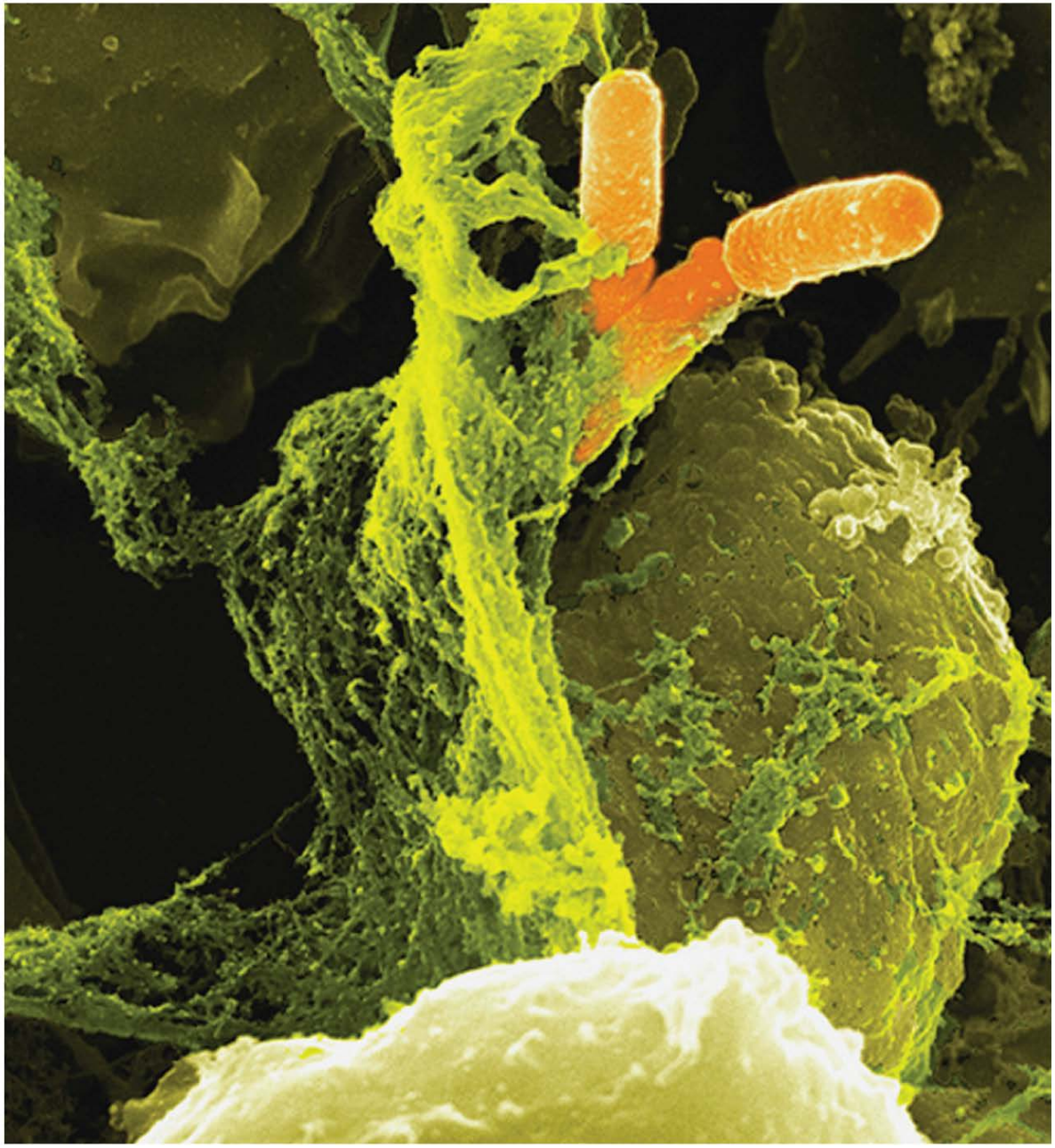


# Fever

- **Advantages**
  - Increases transferrins
  - Increases IL-1 activity
  - Produces interferon
- **Disadvantages**
  - Tachycardia
  - Acidosis
  - Dehydration
  - 44–46° C fatal

# The Concept of Immunity

- 16-1 Differentiate innate and adaptive immunity.
- 16-2 Define *Toll-like receptors*.

