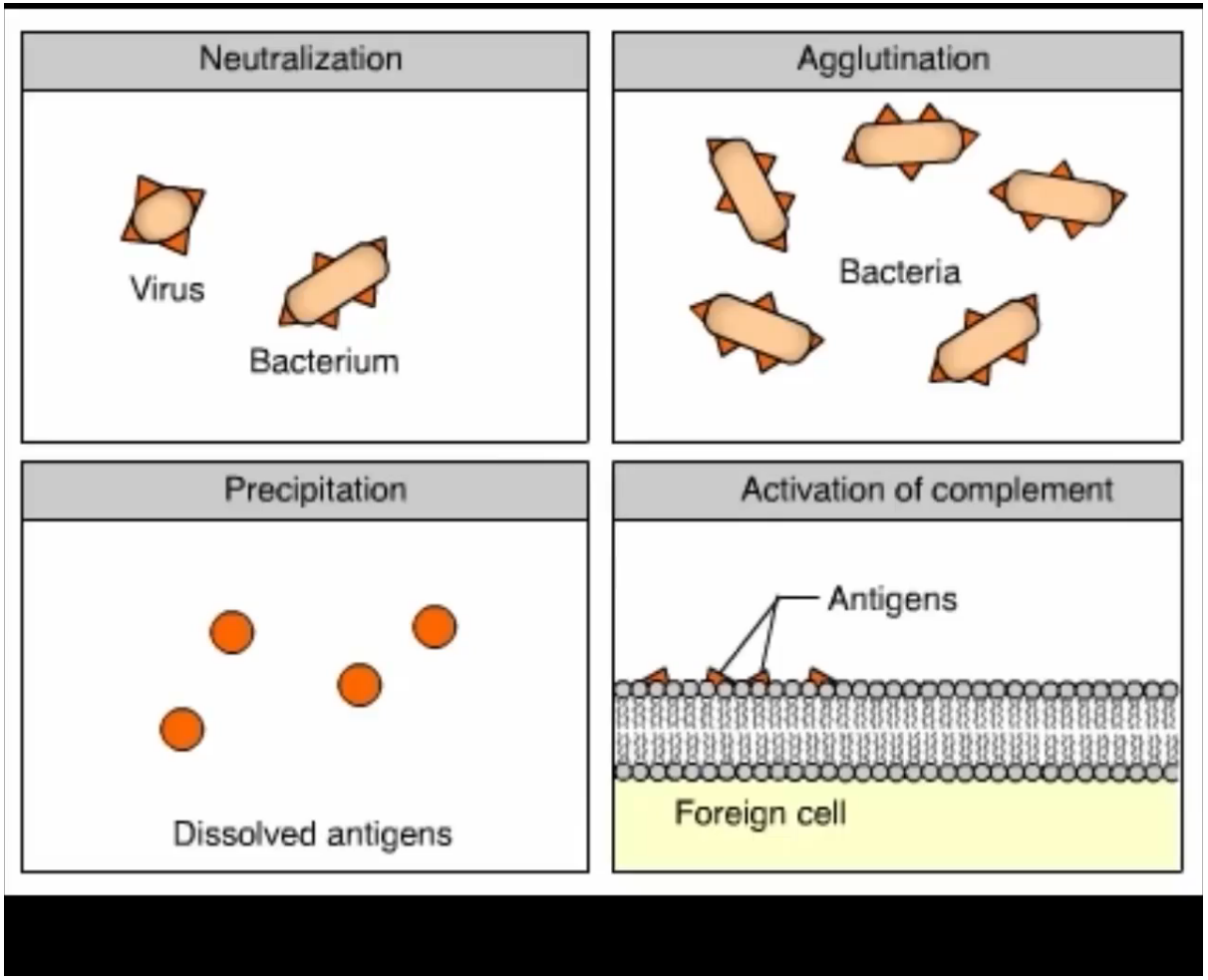
- Antibodies may work with the proteins of the complement system
- Binding of a complement protein to an antigen-antibody complex on a foreign cell leads to formation of a pore in the membrane of the cell
- Water and ions rush into the cell, causing swelling and lysis

Figure 43.21


Complement proteins
Formation of membrane attack complex
Flow of water and ions
Pore
Foreign cell
Antigen
Binding of antibodies activates the complement system
Membrane attack complex forms pores in the foreign cell's membrane. The cell swells and lyses.

