Chapter 15 – Innate Immunity

NIMESH PATEL| HLSC 2400

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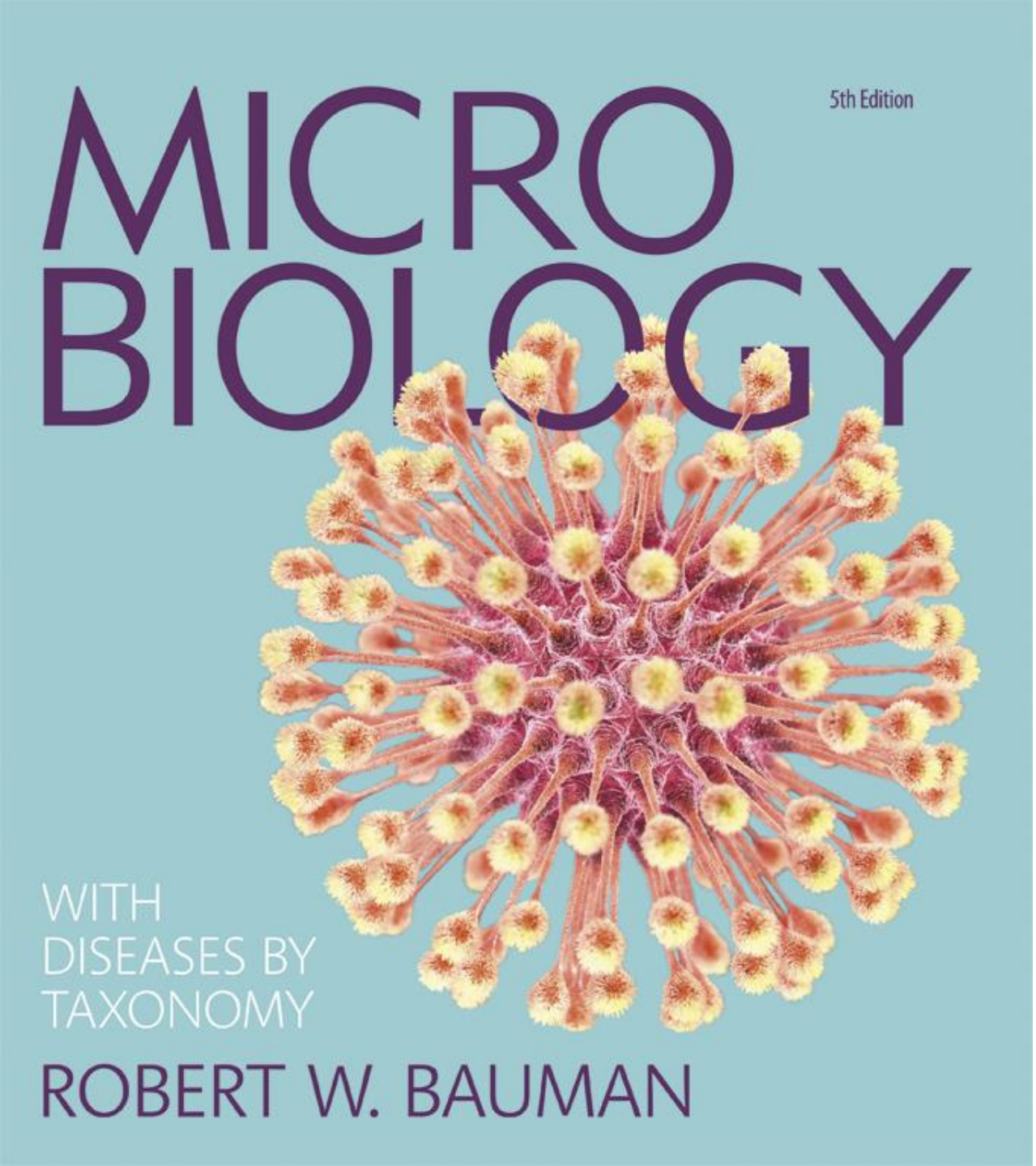


PowerPoint® Lecture Presentations prepared by Mindy Miller-Kittrell, North Carolina State University

CHAPTER **15**

Innate Immunity

An Overview of the Body's Defenses

- Resistance to most plant and animal pathogens
- **Species resistance**
  - Due to physiological processes of humans that are incompatible with those of the pathogen
    - Correct chemical receptors not present on human cells
    - Conditions may be incompatible with those needed for pathogen's survival
- Humans don't have innate resistance to a number of pathogens

- **Innate (Non-specific) defenses**
  - First line of defense
    - External barriers, especially skin and mucous membranes
  - Second line of defense
    - Internal: protective cells, bloodborne chemicals, and processes that inactivate or kill invaders (phagocytosis, inflammation, complement system)
- **Adaptive (specific) defenses**
  - Third line of defense
    - Lymphocytes, antibodies, cytotoxic cells
    - Must be activated by antigen-specific cells
    - More effective against subsequent infections

The Body's First Line of Defense

- Structures, chemicals, and processes that work to prevent pathogens entering the body
- Skin and mucous membranes of the respiratory, digestive, urinary, and reproductive systems

The Body's First Line of Defense

- **The Role of Skin in Innate Immunity**
  - Skin composed of two major layers:
    - **Epidermis**
      - Multiple layers of tightly packed cells
        - Few pathogens can penetrate these layers
        - Shedding of dead skin cells removes microorganisms
      - Epidermal dendritic cells phagocytize pathogens
    - **Dermis**
      - Contains hair follicles, glands, blood vessels, and nerve endings
      - Collagen fibers help skin resist abrasions that could introduce microorganisms

The Body's First Line of Defense

- **The Role of Skin in Innate Immunity**
  - Skin has chemicals that defend against pathogens
    - Perspiration secreted by sweat glands
      - Salt inhibits growth of pathogens
      - Antimicrobial peptides act against microorganisms
      - Lysozyme destroys cell wall of bacteria
    - Sebum secreted by sebaceous (oil) glands
      - Helps keep skin pliable and less likely to break or tear
      - Lowers skin pH to a level inhibitory to many bacteria

The Body's First Line of Defense

- **The Role of Mucous Membranes in Innate Immunity**
  - Mucous membranes line all body cavities open to environment
  - Two distinct layers:
    - *Epithelium*
      - Thin, outer covering of the mucous membranes
      - Epithelial cells are living
      - Tightly packed to prevent entry of many pathogens
      - Continual shedding of cells carries away microorganisms
      - Dendritic cells below epithelium phagocytize pathogens
      - Goblet and ciliated columnar cells help remove invaders
    - Deeper connective layer that supports the epithelium
  - Produce chemicals that defend against pathogens

Figure 15.2 The structure of the respiratory system, which is lined with a mucous membrane.