# The Concept of Immunity

- **Susceptibility**: lack of resistance to a disease
- **Immunity**: ability to ward off disease
- **Innate immunity**: defenses against any pathogen
- **Adaptive immunity**: immunity or resistance to a specific pathogen

# An Overview of the Body's Defenses


ANIMATION Host Defenses: The Big Picture

**Figure 16.1 An overview of the body's defenses.**

| Innate Immunity | | Adaptive Immunity (Chapter 17) |
|---|---|---|
| **First line of defense** | **Second line of defense** | **Third line of defense** |
| • Intact skin<br>• Mucous membranes and their secretions<br>• Normal microbiota | • Phagocytes, such as neutrophils, eosinophils, dendritic cells, and macrophages<br>• Inflammation<br>• Fever<br>• Antimicrobial substances | • Specialized lymphocytes: T cells and B cells<br>• Antibodies |

# The Concept of Immunity

- Host **Toll-like receptors (TLRs)** attach to **pathogen-associated molecular patterns (PAMPs)**
- TLRs induce **cytokines** that regulate the intensity and duration of immune responses

- Which defense system, innate or adaptive immunity, prevents entry of microbes into the body? 16-1
- What relationship do Toll-like receptors have to pathogen-associated molecular patterns? 16-2

# First Line of Defense: Skin and Mucous Membranes

16-3 Describe the role of the skin and mucous membranes in innate immunity.

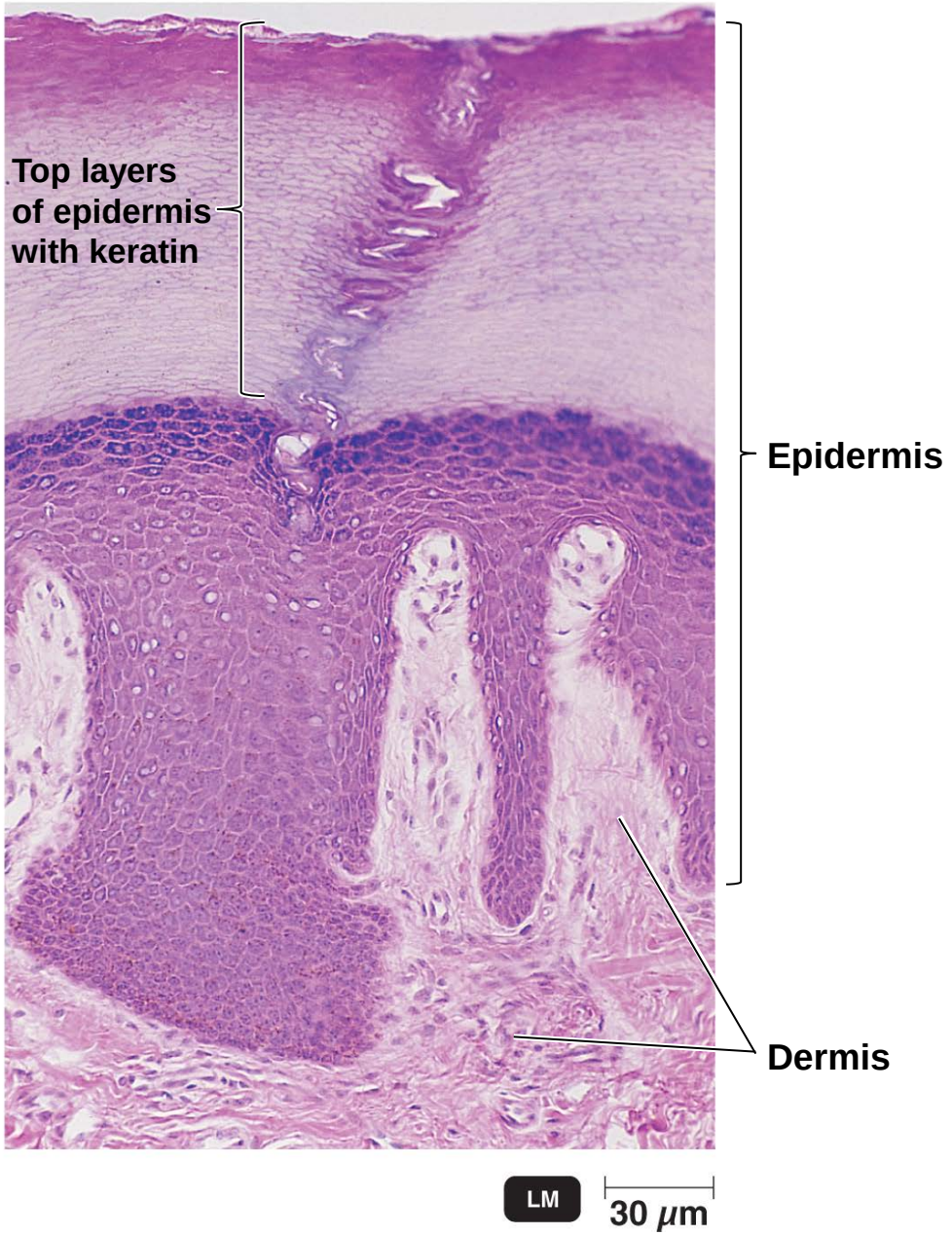
16-4 Differentiate physical from chemical factors, and list five examples of each.