- 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

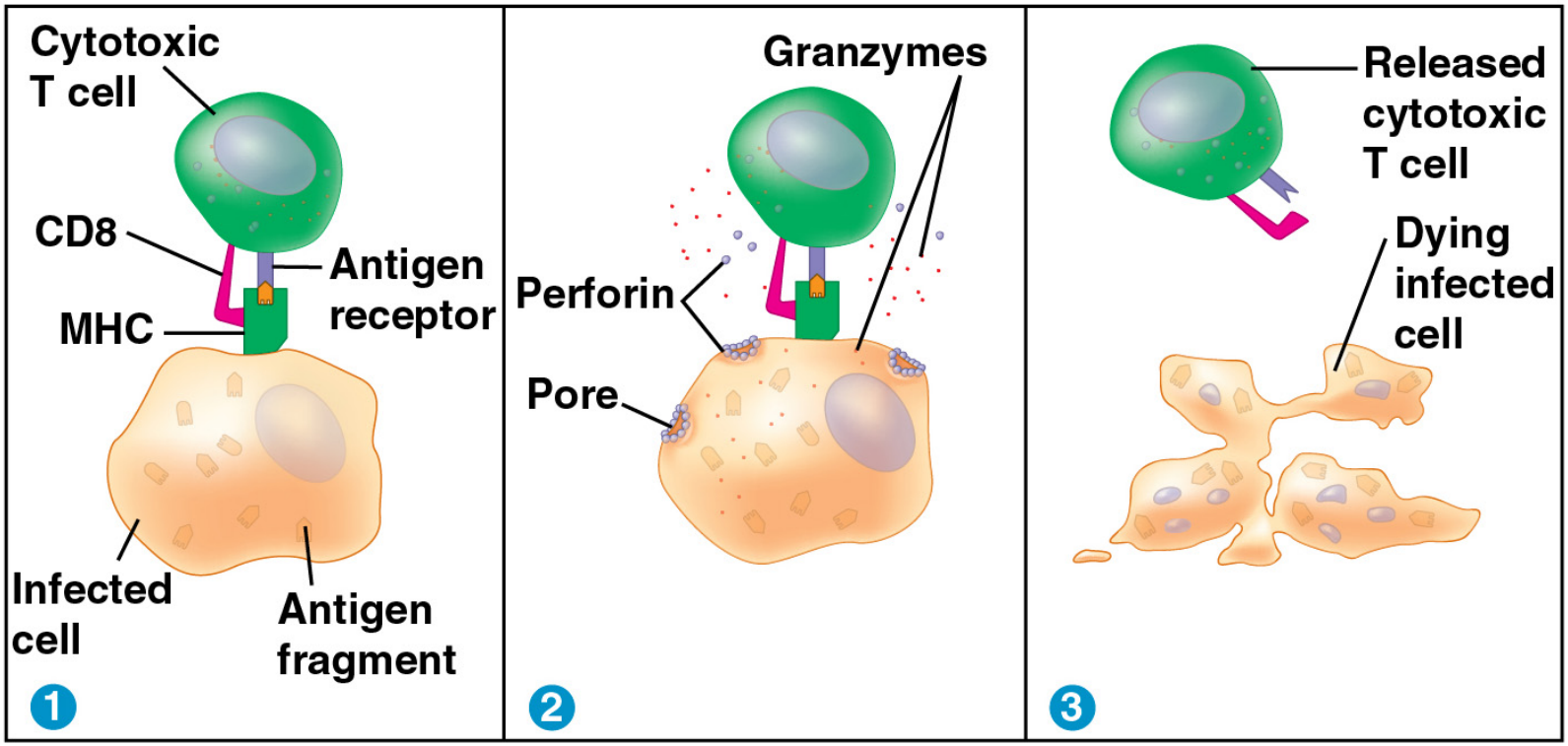
Animation: Antibodies



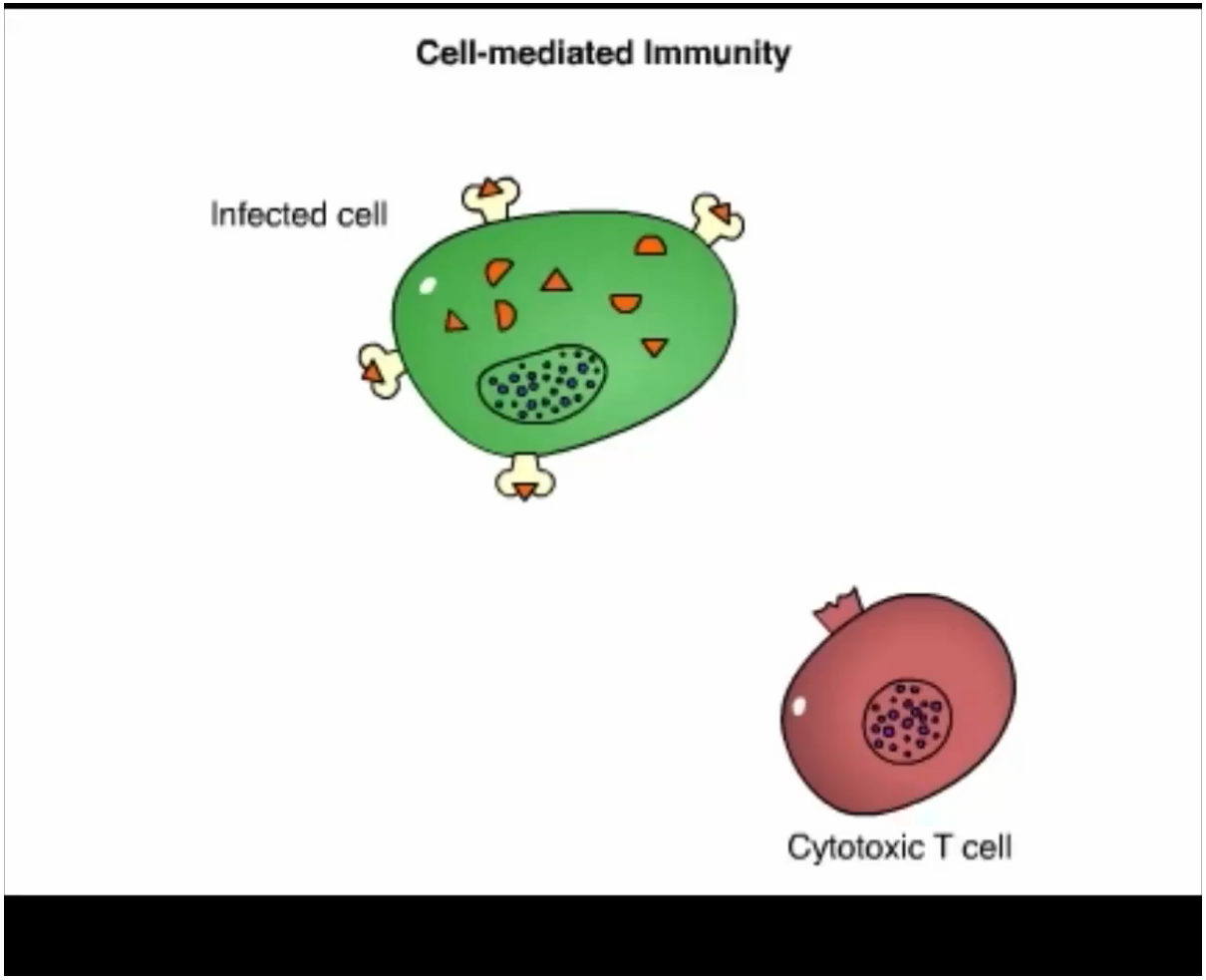
Cytotoxic T Cells: A Response to Infected Host Cells

- **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 43.22


Cytotoxic T cell
CD8
Antigen receptor
MHC
Infected cell
Antigen fragment
1
Granzymes
Perforin
Pore
2
Released cytotoxic T cell
Dying infected cell
3