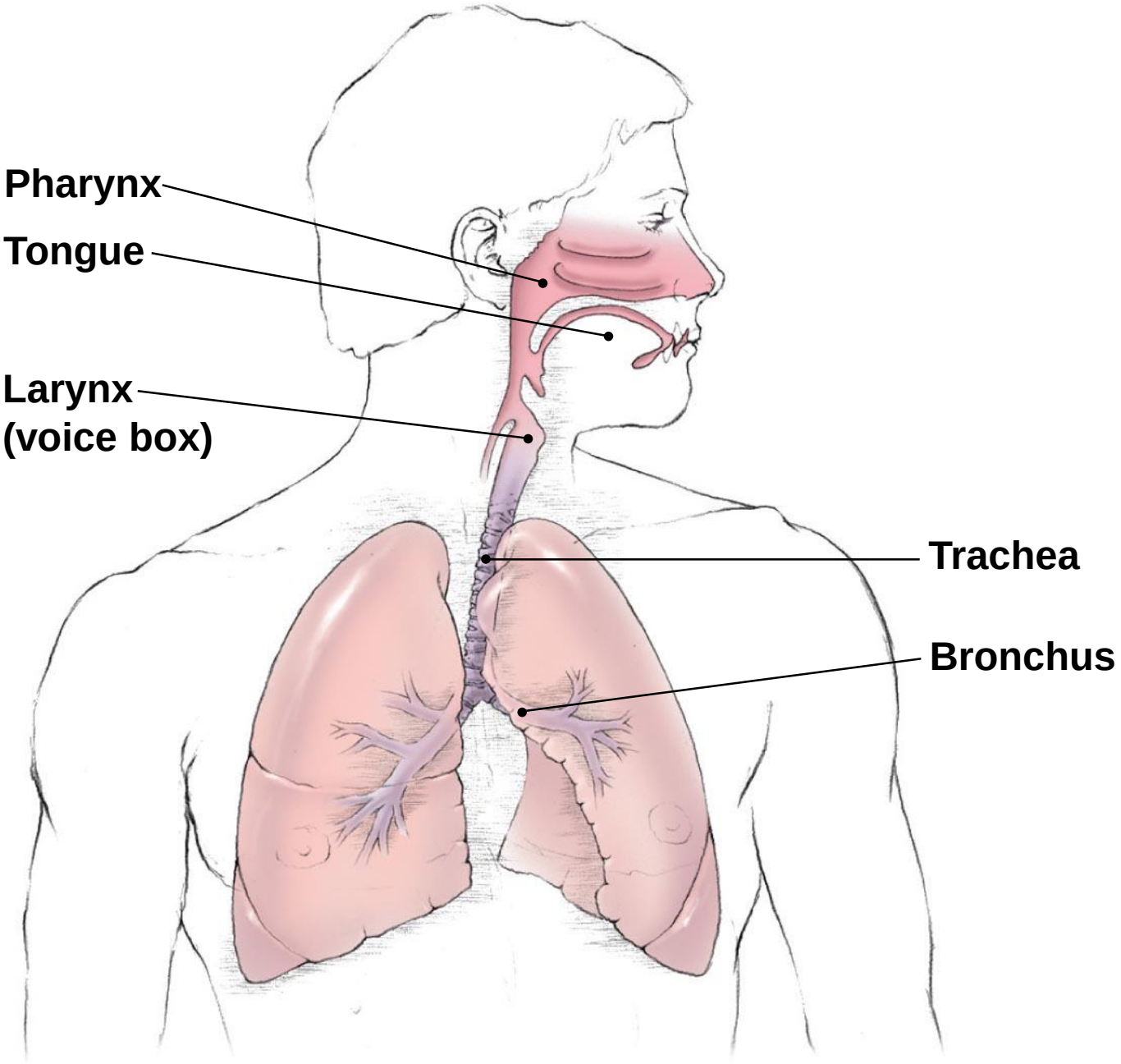


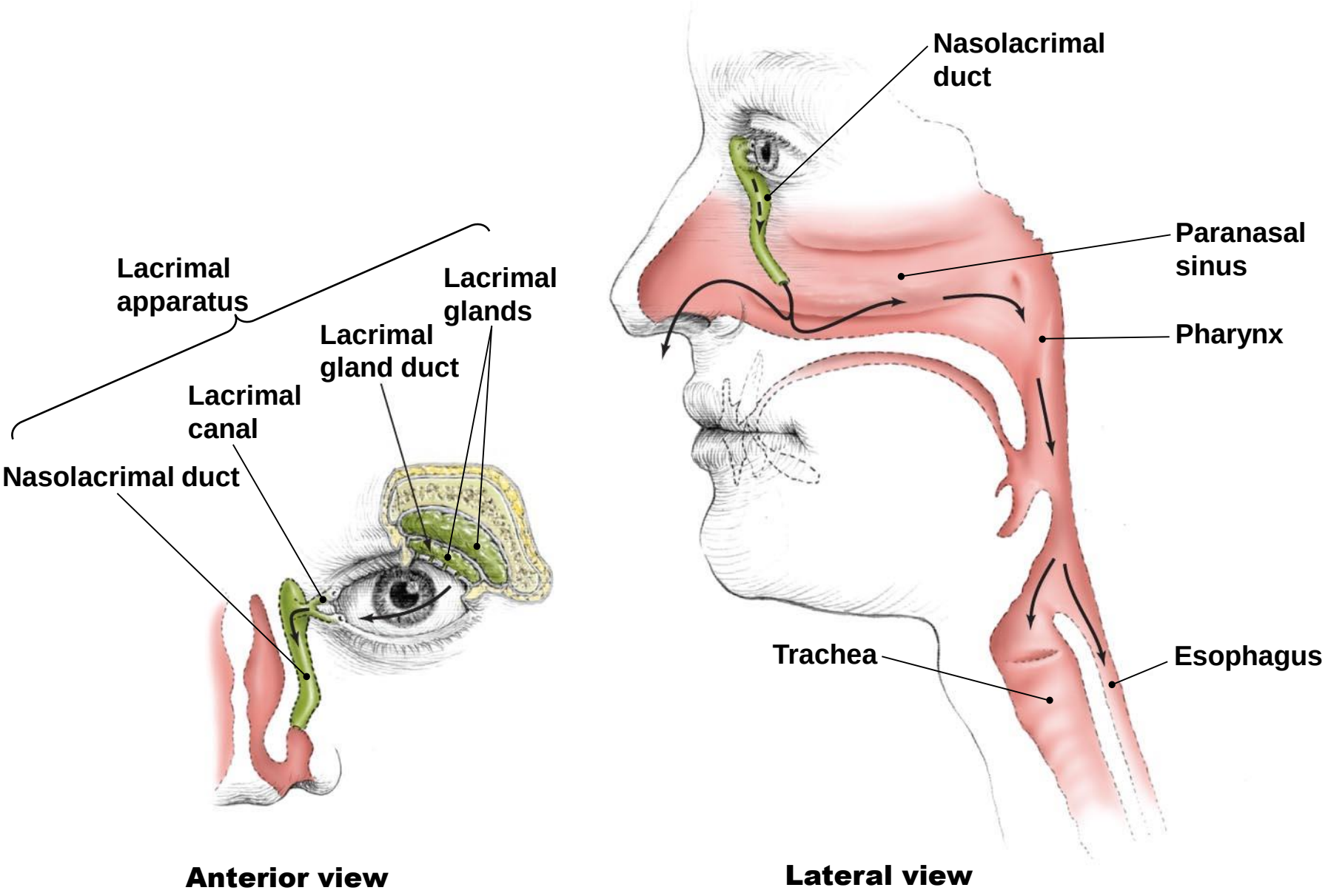
TABLE 15.1 The First Line of Defense: A Comparison of the Skin and Mucous Membranes

	Skin	Mucous Membrane
Number of Cell Layers	Many	One to a few
Cells Tightly Packed?	Yes	Yes
Cells Dead or Alive?	Outer layers: dead; inner layers: alive	Alive
Mucus Present?	No	Yes
Relative Water Content	Dry	Moist
Defensins Present?	Yes	With some
Lysozyme Present?	Yes	With some
Sebum Present?	Yes	No
Cilia Present?	No	Trachea, uterine tubes
Constant Shedding and Replacement of Cells?	Yes	Yes

The Body's First Line of Defense

- **The Role of the Lacrimal Apparatus in Innate Immunity**
  - Lacrimal apparatus
    - Produces and drains tears
    - Blinking spreads tears and washes surface of the eye
    - Lysozyme in tears destroys bacteria

Figure 15.3 The lacrimal apparatus.



The Body's First Line of Defense

- **The Role of Normal Microbiota in Innate Immunity**
  - **Microbial antagonism**
    - **Normal microbiota** compete with potential pathogens aka microbial antagonism
  - Activities of normal microbiota make it hard for pathogens to compete
    - Consumption of nutrients
    - Create an environment unfavorable to other microorganisms
    - Help stimulate the body's second line of defense
      - Normal microbiota in intestines
    - Promote overall health by providing vitamins to host

The Body's First Line of Defense

- **Other First-Line Defenses**
  - Antimicrobial Peptides
    - Present in skin, mucous membranes, neutrophils
    - Act against a variety of microbes
    - Work in several ways
      - Punch holes in cytoplasmic membranes of pathogens
      - Interrupt enzymatic reaction
      - Recruit leukocyte to a site
  - Other Processes and Chemicals
    - Many organs secrete chemicals with antimicrobial properties

TABLE 15.2 Secretions and Activities That Contribute to the First Line of Defense

Secretion/Activity	Function
Digestive System	
Saliva	Washes microbes from teeth, gums, tongue, and palate; contains lysozyme, an antibacterial enzyme
Stomach acid	Digests and/or inhibits microorganisms
Gastroferritin	Sequesters iron being absorbed, making it unavailable for microbial use
Bile	Inhibitory to most microorganisms
Intestinal secretions	Digests and/or inhibits microorganisms
Peristalsis	Moves gastrointestinal (GI) contents through GI tract, constantly eliminating potential pathogens
Defecation	Eliminates microorganisms
Vomiting	Eliminates microorganisms
Urinary System	
Urine	Contains lysozyme; urine's acidity inhibits microorganisms; may wash microbes from ureters and urethra during urination

TABLE 15.2 Secretions and Activities That Contribute to the First Line of Defense *(Continued)*

Secretion/Activity	Function
Reproductive System	
Vaginal secretions	Acidity inhibits microorganisms; contains iron-binding proteins that sequester iron, making it unavailable for microbial use
Menstrual flow	Cleanses uterus and vagina
Prostate secretion	Contains iron-binding proteins that sequester iron, making it unavailable for microbial use
Cardiovascular System	
Blood flow	Removes microorganisms from wounds
Coagulation	Prevents entrance of many pathogens

The Body's Second Line of Defense

- Operates when pathogens penetrate the skin or mucous membranes
- Composed of cells, antimicrobial chemicals, and processes
  - Many of these components are contained in or originate in the blood

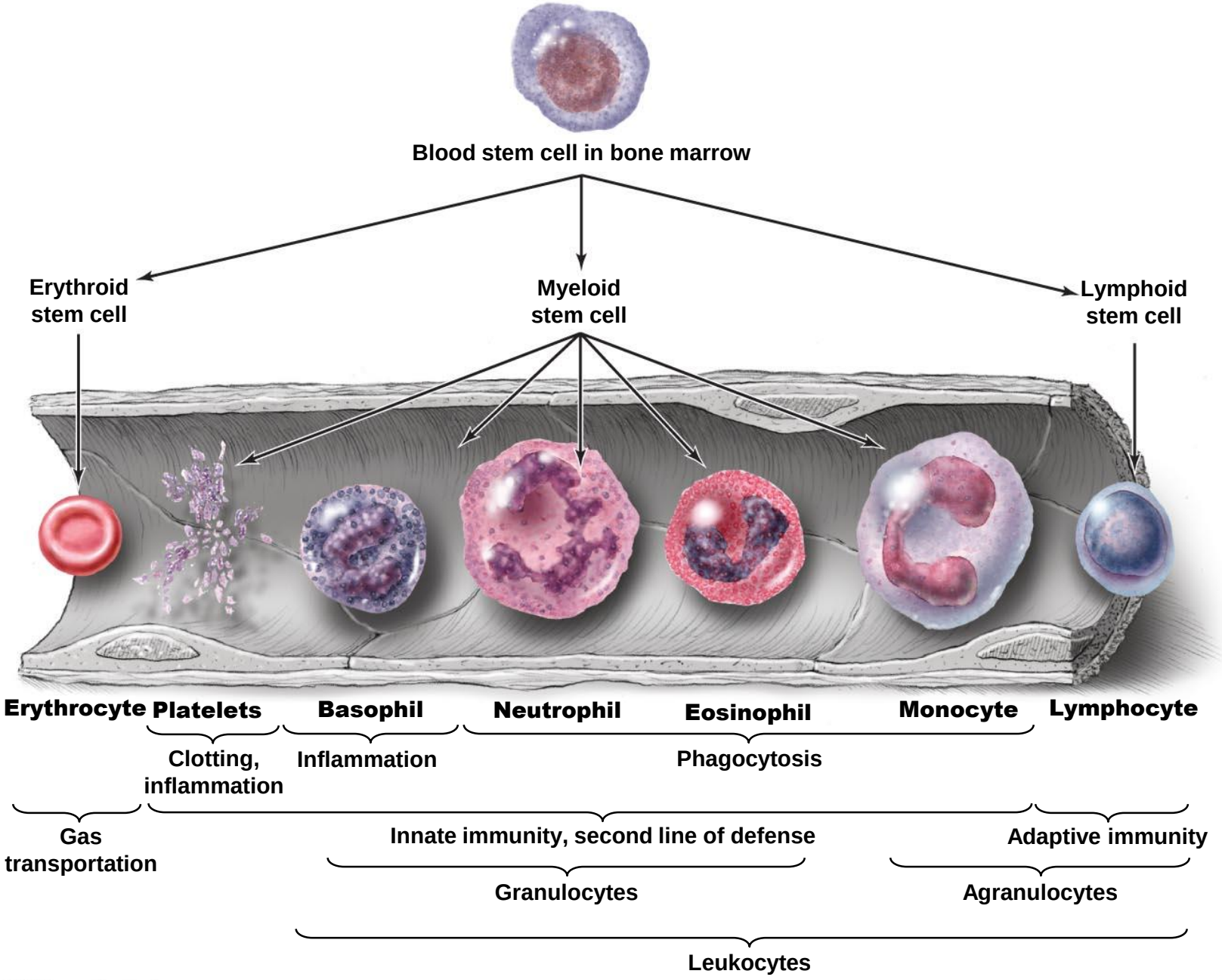
The Body's Second Line of Defense

- **Defense Components of Blood**
  - **Plasma**
    - Mostly water containing electrolytes, dissolved gases, nutrients, and proteins
    - Serum is the fluid remaining when clotting factors are removed
    - Contains iron-binding compounds
      - Iron needed for metabolism
      - Some microbes produce proteins that bind iron
    - Complement proteins and antibodies are also found in plasma

The Body's Second Line of Defense

- **Defense Components of Blood**
  - Defensive Blood Cells: Leukocytes
    - Cells and cell fragments in plasma called **formed elements**
    - Three types of formed elements:
      - **Erythrocytes**
        - Carry oxygen and carbon dioxide in the blood
      - **Platelets**
        - Involved in blood clotting
      - **Leukocytes**
        - Involved in defending the body against invaders
        - Divided into granulocytes and agranulocytes

Figure 15.4 A schematic representation of hematopoiesis.