16-5 Describe the role of normal microbiota in innate immunity.

# Physical Factors

- **Skin**
- **Epidermis** consists of tightly packed cells with
  - **Keratin**, a protective protein

**Figure 16.2 A section through human skin.**



# Physical Factors

- **Mucous membranes**
- **Mucus**: traps microbes
- **Ciliary escalator**: transports microbes trapped in mucus away from the lungs

**Figure 24.7 Ciliated cells of the respiratory system infected with *Bordetella pertussis*.**

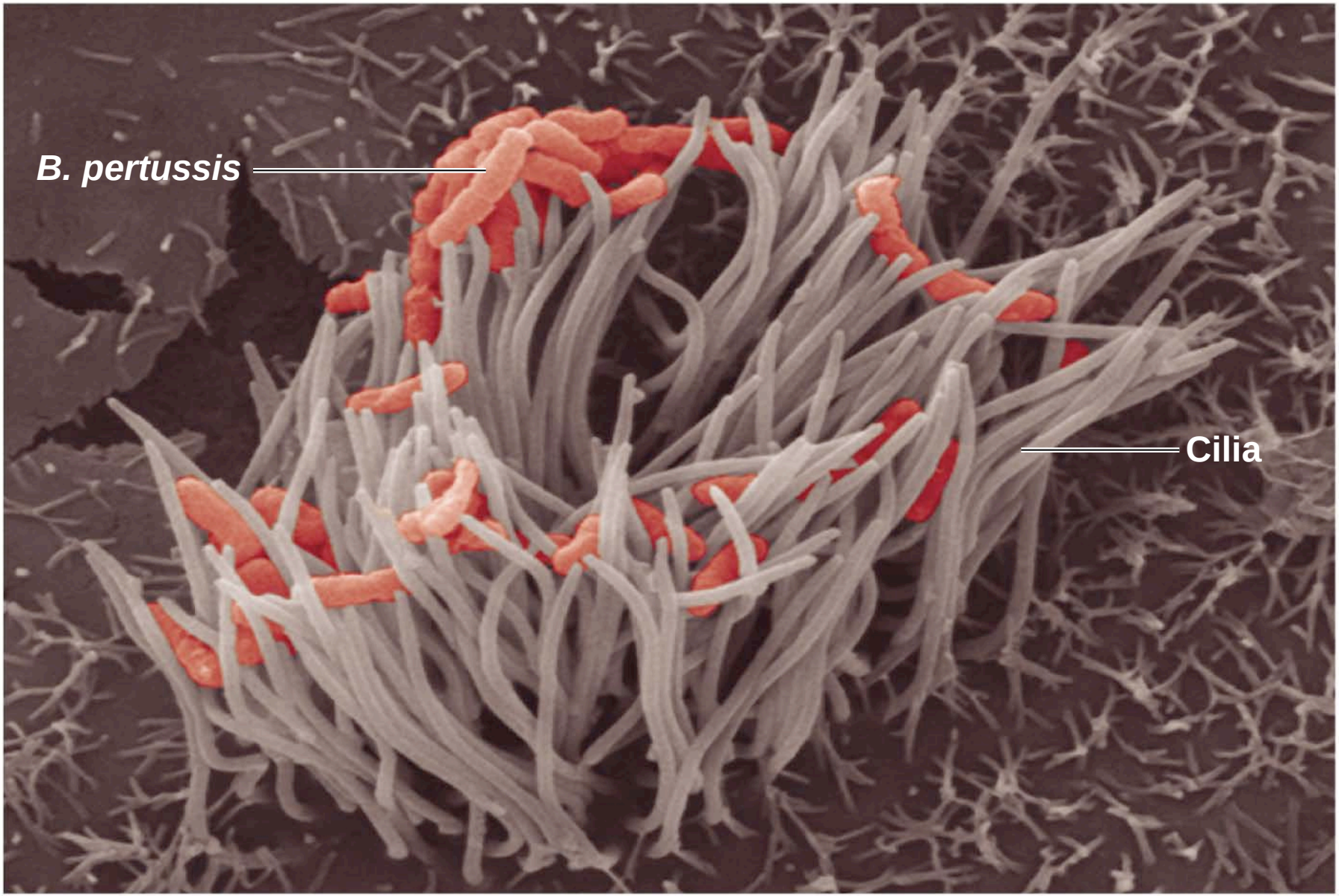
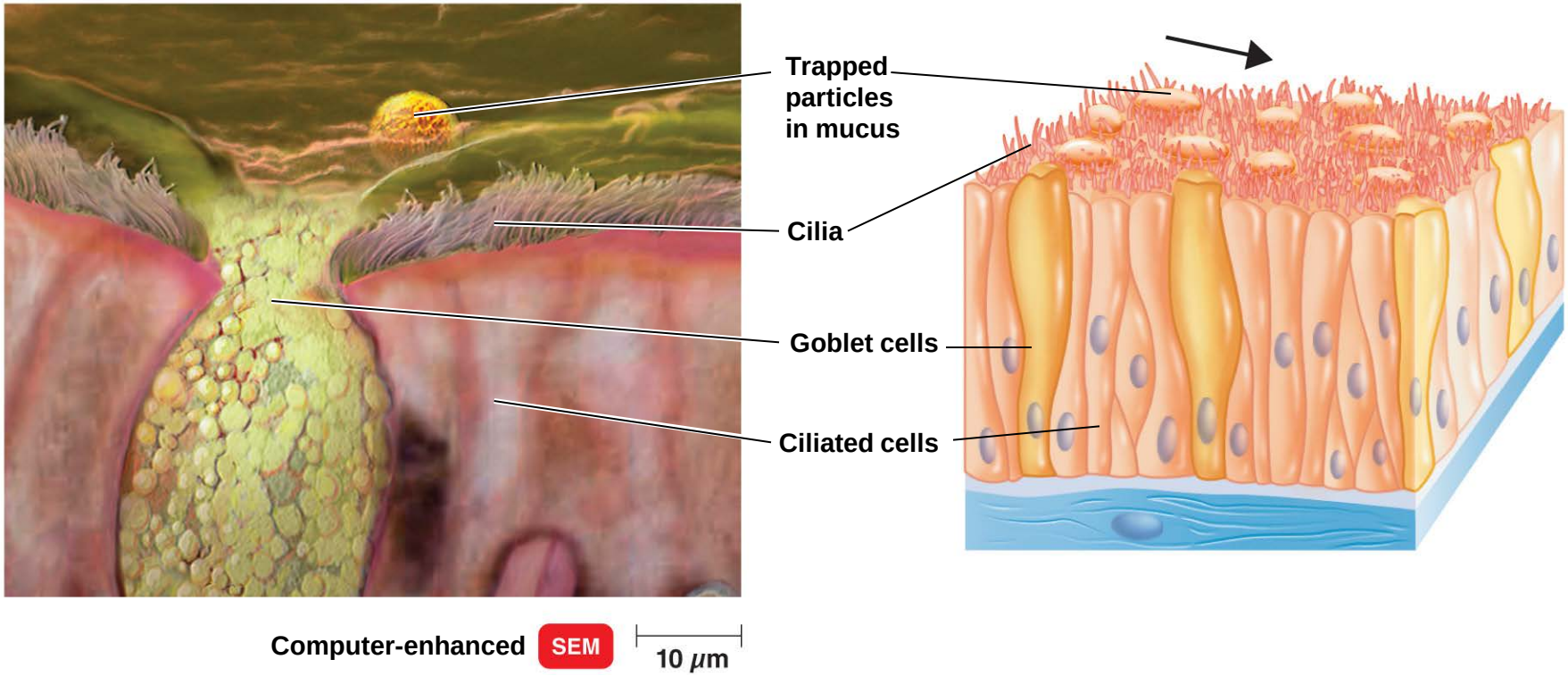