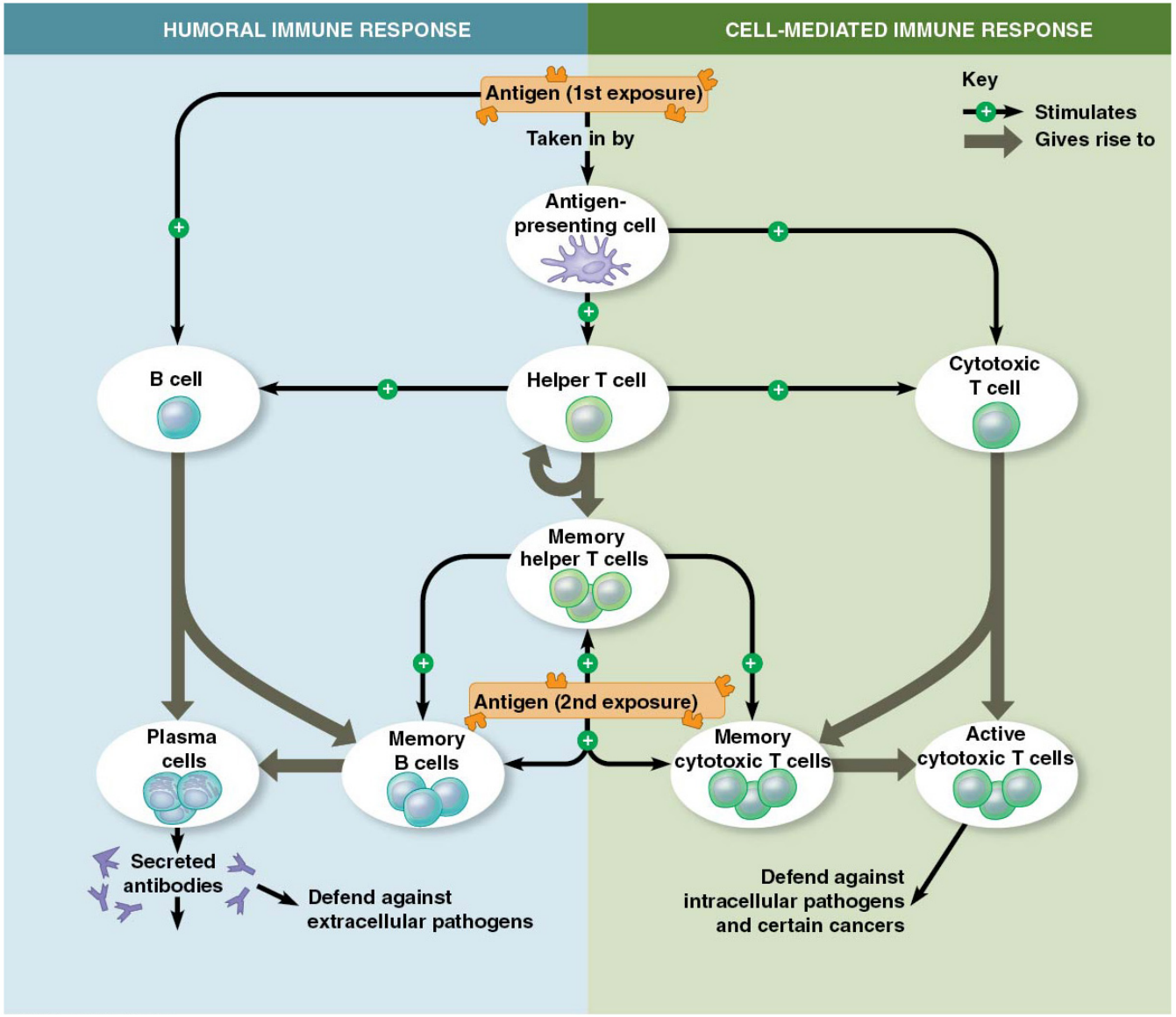
BioFlix® Animation: Adaptive Defenses: Cytotoxic T Cells



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 of each type enable the secondary response

Figure 43.23

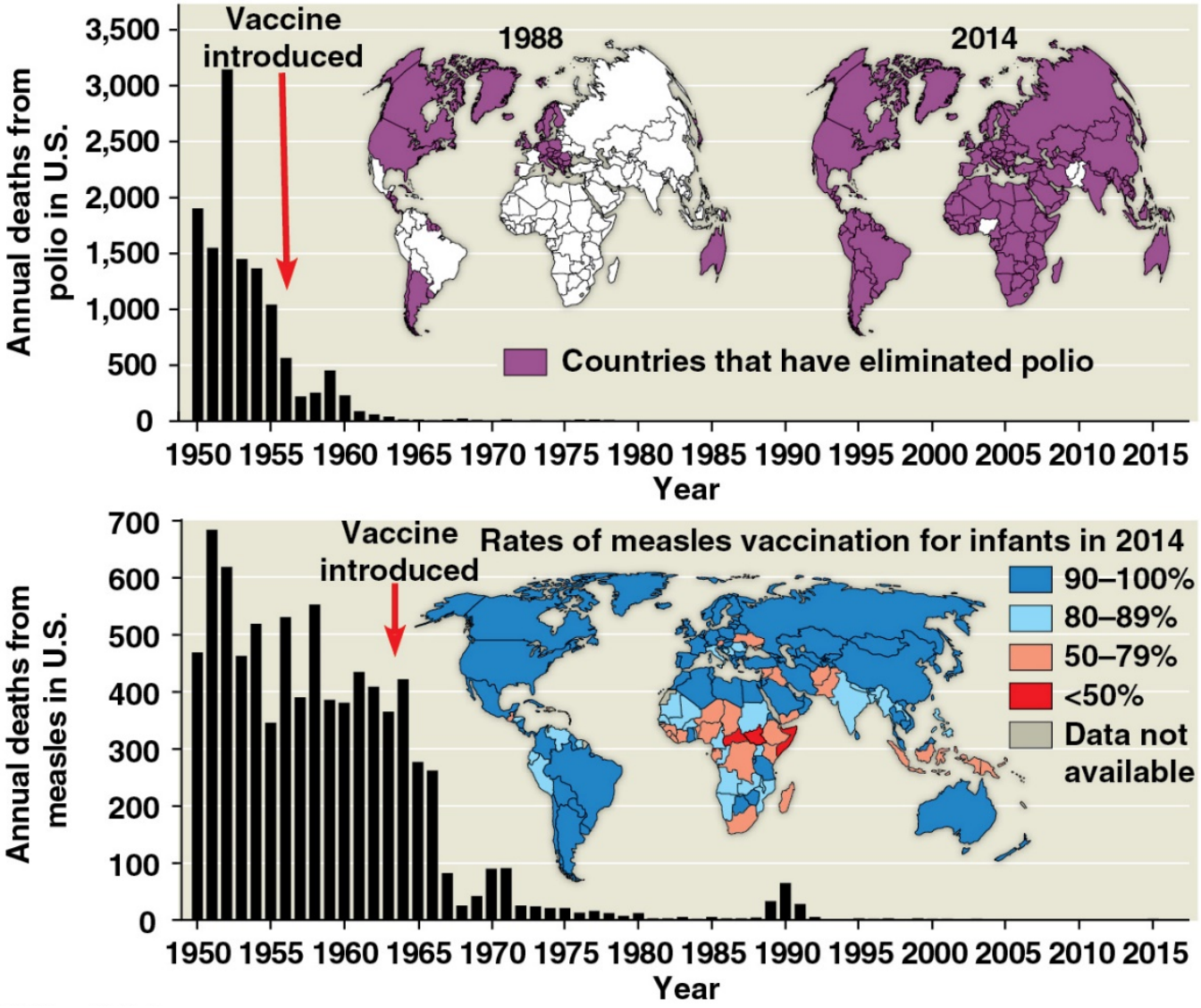

HUMORAL IMMUNE RESPONSE
CELL-MEDIATED IMMUNE RESPONSE
Key
Stimulates
Gives rise to
Antigen (1st exposure)
Taken in by
Antigen-presenting cell
B cell
Helper T cell
Cytotoxic T cell
Memory helper T cells
Antigen (2nd exposure)
Plasma cells
Memory B cells
Memory cytotoxic T cells
Active cytotoxic T cells
Secreted antibodies
Defend against extracellular pathogens
Defend against intracellular pathogens and certain cancers

Immunization

- The protection provided by a second immune response provides the basis for **immunization**
- Antigens are artificially introduced into the body to generate adaptive immune response and memory cell formation
- Vaccines used today for immunization are made with inactivated bacterial toxins, killed or weakened pathogens, or even genes encoding microbial proteins

- Vaccination programs have been successful against many infectious diseases
- Not all pathogens are easily managed by vaccination and some vaccines are not readily available in impoverished areas
- Misinformation about vaccine safety has led to a growing public health problem