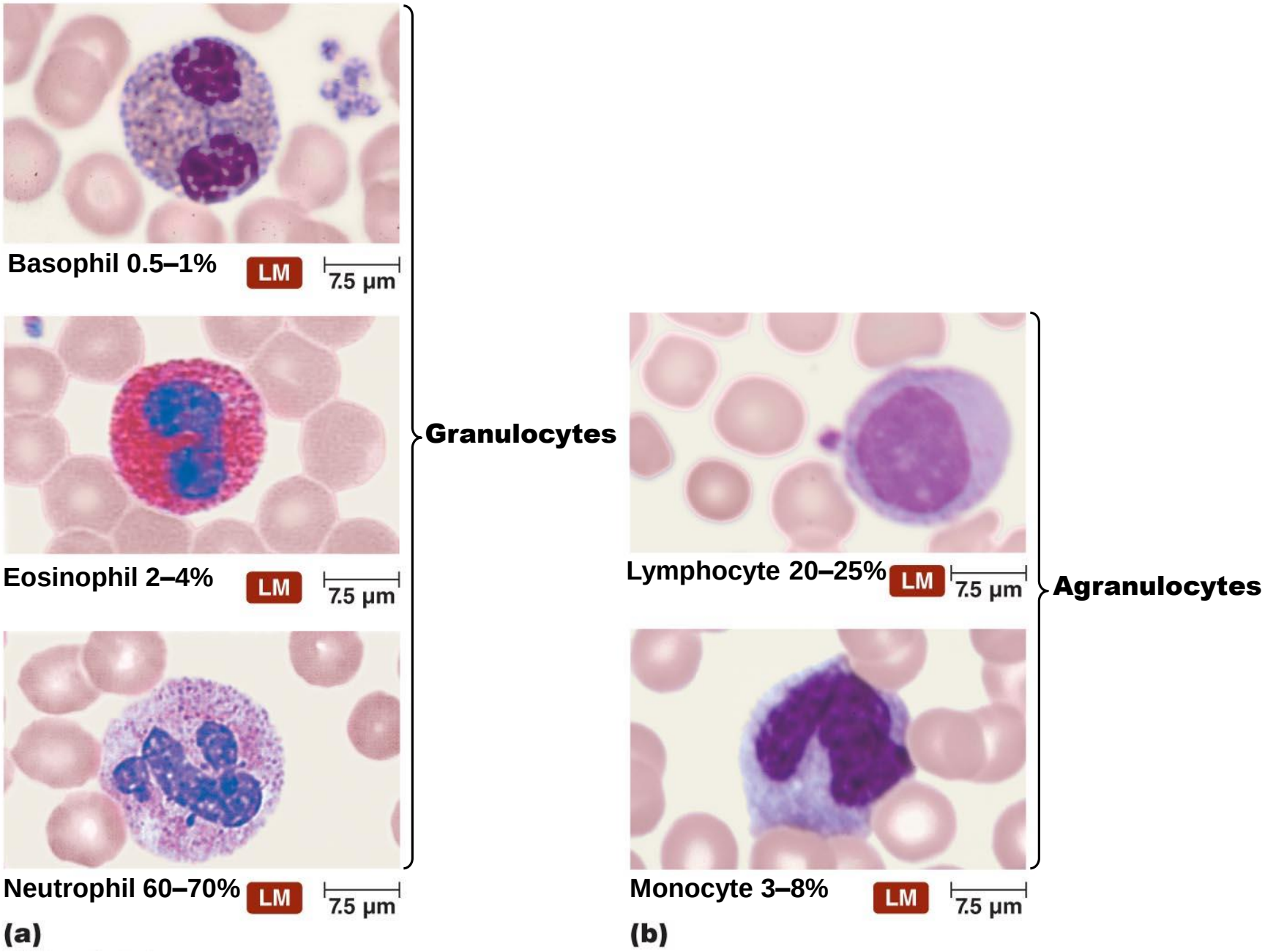
The Body's Second Line of Defense

- **Defense Components of Blood**
  - Defensive Blood Cells: Leukocytes
    - **Granulocytes**
      - Contain large granules that stain different colors
      - Three types:
        - **Basophils** — stain blue with basic dye methylene blue
        - **Eosinophils** — stain red/orange with acidic dye eosin
        - **Neutrophils** — stain lilac with mix of acidic and basic dyes
      - Neutrophils and eosinophils
        - Phagocytize pathogens
        - Capable of diapedesis

The Body's Second Line of Defense

- **Defense Components of Blood**
  - Defensive Blood Cells: Leukocytes
    - **Agranulocytes**
      - Cytoplasm appears uniform under a light microscope
      - Two types:
        - **Lymphocytes**
          - Most involved in adaptive immunity
          - Natural killer lymphocytes
        - **Monocytes**
          - Leave the blood and mature into macrophages
          - Phagocytic cells that devour foreign objects

Figure 15.5 Leukocytes as seen in stained blood smears.



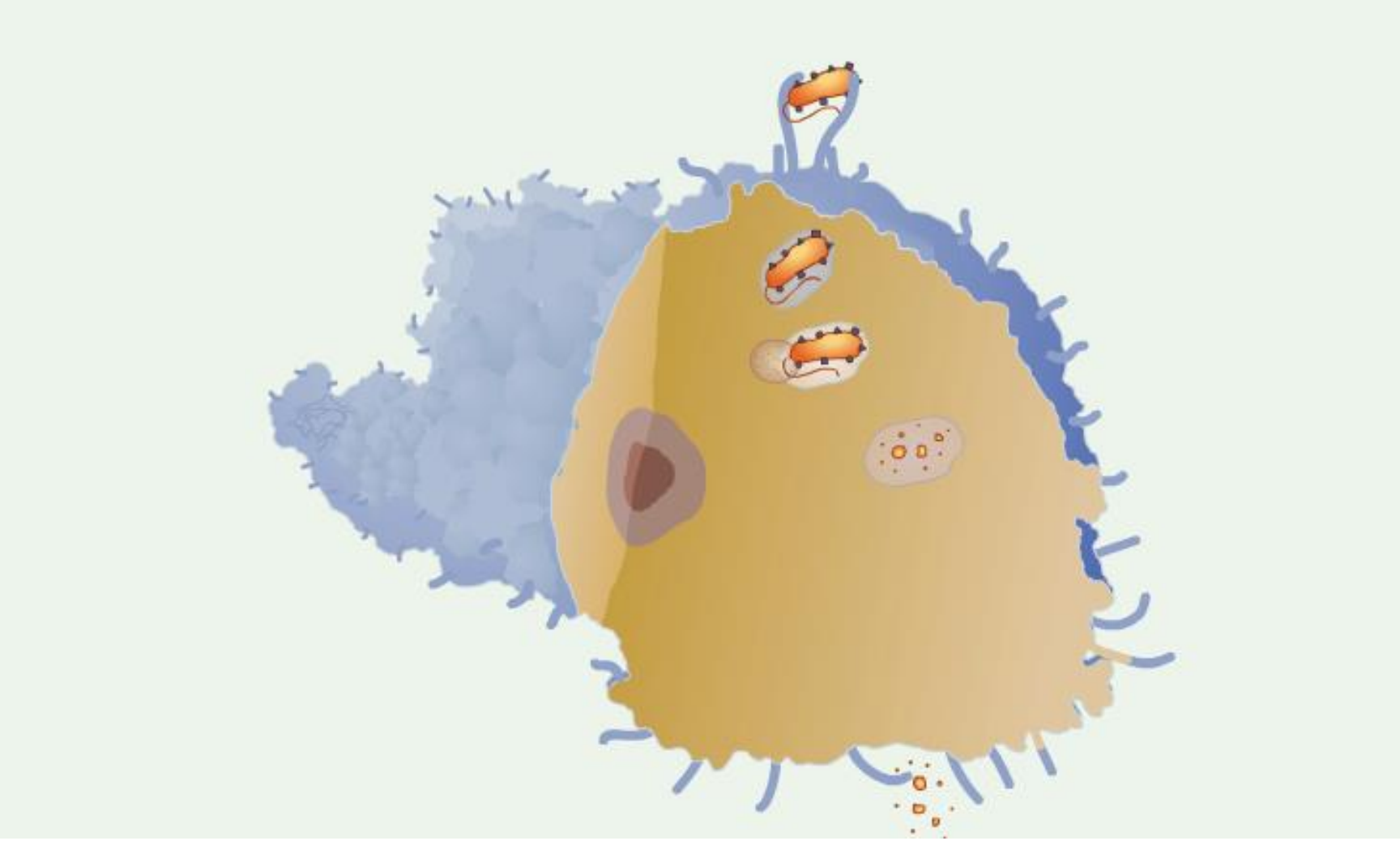
The Body's Second Line of Defense

- **Defense Components of Blood**
  - Defensive Blood Cells: Leukocytes
    - Lab Analysis of Leukocytes
      - **Differential white blood cell count** can signal disease
        - Increased eosinophils indicate allergies or parasitic worm infection
        - Bacterial diseases often show increase in leukocytes and neutrophils
        - Viral infections show increase in lymphocytes