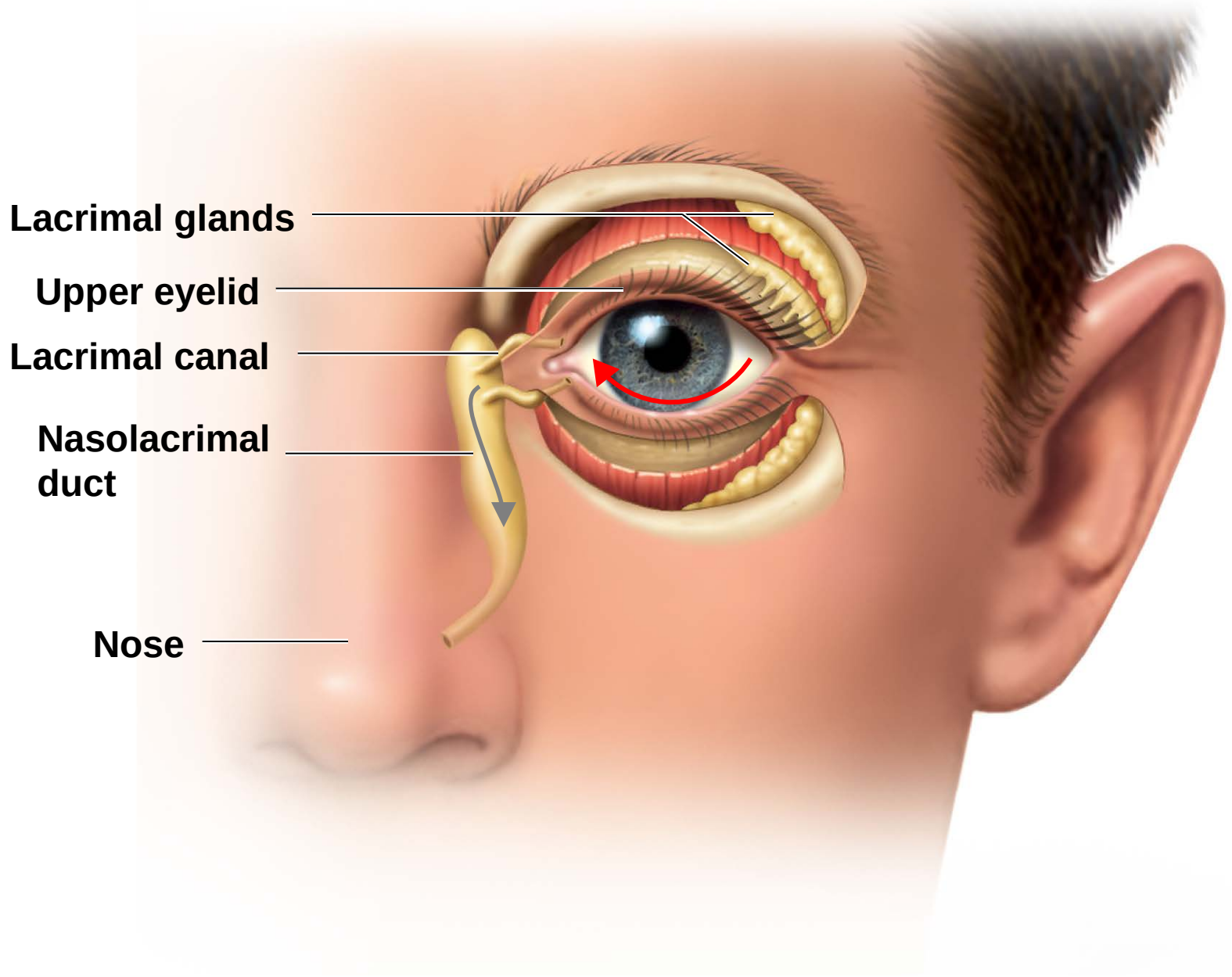
**Figure 16.4 The ciliary escalator.**



# Physical Factors

- **Lacrimal apparatus**: washes eye
- **Saliva**: washes microbes off
- **Urine**: flows out
- **Vaginal secretions**: flow out

**Figure 16.3 The lacrimal apparatus.**



# Chemical Factors

- Fungistatic fatty acid in **sebum**
- Low pH (3–5) of skin
- **Lysozyme** in **perspiration**, tears, saliva, and **urine**
- Low pH (1.2–3.0) of **gastric juice**
- Low pH (3–5) of **vaginal secretions**

# Normal Microbiota and Innate Immunity

- Microbial antagonism/competitive exclusion: **normal microbiota** compete with pathogens or alter the environment
- Commensal microbiota: one organism (microbe) benefits, and the other (host) is unharmed
  - May be opportunistic pathogens

- Identify one physical factor and one chemical factor that prevent microbes from entering the body through skin and mucous membranes. 16-3
- Identify one physical factor and one chemical factor that prevent microbes from entering or colonizing the body through the eyes, digestive tract, and respiratory tract. 16-4
- Distinguish microbial antagonism from commensalism. 16-5

# Second Line of Defense

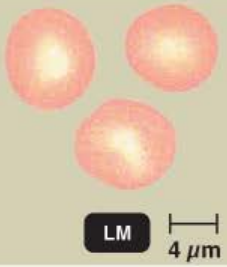
- 16-6 Classify leukocytes, and describe the roles of granulocytes and monocytes.
- 16-7 Define *differential white blood cell count*.
- 16-8 Differentiate the lymphatic and blood circulatory systems.

# Table 16.1 Formed Elements in Blood (Part 1 of 2)

## TABLE 16.1 Formed Elements in Blood

**I. Erythrocytes (Red Blood Cells)**

4.8–5.4 million per µl or $mm^3$
Function: Transport of $O_2$ and $CO_2$

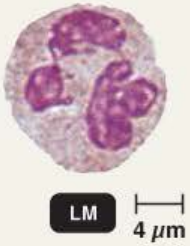



**II. Leukocytes (White Blood Cells)**

5000–10,000 per µl or $mm^3$

A. Granulocytes (stained)

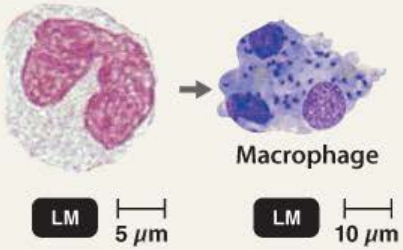
1. Neutrophils (PMNs)
(60–70% of leukocytes)
Function: Phagocytosis