Figure 43.24


Vaccine introduced
1988
2014
Annual deaths from polio in U.S.
3,500
3,000
2,500
2,000
1,500
1,000
500
0
Countries that have eliminated polio
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015
Year
Vaccine introduced
Rates of measles vaccination for infants in 2014
90–100%
80–89%
50–79%
<50%
Data not available
Annual deaths from measles in U.S.
700
600
500
400
300
200
100
0
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015
Year

Active and Passive Immunity

- **Active immunity** develops naturally when 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

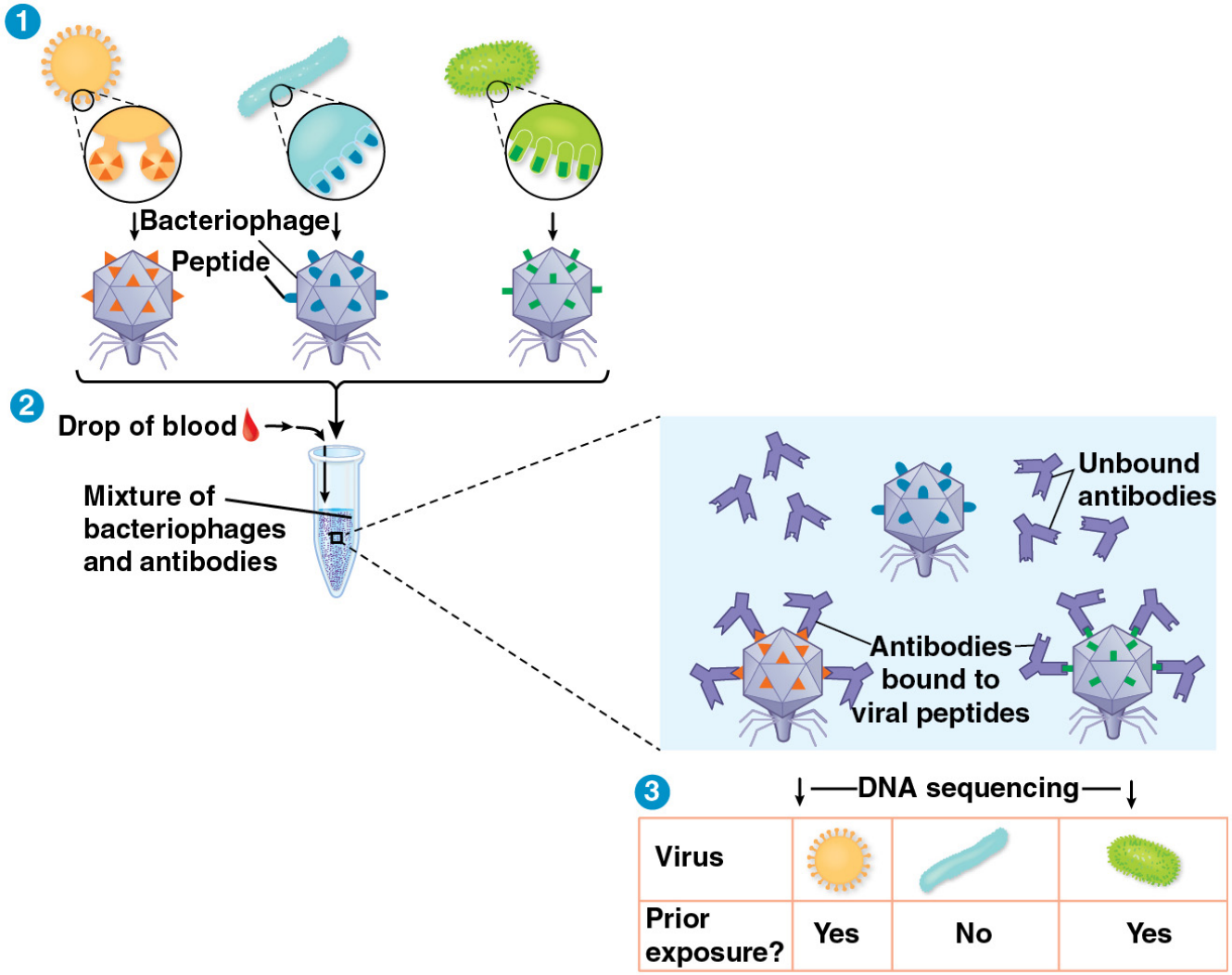
- In artificial passive immunization, antibodies from an immune animal are injected into a nonimmune animal
- For example humans bitten by venomous snakes are sometimes treated with antivenin
- This is serum from sheep or horses immunized against snake venom
- Antibodies in antivenin can neutralize toxins in the snake venom

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 the same epitope
- Monoclonal antibodies are used in many types of medical diagnoses and treatments

- Home pregnancy kits use monoclonal antibodies to detect human chorionic gonadotropin (hCG)
- This hormone is a reliable indicator of early pregnancy
- Monoclonal antibodies are used as therapies for some cancers
- They can also be used to identify every virus a person has encountered, either through infection or immunization

Figure 43.25


1
Bacteriophage
Peptide
2
Drop of blood
Mixture of bacteriophages and antibodies
Unbound antibodies
Antibodies bound to viral peptides
3
DNA sequencing
Virus
Prior exposure?
Yes
No
Yes

Immune Rejection

- Cells transferred from one person to another can be attacked by immune defenses
- This complicates the transplantation of tissues or organs
- To minimize rejection of a transplant or graft, surgeons use donor tissue with MHC molecules as similar as possible to those of the recipient
- In addition, the recipient takes medicines that suppress immune responses

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 can lead to lysis of the introduced cells, and chills, fever, shock, and perhaps kidney malfunction

CONCEPT 43.4: Disruptions in immune system function can elicit or exacerbate disease