The Body's Second Line of Defense

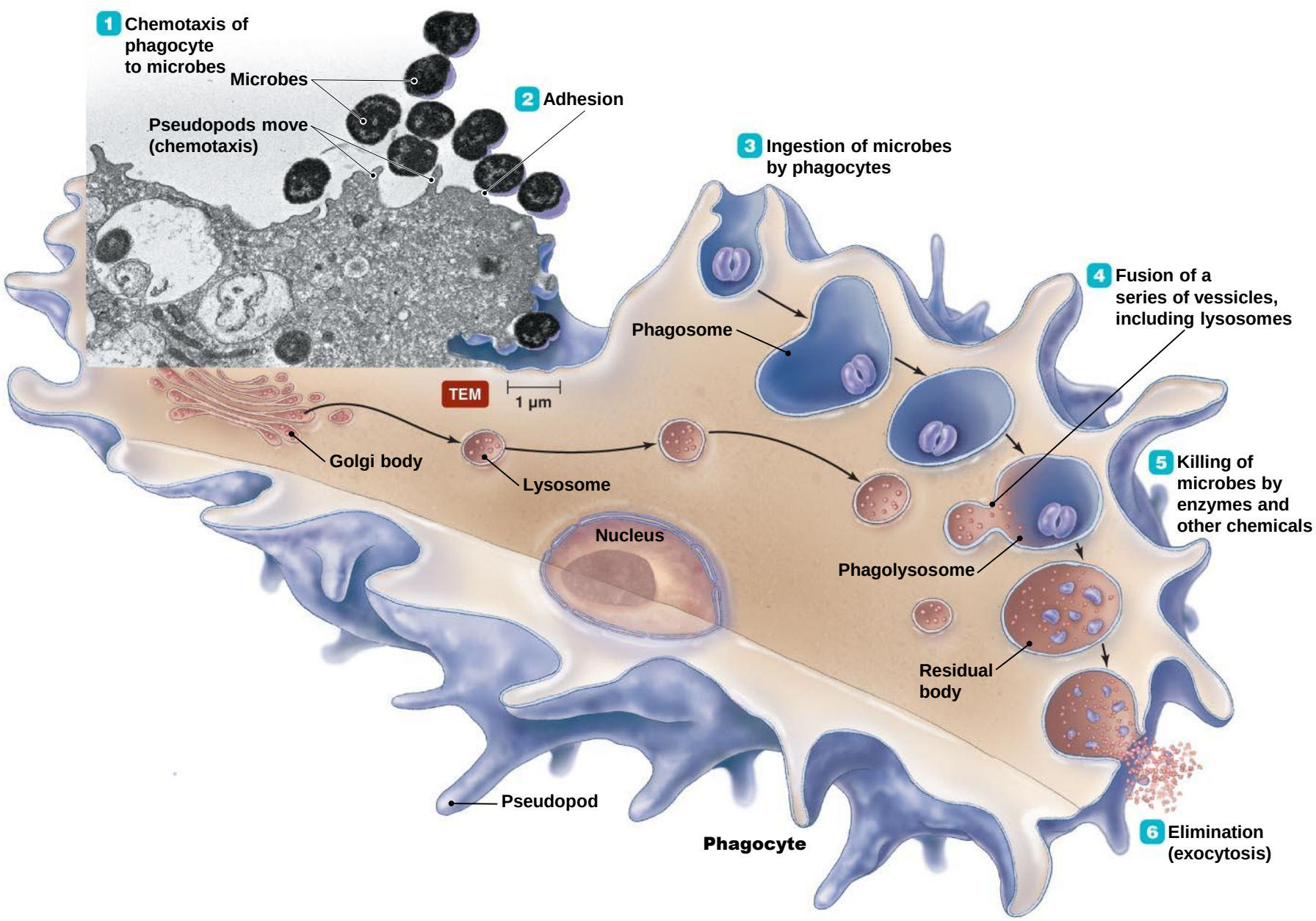
- **Phagocytosis**
  - Cells capable of phagocytosis are called phagocytes
    - Macrophages and neutrophils
  - Phagocytosis is not completely understood
  - Can be divided into six stages
    - Chemotaxis
    - Adhesion
    - Ingestion
    - Maturation
    - Killing
    - Elimination

Phagocytosis: Overview



PLAY **Phagocytosis: Overview**

Figure 15.6 The events in phagocytosis.



The Body's Second Line of Defense

- **Nonphagocytic Killing**
  - Killing by Eosinophils
    - Attack parasitic helminths by adhering to their surface
      - Secrete toxins that weaken or kill the helminth
      - Eosinophilia is often indicative of a helminth infestation or allergies
    - Eosinophil mitochondrial DNA and proteins form structure that kills some bacteria

The Body's Second Line of Defense

- **Nonphagocytic Killing**
  - Killing by **Natural Killer Lymphocytes (NK Cells)**
    - Secrete toxins onto surface of virally infected cells and tumors
    - Differentiate normal body cells because they have membrane proteins similar to the NK cells

The Body's Second Line of Defense

- **Nonphagocytic Killing**
  - Killing by Neutrophils
    - Can destroy microbes without phagocytosis
    - Produce chemicals that kill nearby invaders
    - Generate extracellular fibers called neutrophil extracellular traps (NETs) that bind to and kill bacteria

The Body's Second Line of Defense

- **Nonspecific Chemical Defenses Against Pathogens**
  - **Toll-like Receptors (TLRs)**
    - Integral membrane proteins produced by phagocytic cells
    - Bind **pathogen-associated molecular patterns (PAMPs)**
    - Initiate defensive responses
      - Secretion of inflammatory mediators
      - Stimulate adaptive immune response
      - Apoptosis

TABLE 15.3 Toll-Like Receptors and Their Natural Microbial Binding Partners

TLR	PAMP (Microbial Molecule)
In Cytoplasmic Membrane	
TLR1	Bacterial lipopeptides and certain proteins in multicellular parasites
TLR2	Bacterial lipopeptides, lipoteichoic acid (found in Gram-positive cell wall), and cell wall of yeast
TLR4	Lipid A (found in outer membrane of Gram-negative bacteria)
TLR5	Flagellin (bacterial flagella)
TLR6	Bacterial lipopeptides, lipoteichoic acid (found in Gram-positive cell wall), and cell wall of yeast
TLR10	Unknown component of influenzaviruses
In Phagosome Membrane	
TLR3	Double-stranded RNA (found only in viruses)
TLR7	Single-stranded viral RNA
TLR8	Single-stranded viral RNA
TLR9	Unmethylated cytosine-guanine pairs of viral and bacterial DNA

The Body's Second Line of Defense

- **Nonspecific Chemical Defenses Against Pathogens**
  - **NOD Proteins**
    - Cytosolic proteins that bind PAMPs
    - Trigger inflammation, apoptosis, and other innate responses
    - Mechanism of action still being researched

The Body's Second Line of Defense

- **Nonspecific Chemical Defenses Against Pathogens**
  - Interferons
    - Protein molecules released by host cells to nonspecifically inhibit the spread of viral infections
    - Cause many symptoms associated with viral infections
    - Two types:
      - Types I (alpha and beta)
        - Released within hours of infection
      - Type II (gamma)
        - Released several days after initial infection

Figure 15.7 The actions of alpha and beta interferons.