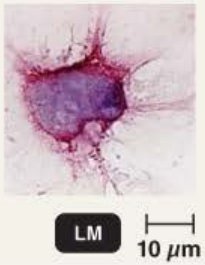

2. Basophils (0.5–1%)
Function: Production of histamine


B. Agranulocytes (stained)

1. Monocytes (3–8%)
Function: Phagocytosis (when they mature into macrophages)



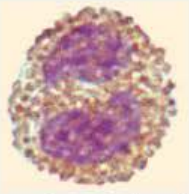

2. Dendritic cells
Functions: Derived from monocytes; phagocytosis and initiation of adaptive immune responses



# Table 16.1 Formed Elements in Blood (Part 2 of 2)

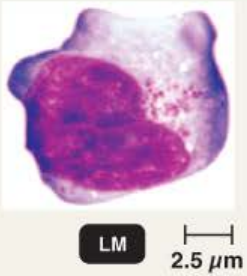
## TABLE 16.1 Formed Elements in Blood

3. Eosinophils (2–4%)
Functions: Production of toxic proteins against certain parasites; some phagocytosis

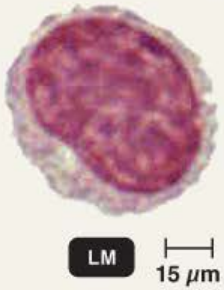



3. Lymphocytes (20–25%)

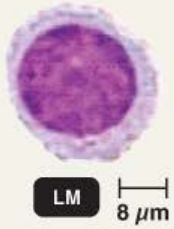
- Natural killer (NK) cells
Function: Destroy target cells by cytolysis and apoptosis




- T cells
Function: Cell-mediated immunity (discussed in Chapter 17)




- B cells
Function: Descendants of B cells (plasma cells) produce antibodies




**III. Platelets**

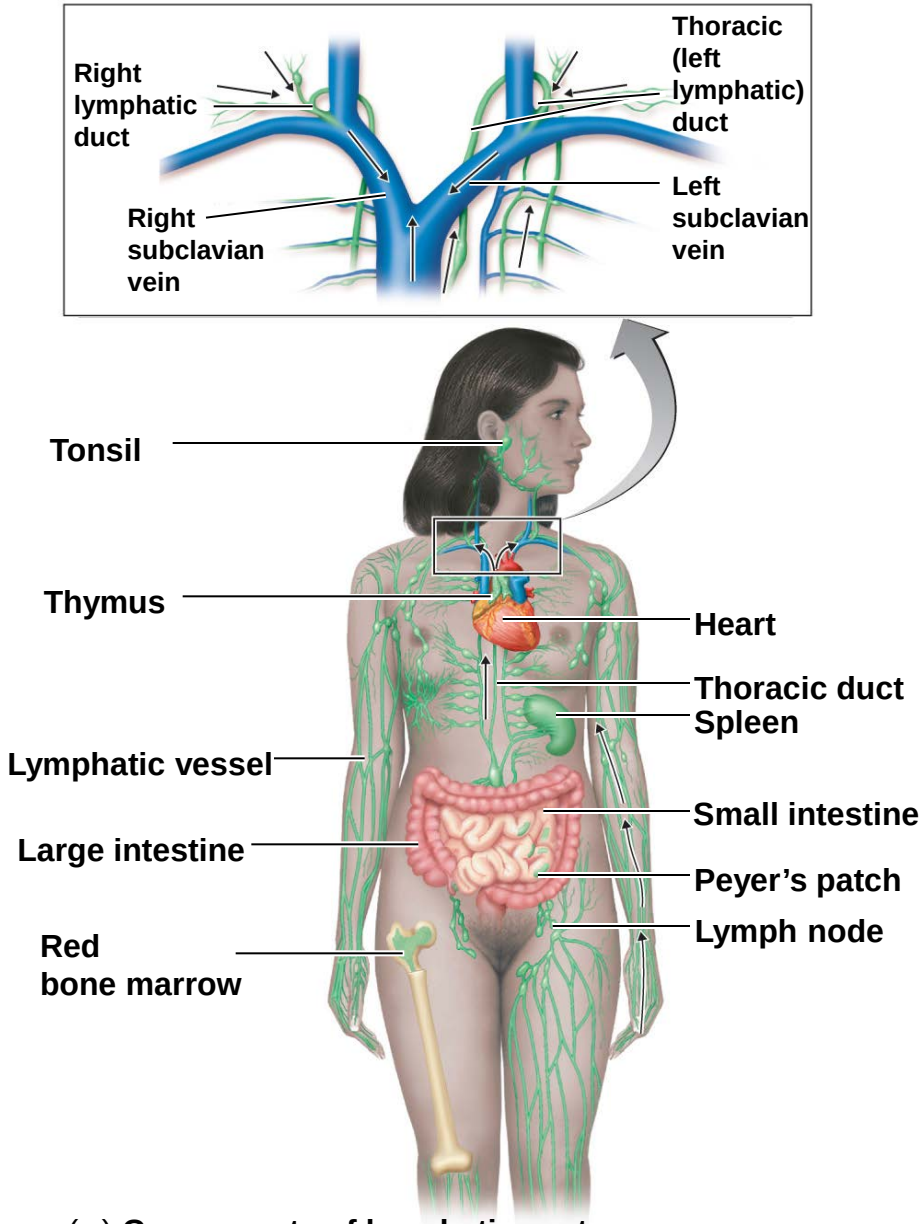
150,000–400,000 per μl or $mm^3$
Function: Blood clotting