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

Exaggerated, Self-Directed, and Diminished Immune Responses

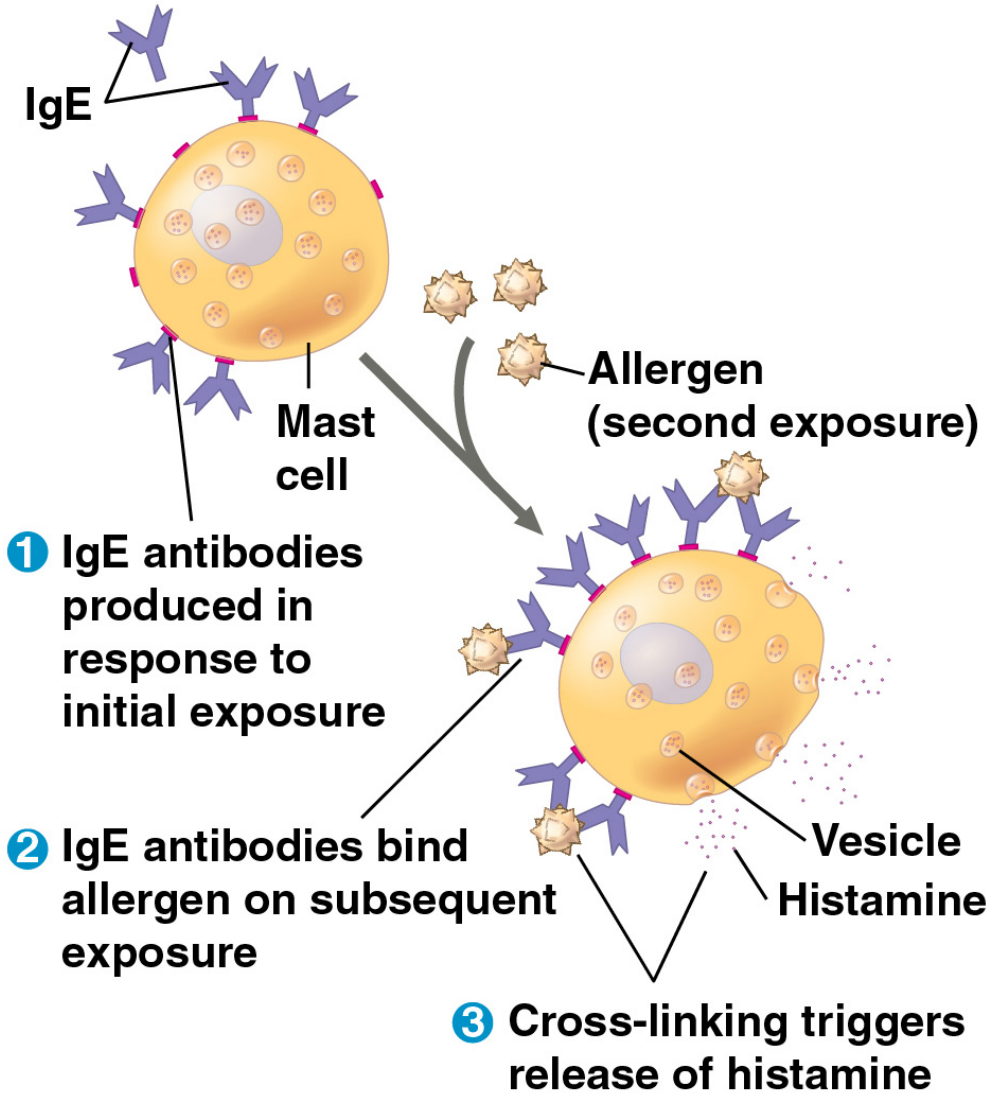
- When allergic, autoimmune, or immunodeficiency disorders disrupt the delicate balance of immune responses, the effects can be severe

Allergies

- Allergies are exaggerated (hypersensitive) responses to antigens called allergens
- Hay fever occurs when plasma cells secrete IgE antibodies specific for antigens on the surface of pollen grains
- The next time pollen grains enter the body, they bind the IgE antibodies and induce mast cells to release histamine and other inflammatory chemicals

- Typical allergy symptoms include: sneezing, runny nose, teary eyes, and smooth muscle contractions in the lungs
- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction, within seconds of allergen exposure
- An injection of epinephrine can rapidly counteract the allergic response

Figure 43.26

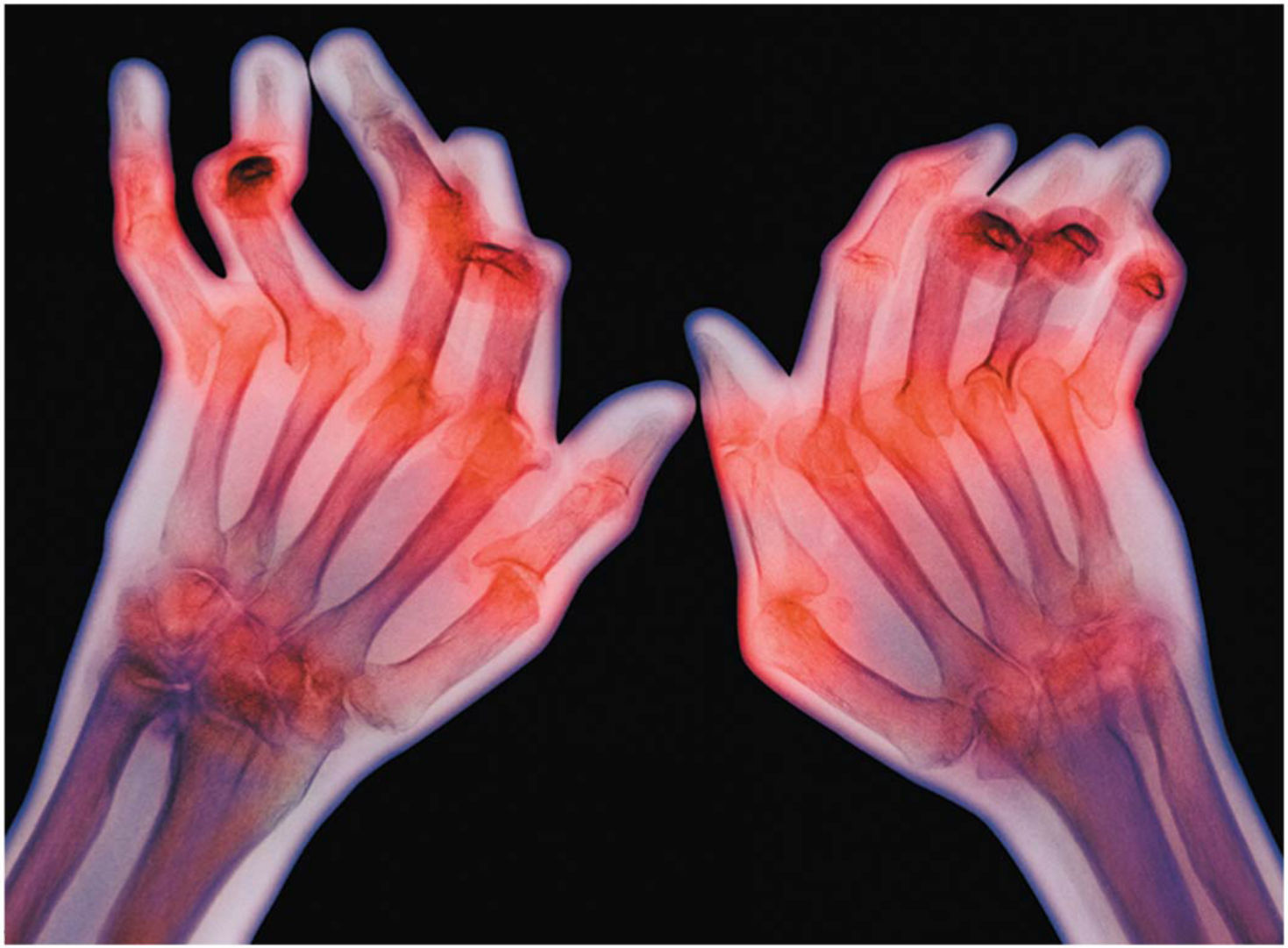

IgE
Mast cell
Allergen (second exposure)
1 IgE antibodies produced in response to initial exposure
2 IgE antibodies bind allergen on subsequent exposure
Vesicle
Histamine
3 Cross-linking triggers release of histamine