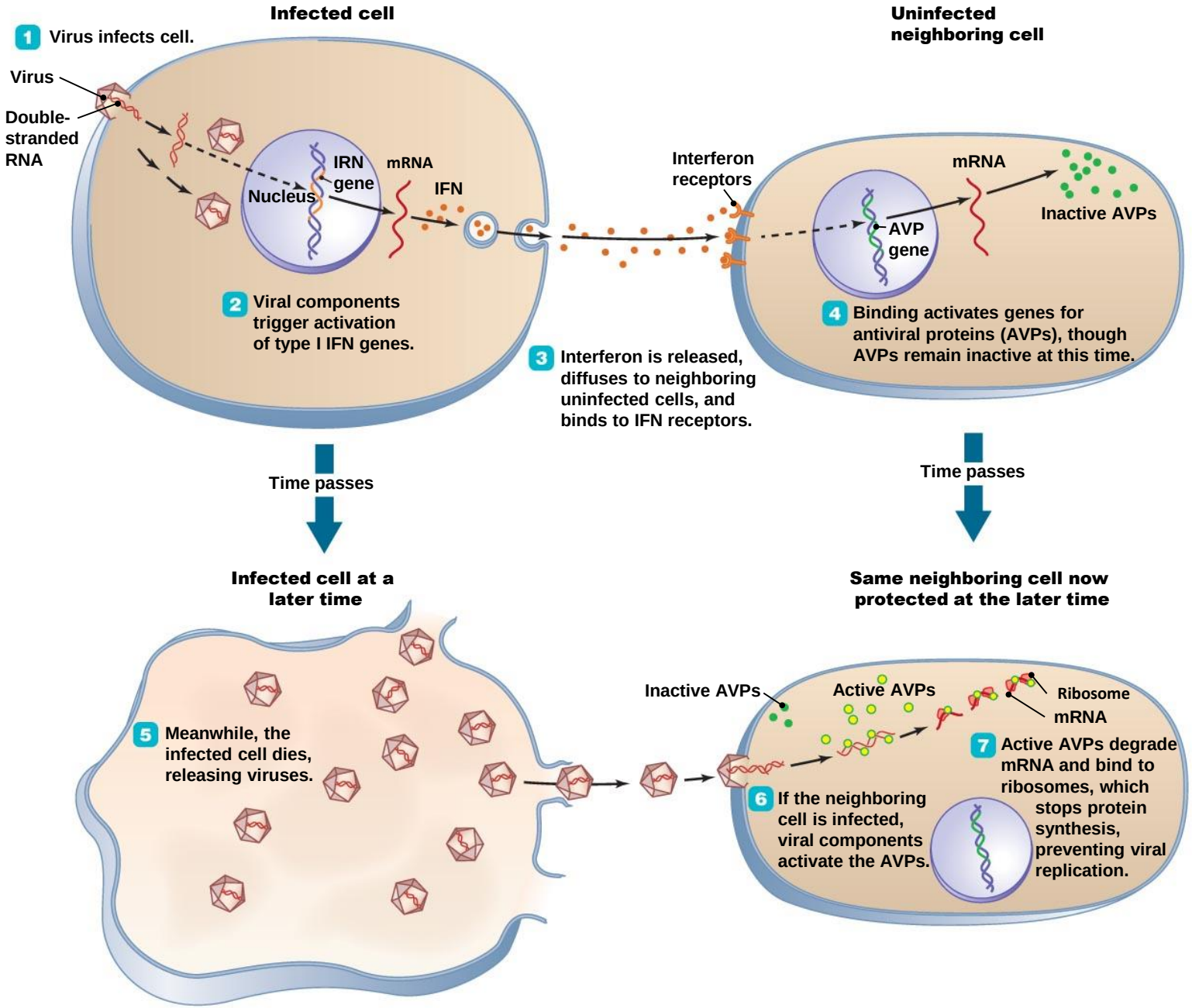


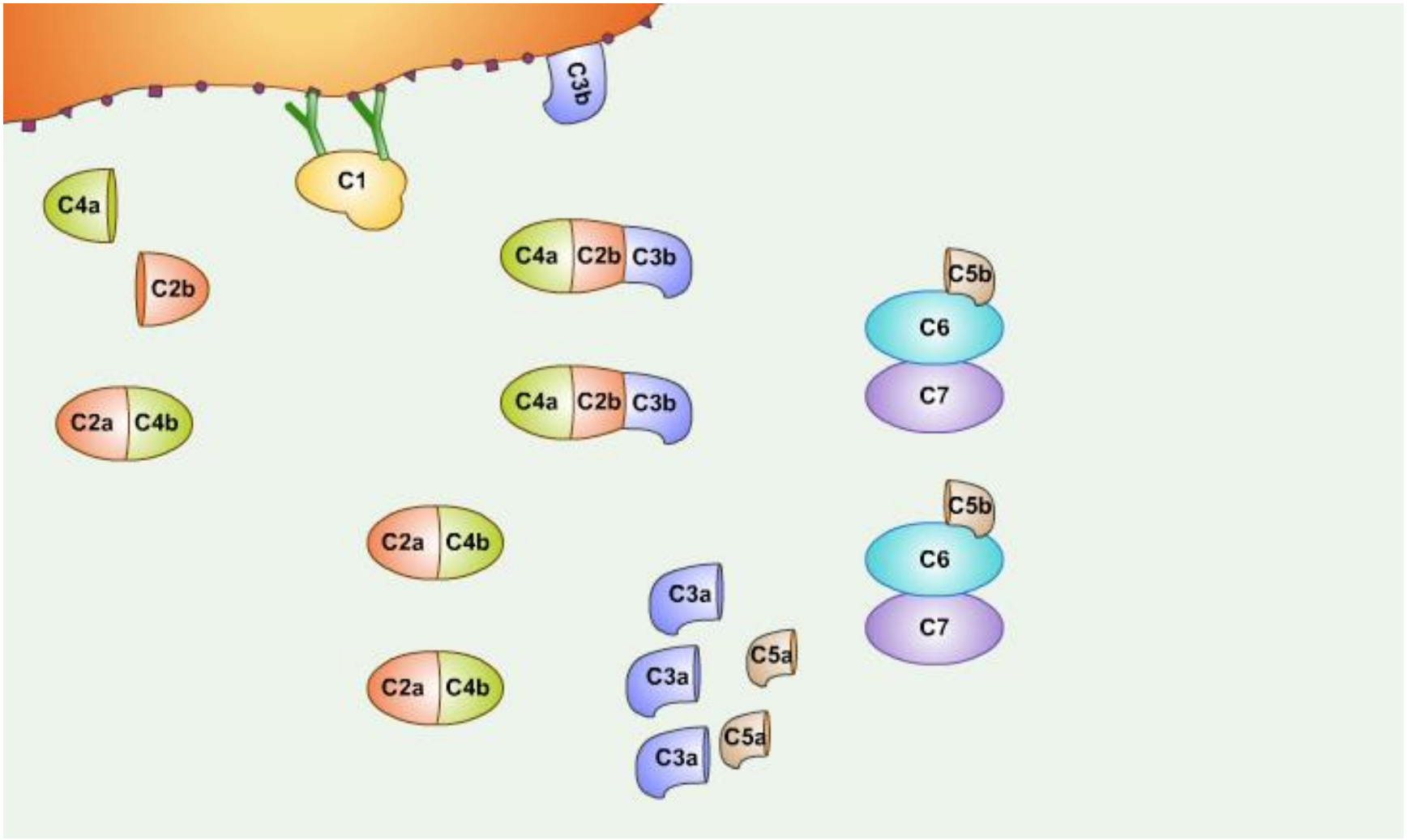
TABLE 15.4 The Characteristics of Human Interferons

	Type I		Type II
Property	**Alpha Interferon (IFN-α)**	**Beta Interferon (IFN-β)**	**Gamma Interferon (IFN-γ)**
Principal source	Epithelium, leukocytes	Fibroblasts	Activated T lymphocytes and NK lymphocytes
Inducing agent	Viruses	Viruses	Adaptive immune responses
Action	Stimulates production of antiviral proteins	Stimulates production of antiviral proteins	Stimulates phagocytic activity of macrophages and neutrophils
Other names	Leukocyte-IFN	Fibroblast-IFN	Immune-IFN, macrophage activation factor

The Body's Second Line of Defense

- **Nonspecific Chemical Defenses Against Pathogens**
  - Complement
    - Set of serum proteins designated numerically according to their order of discovery
    - Complement activation results in lysis of the foreign cell
    - Indirectly trigger inflammation and fever
    - Complement can be activated in three ways:
      - *Classical pathway*
      - *Alternative pathway*
      - *Lectin pathway*

Complement: Overview



PLAY **Complement: Overview**

Figure 15.8 Pathways by which complement is activated.

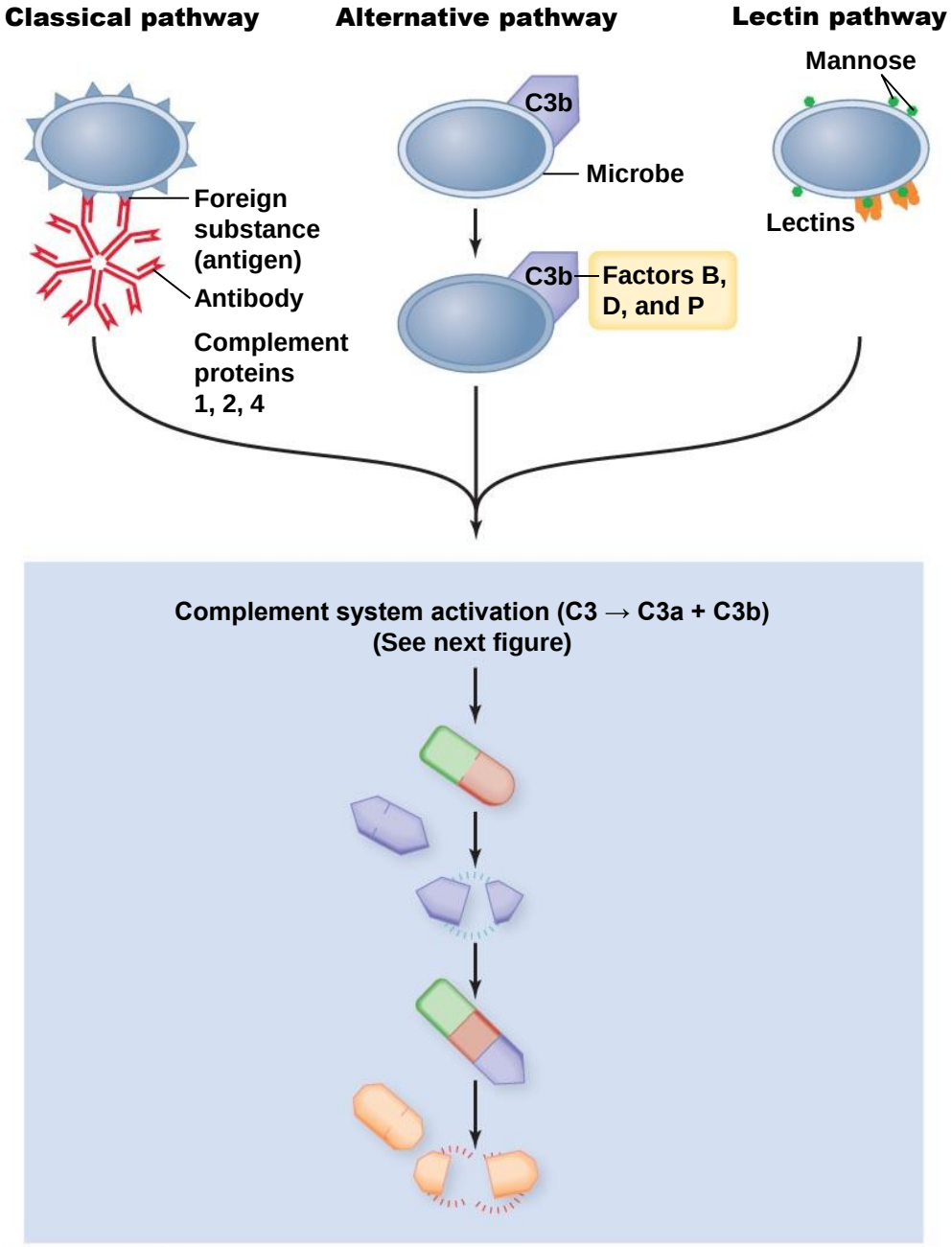
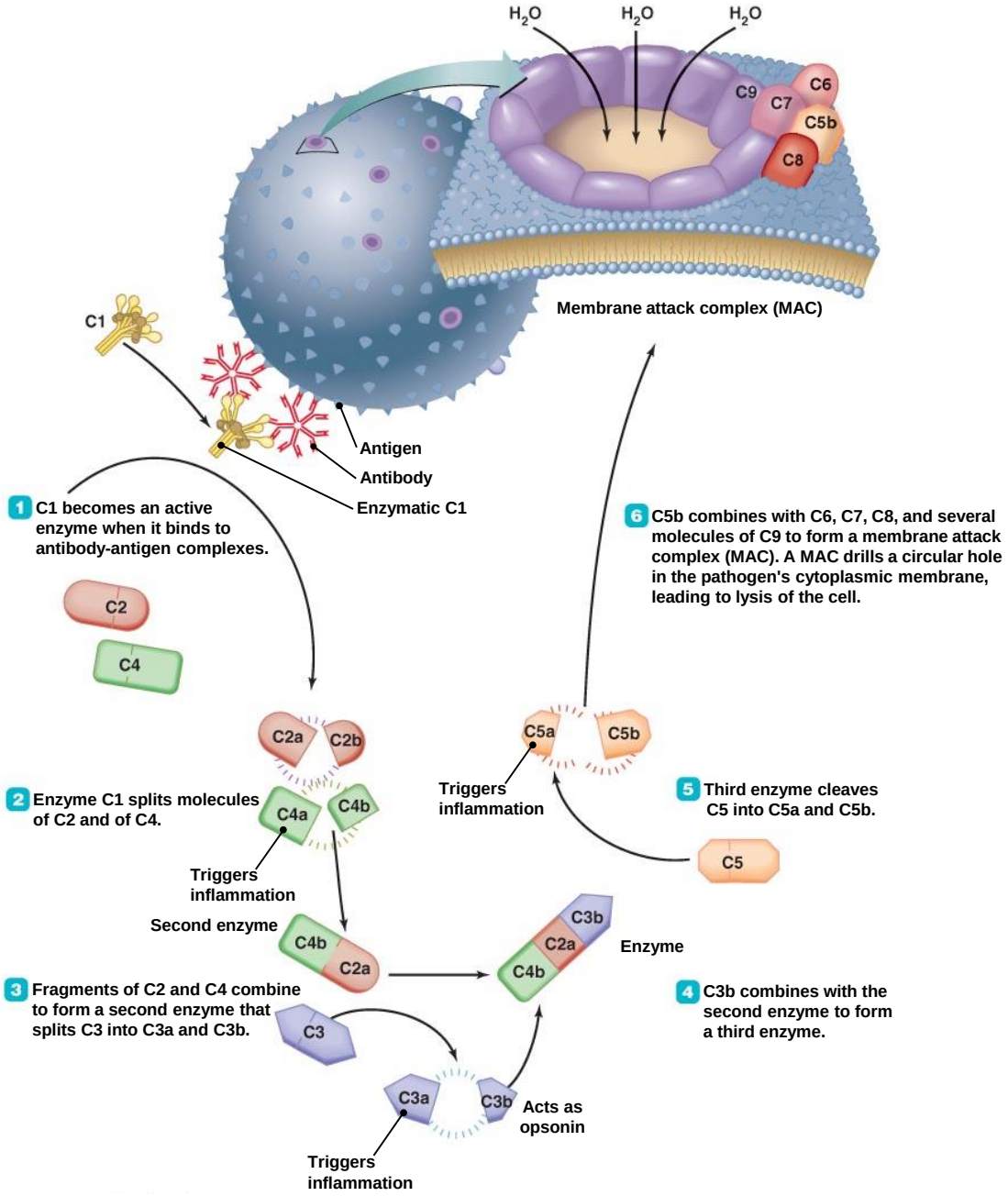
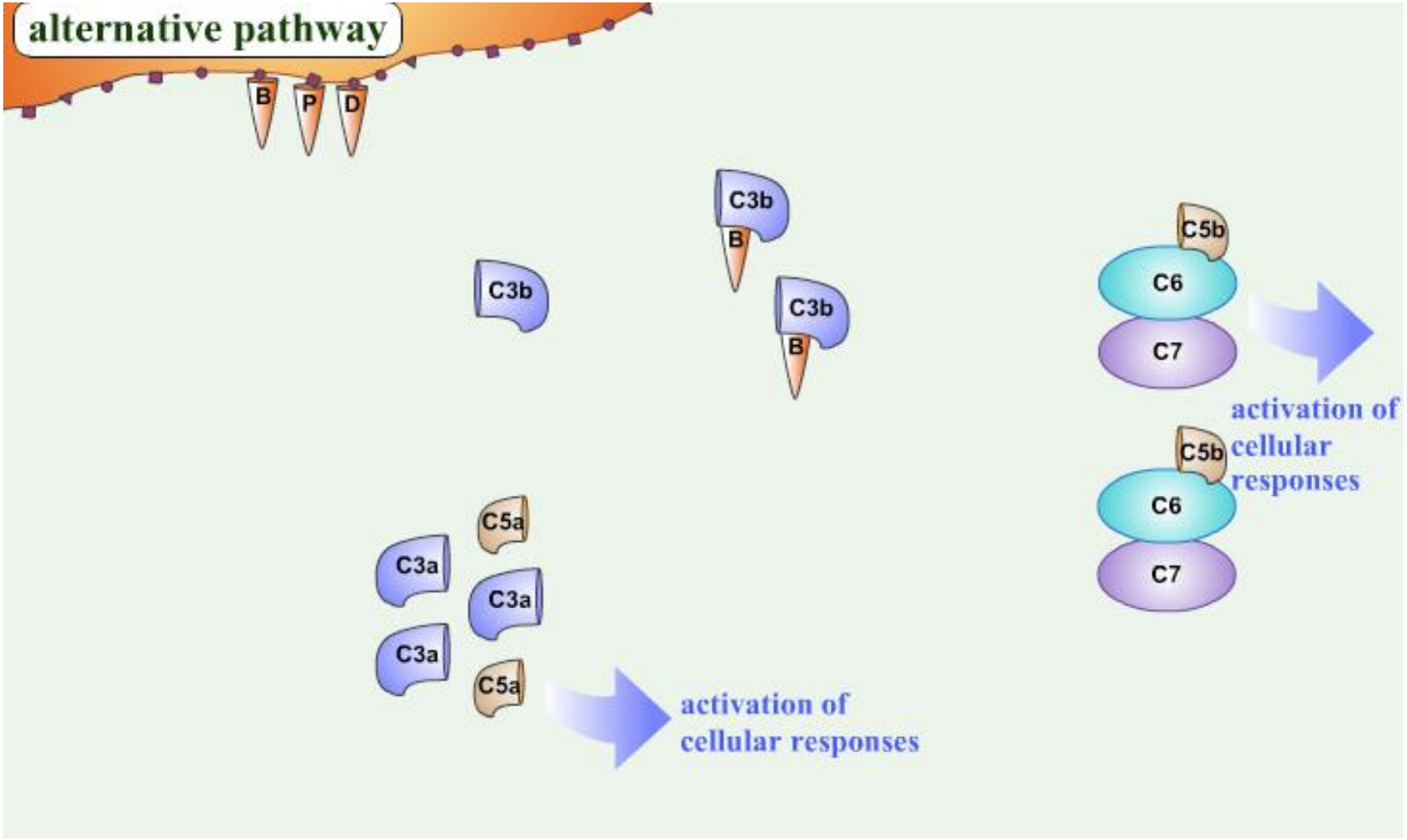