# Differential White Cell Count

- Percentage of each type of white cell in a sample of 100 white blood cells

| | |
|---|---|
| **Neutrophils** | 60–70% |
| **Basophils** | 0.5–1% |
| **Eosinophils** | 2–4% |
| **Monocytes** | 3–8% |
| **Lymphocytes** | 20–25% |

**Figure 16.5a The lymphatic system.**

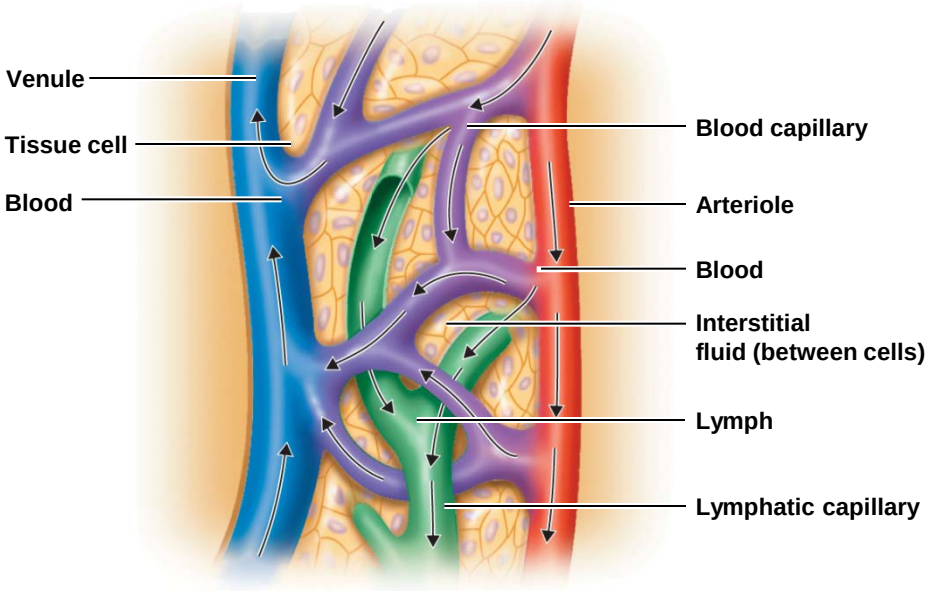



(a) **Components of lymphatic system**

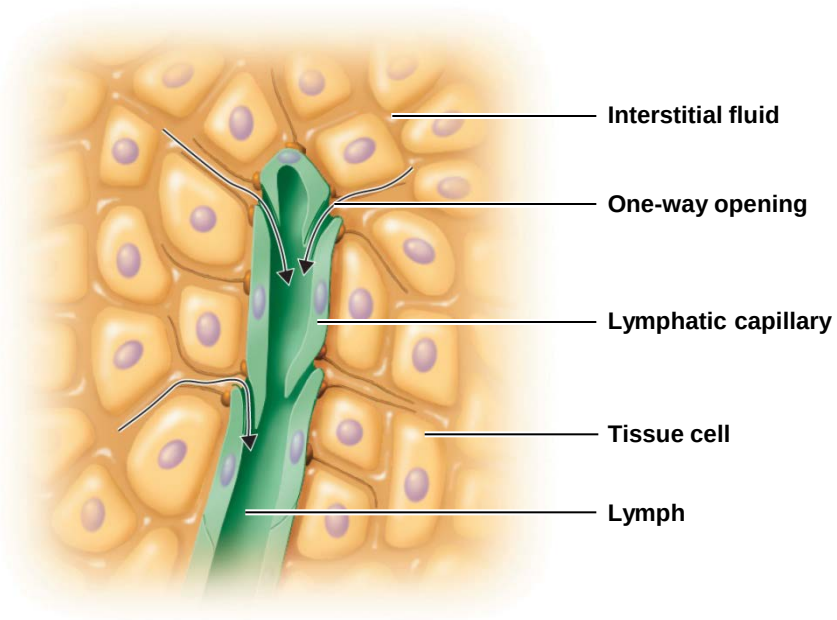
# The Lymphatic System


ANIMATION Host Defenses: Overview

# Figure 16.5b-c The lymphatic system.




(b) Relationship of lymphatic capillaries to tissue cells and blood capillaries




(c) Details of a lymphatic capillary

- Compare the structures and function of monocytes and neutrophils. 16-6
- Describe the six different types of white blood cells, and name a function for each type. 16-7
- What is the function of lymph nodes? 16-8