Autoimmune Diseases

- In individuals with **autoimmune diseases**, the immune system loses tolerance for self and turns against certain molecules of the body
- In systemic lupus, the immune system generates antibodies against histones and DNA released by normal breakdown of body cells
- These self-reactive antibodies cause rashes, fever, arthritis, and kidney dysfunction

- Type 1 diabetes is another autoimmune condition
- Heredity, gender, and environment all influence susceptibility to autoimmune disorders
- Many such diseases affect females more often than males
- Rheumatoid arthritis is a damaging and painful inflammation of the cartilage and bone in joints

Figure 43.27



Exertion, Stress, and the Immune System

- Moderate exercise improves immune system function, though exercise to exhaustion leads to more frequent infections
- 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

- Some pathogens can change epitope expression and prevent recognition by the host
- This is called *antigenic variation*
- The parasite that causes sleeping sickness is an extreme example; it can switch at random among 1,000 versions of the protein found on its surface

- Antigenic variation is the main reason the influenza virus remains a major public health problem
- Because the virus mutates rapidly, 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 may be 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
- A stimulus such as fever, emotional stress, or menstruation can reactivate the virus

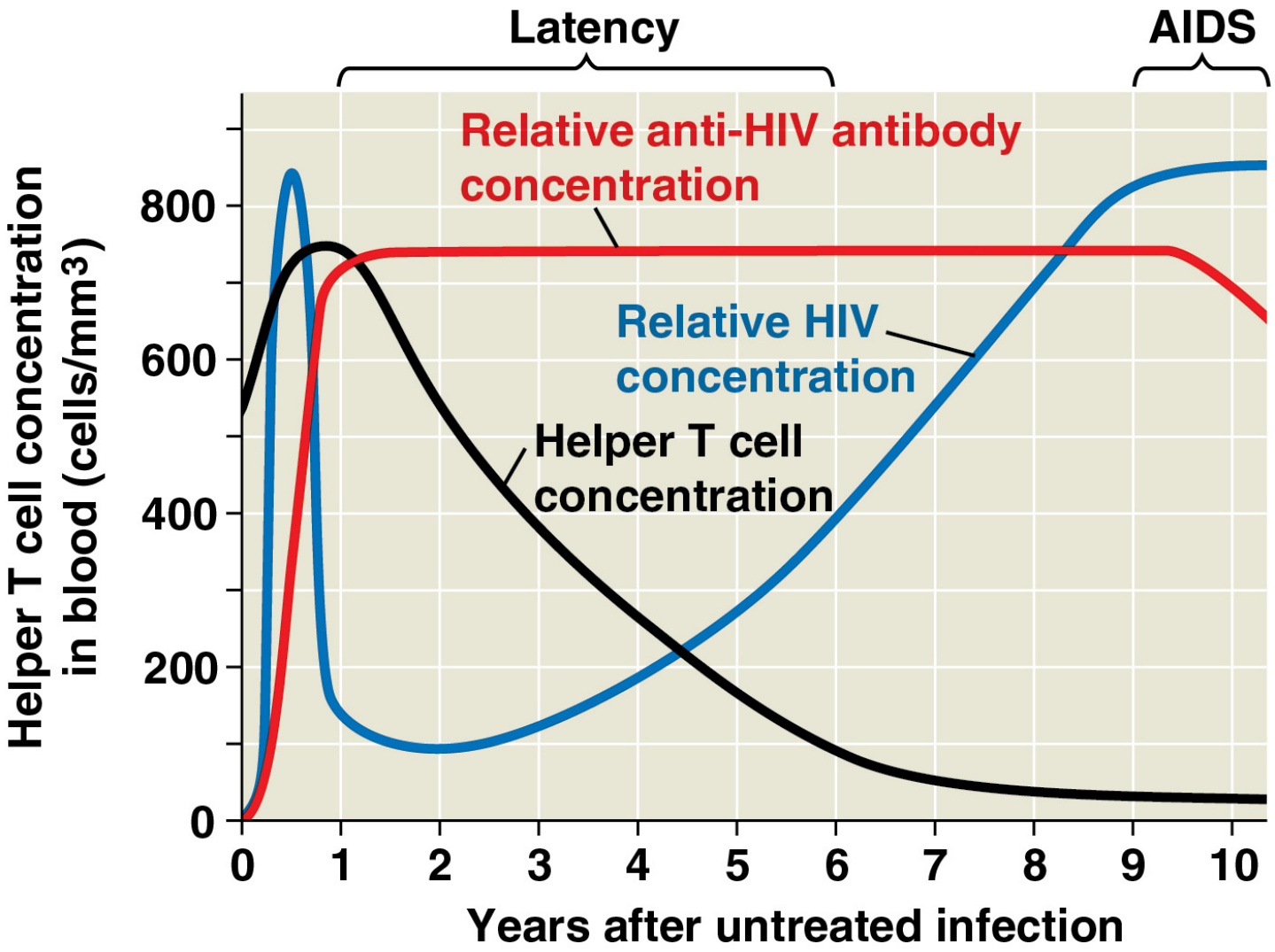
Table 43.1 Latency as a shared characteristic of human herpes virus

Human Herpesvirus	Main Sites of Latency	Associated Diseases or Disorders
Herpes simplex virus-1 (HSV-1)	Clusters of neurons in spinal nerves	Cold sores
Herpes simplex virus-2 (HSV-2)	Clusters of neurons in spinal nerves	Genital ulcers
Varicella-zoster virus (VZV)	Clusters of neurons in spinal nerves	Chicken pox, shingles
Epstein-Barr virus (EBV)	Memory B cells	Some lymphoma, mononucleosis
Cytomegalovirus (CMV)	Monocytes and lymphocytes	Abnormal fetal development
Human herpesvirus 8 (HHV-8)	B cells	Kaposi's sarcoma

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 also abolishes it

Figure 43.28


Latency
AIDS
Relative anti-HIV antibody concentration
Relative HIV concentration
Helper T cell concentration
Helper T cell concentration in blood (cells/mm³)
800
600
400
200
0
0
1
2
3
4
5
6
7
8
9
10
Years after untreated infection

- HIV infection leads to **acquired immunodeficiency syndrome (AIDS)**
- People with AIDS are highly susceptible to opportunistic infections and cancers that a normal immune system would usually defeat
- The spread of HIV is a worldwide problem
- The best approach for slowing this spread is education about practices that transmit the virus

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
- Scientists have identified six viruses that can cause cancer in humans

- Kaposi's sarcoma herpes virus is associated with cancer
- Hepatitis B virus, can trigger liver cancer; a vaccine for this virus was introduced in 1986
- Human papilloma virus (HPV) is associated with cervical and some oral cancers
- In 2006, a vaccine to protect against HPV was first released