Figure 15.9 The classical pathway and the complement cascade.

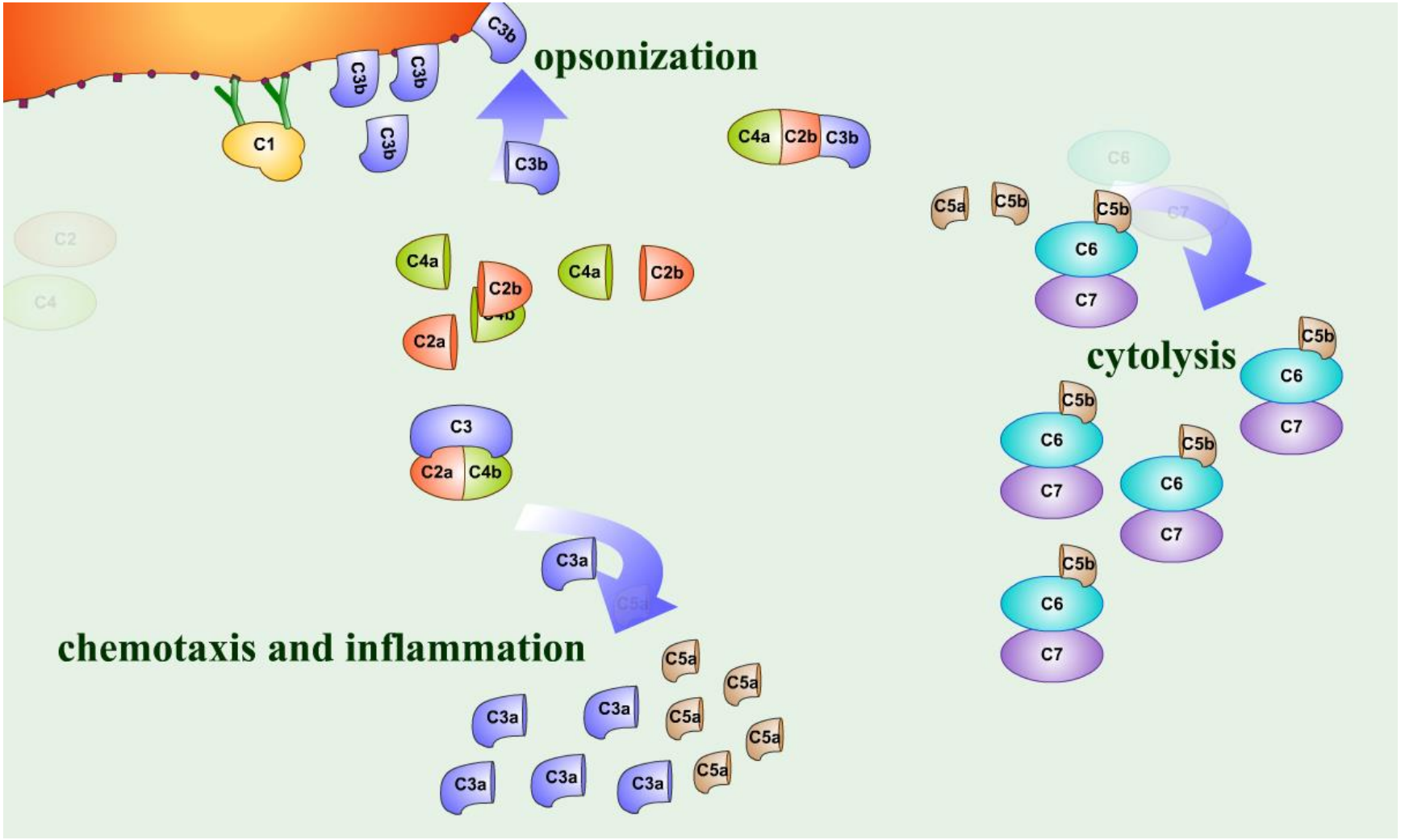


Complement: Activation



PLAY **Complement: Activation**

Complement: Results



PLAY **Complement: Results**

The Body's Second Line of Defense

- **Inflammation**
  - Nonspecific response to tissue damage from various causes
  - Characterized by redness (rubor), heat (calor), edema (swelling), and pain (dolor)
  - Two types:
    - Acute
    - Chronic
  - Three functions:
    - To destroy the agent causing injury
    - To limit the effects of the agent on the rest of the body
    - To repair or replace the damaged tissue

The Body's Second Line of Defense

- **Inflammation**
  - **Acute inflammation**
    - Develops quickly and is short lived
    - Is typically beneficial
    - Is important in the second line of defense
      - Dilation and increased permeability of the blood vessels
      - Migration of phagocytes
      - Tissue repair
  - **Chronic inflammation**
    - Long-lasting
    - Damage to tissues can cause disease

Figure 15.11 The dilating effect of inflammatory mediators on small blood vessels.

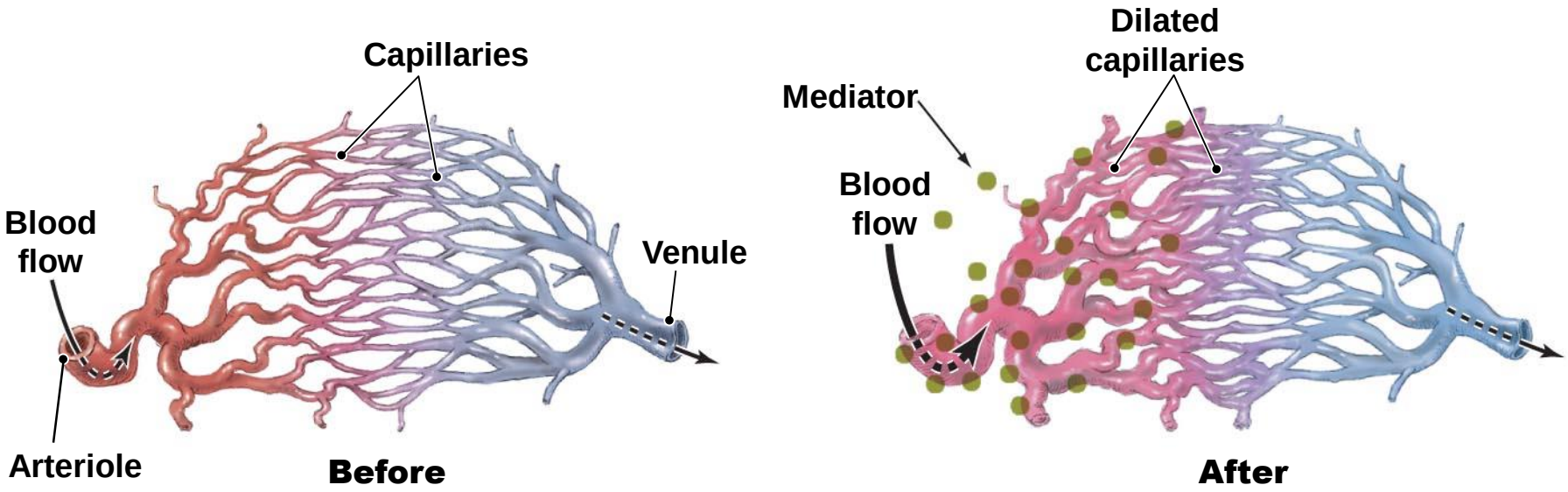


Figure 15.12 The stimulation of inflammation by complement.

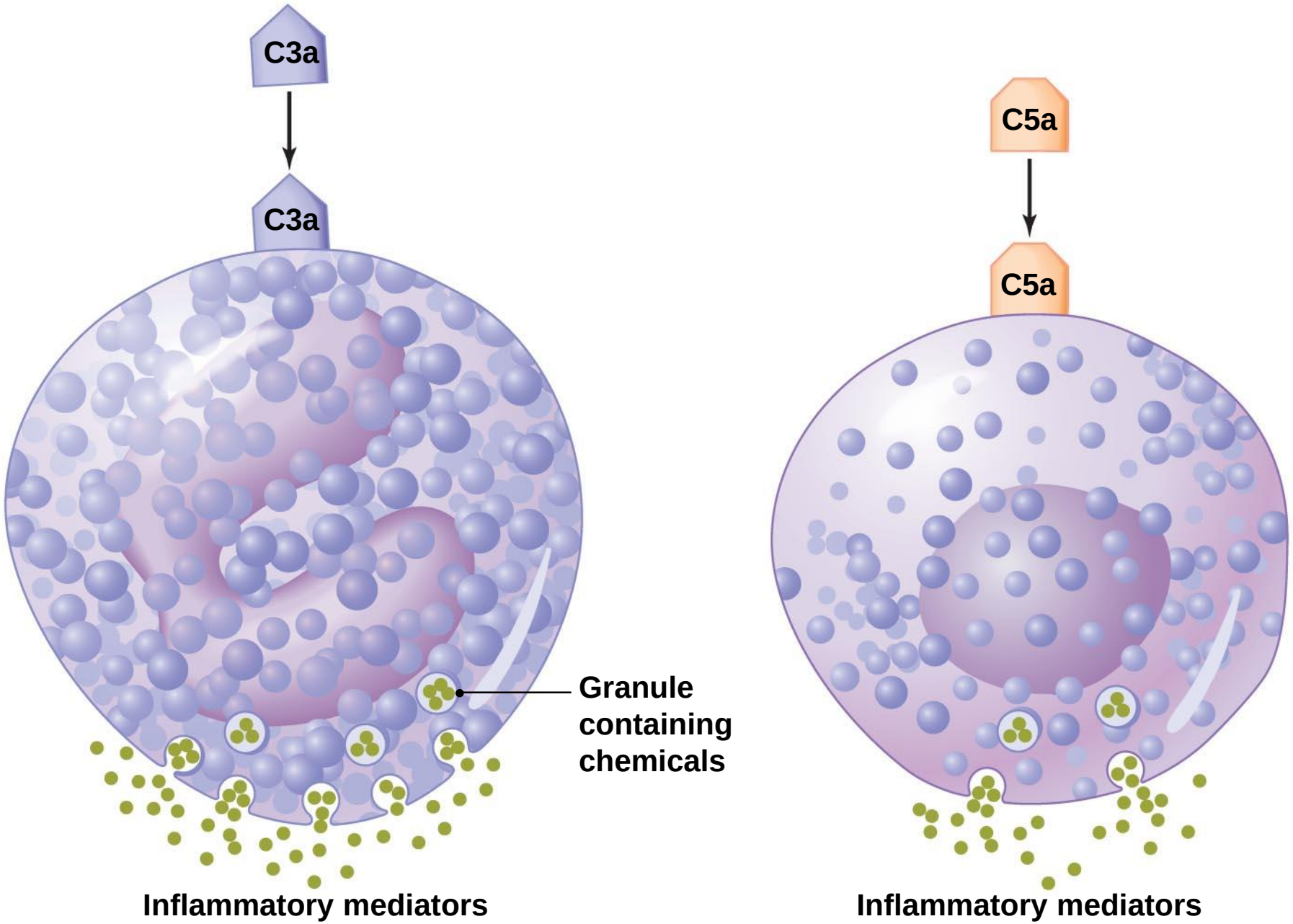


Figure 15.13 Increased vascular permeability during inflammation.

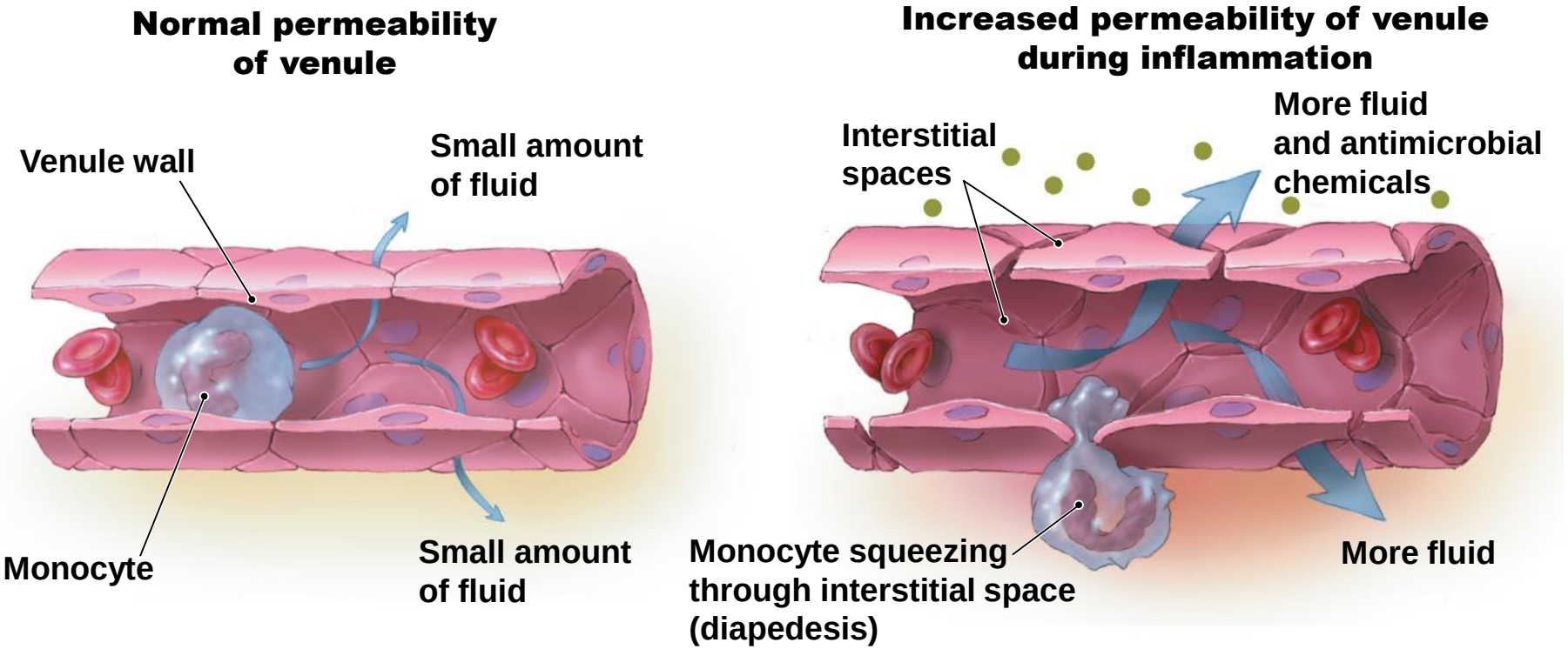
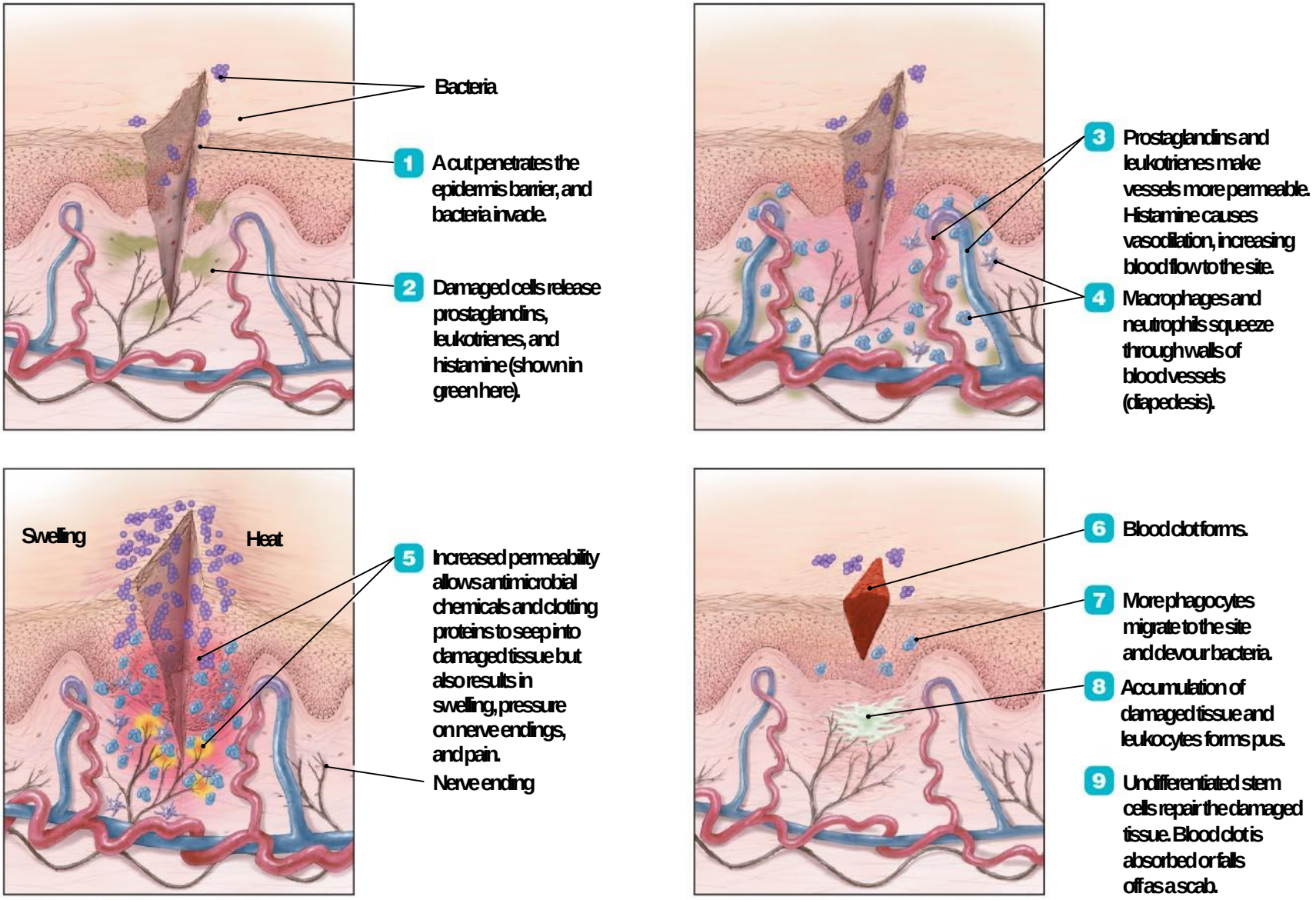
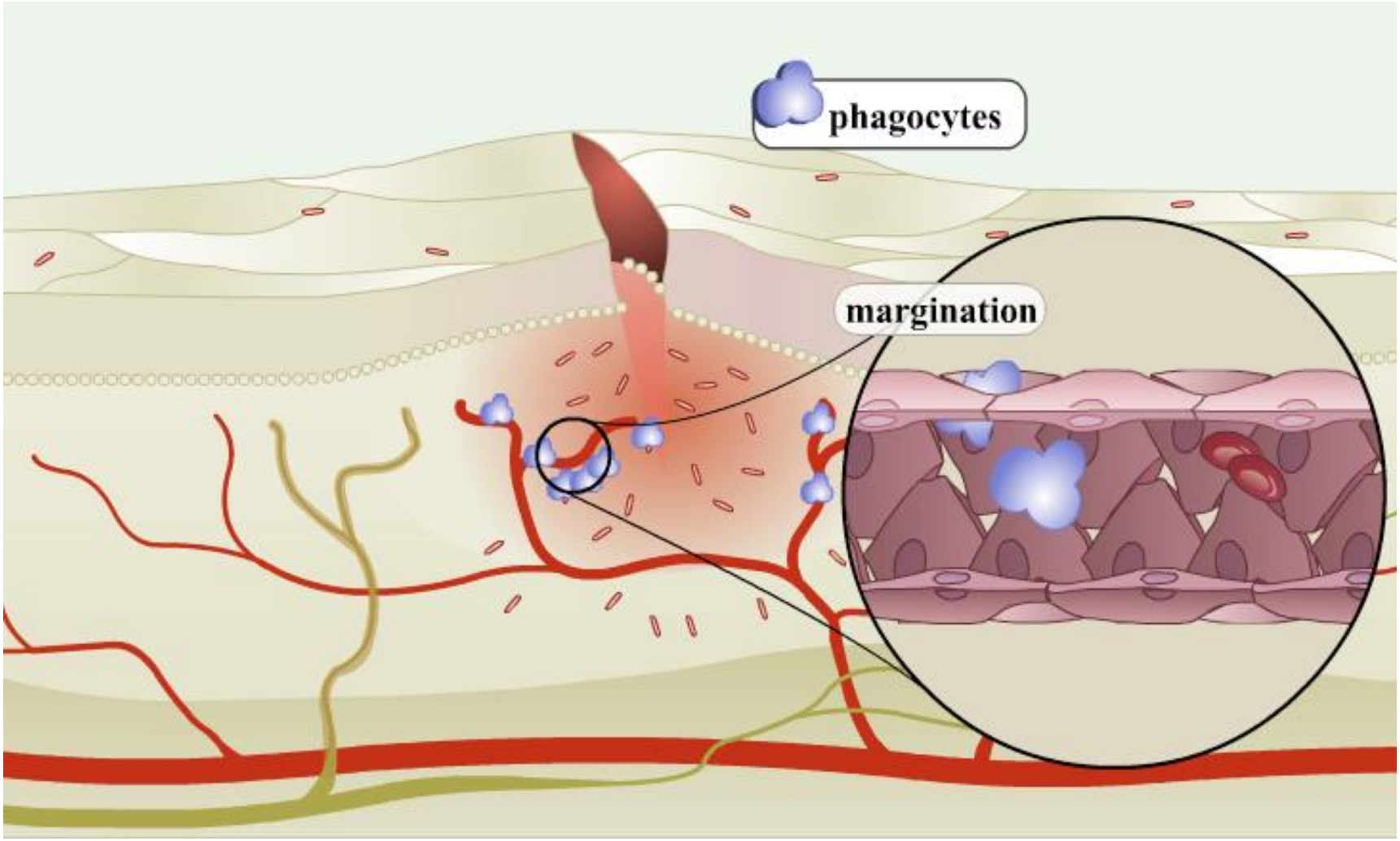