Figure 43.29

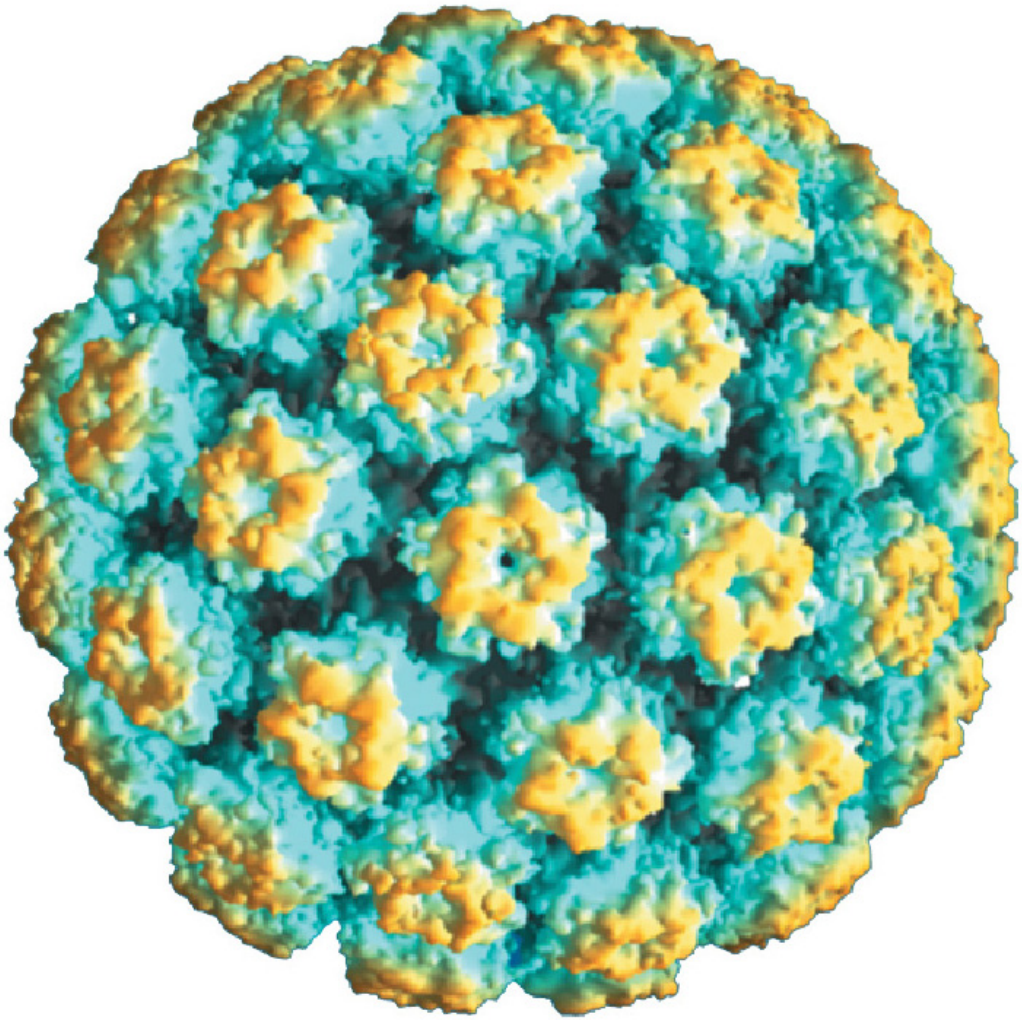


Figure 43.UN01

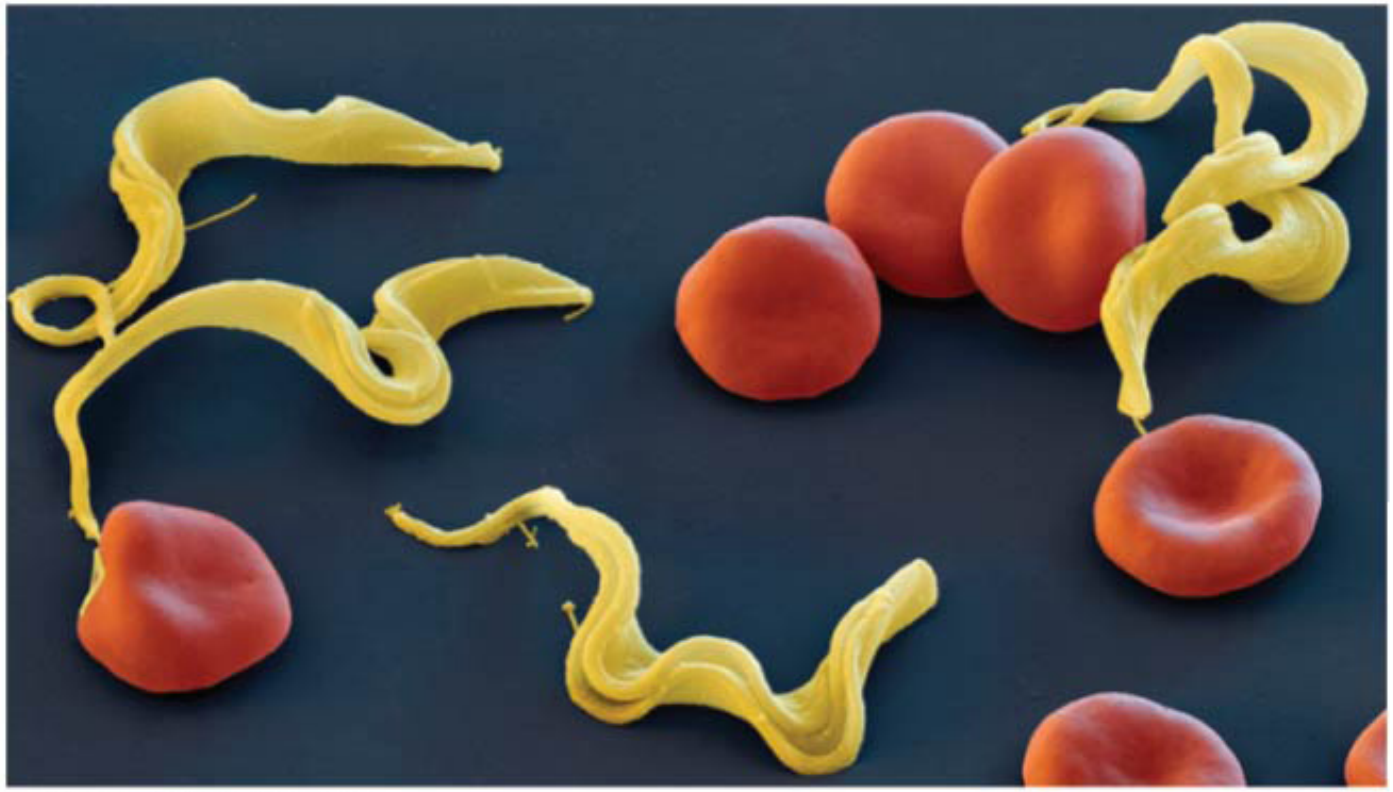