Figure 15.14 An overview of the events in inflammation following a cut and infection.



Inflammation: Steps



PLAY **Inflammation: Steps**

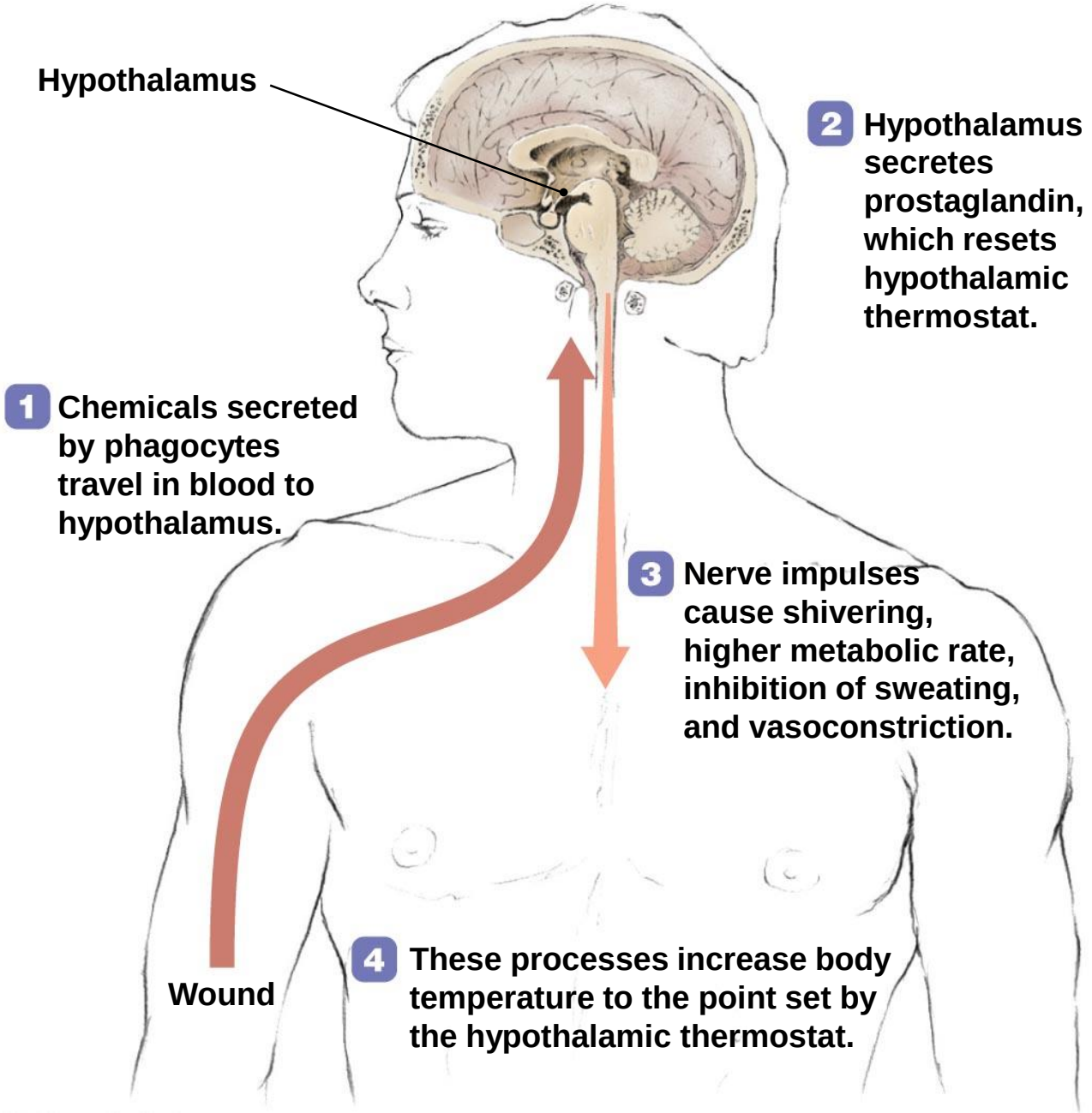
TABLE 15.5 Chemical Mediators of Inflammation

Vasodilating Chemicals	Histamine, serotonin, bradykinin, prostaglandins
Chemotactic Factors	Fibrin, collagen, mast cell chemotactic factors, bacterial peptides
Substances with Both Vasodilating and Chemotactic Effects	Complement fragment C5a, interferons, interleukins, leukotrienes, platelet secretions

The Body's Second Line of Defense

- **Fever**
  - A body temperature over 37°C
  - Results when pyrogens trigger the hypothalamus to increase the body's core temperature
  - Various types of pyrogens:
    - Bacterial toxins
    - Cytoplasmic contents of bacteria released by lysis
    - Antibody-antigen complexes
    - Pyrogens released by phagocytes that have phagocytized bacteria
  - Exact mechanism of fever is not known

Figure 15.15 One theoretical explanation for the production of fever in response to infection.



The Body's Second Line of Defense

- **Fever**
  - Continues as long as pyrogens are present
  - Outcomes of fever:
    - Enhances effects of interferons
    - Inhibits growth of some microbes
    - May enhance the activities of phagocytes, cells of specific immunity, and the process of tissue repair

TABLE 15.6 A Summary of Some Nonspecific Components of the First and Second Lines of Defense (Innate Immunity)

First Line	Second Line						
Barriers and Associated Chemicals	**Phagocytes**	**Extracellular Killing**	**Complement**	**Interferons**	**Antimicrobial Peptides**	**Inflammation**	**Fever**
Skin and mucous membranes prevent the entrance of pathogens; chemicals (e.g., sweat, acid, lysozyme, mucus) enhance the protection	Macrophages, neutrophils, and eosinophils ingest and destroy pathogens	Eosinophils and NK lymphocytes kill pathogens without phagocytizing them; neutrophils can also kill without phagocytosis	Components attract phagocytes, stimulate inflammation, and attack a pathogen's cytoplasmic membrane	Increase resistance of cells to viral infection, slow the spread of disease	Interfere with membranes, internal signaling, and metabolism; act against pathogens	Increases blood flow, capillary permeability, and migration of leukocytes into infected area; walls off infected region, increases local temperature	Mobilizes defenses, accelerates repairs, inhibits pathogens