Figure 43.UN02

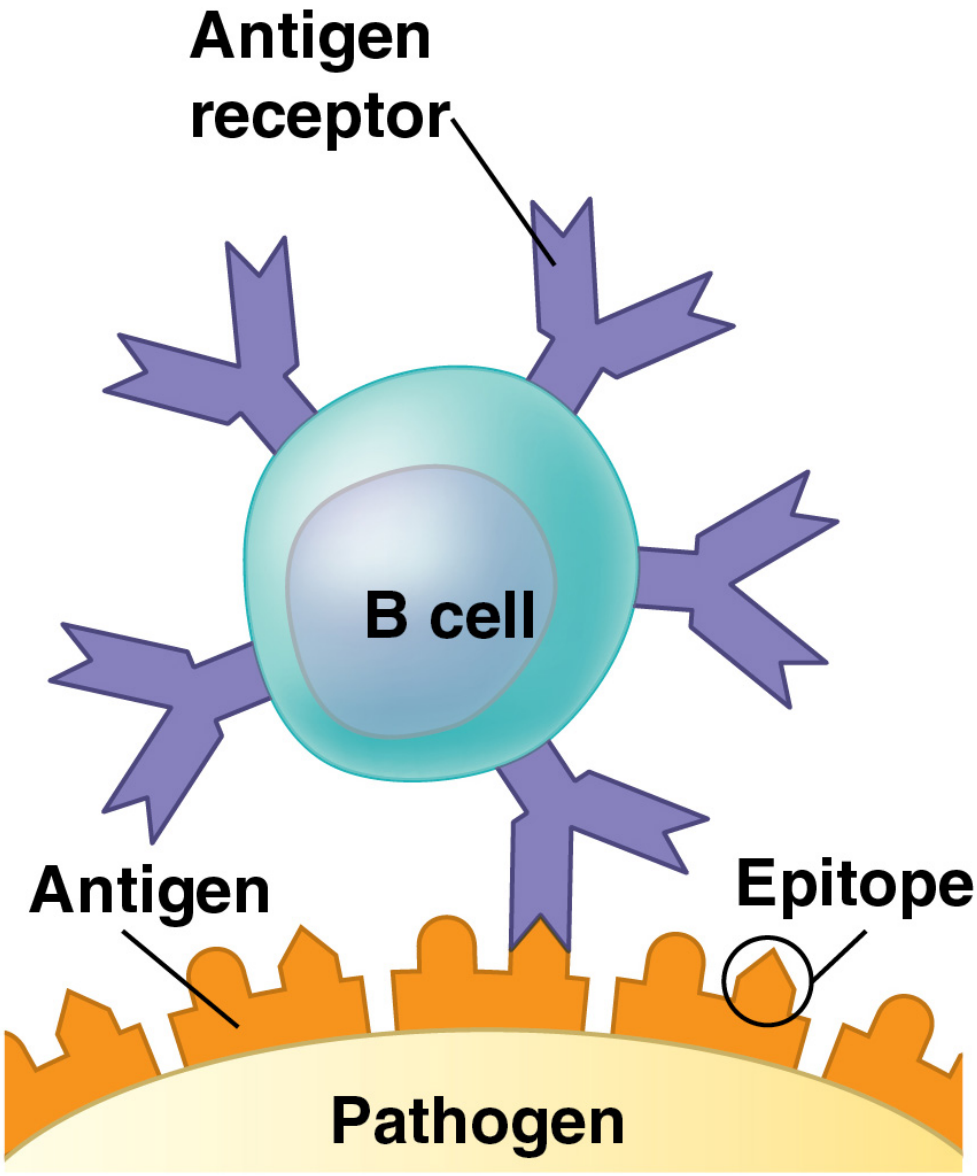


Figure 43.UN03

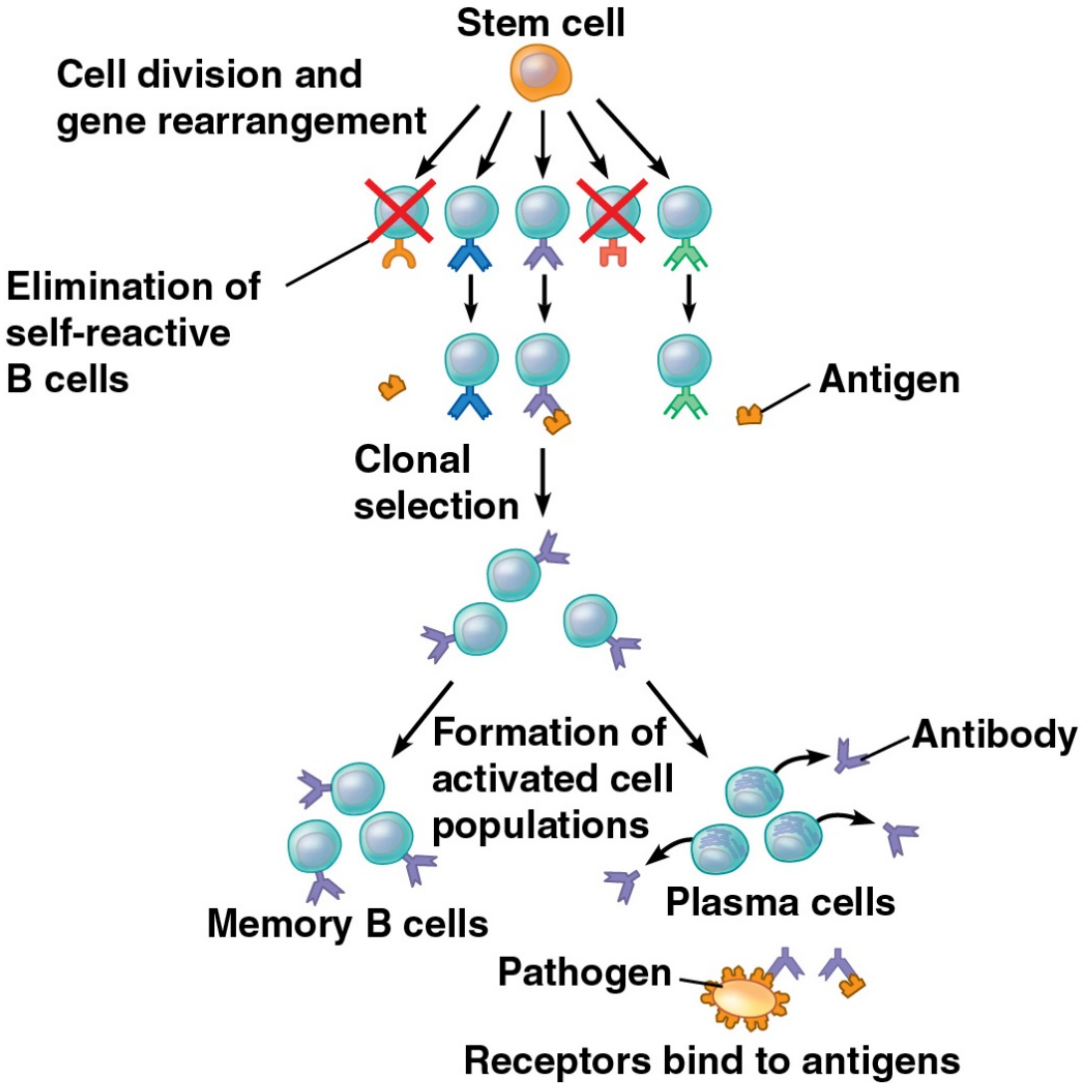


Figure 43.UN04