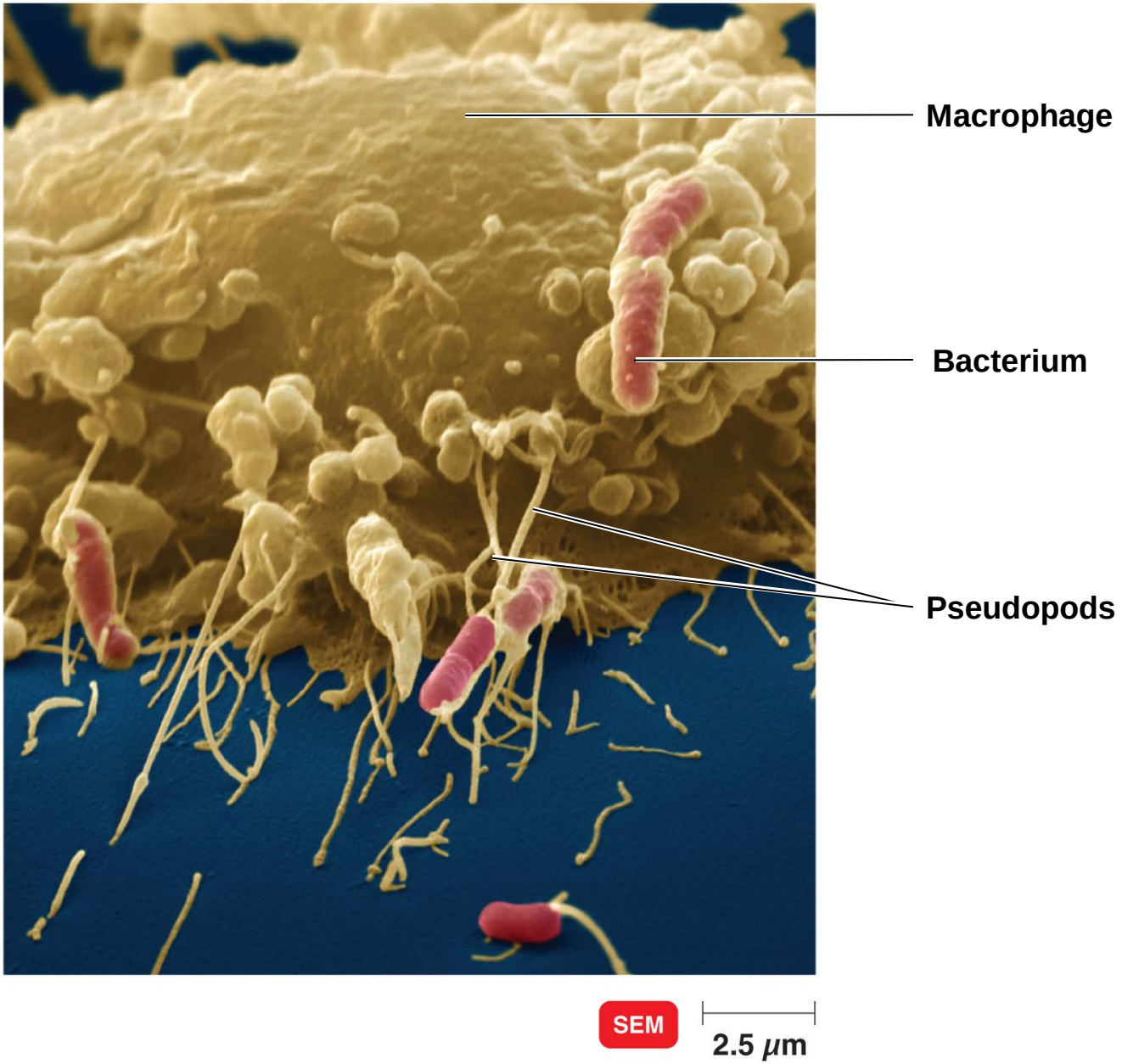
# Second Line of Defense

- 16-9 Define *phagocyte* and *phagocytosis*.
- 16-10 Describe the process of phagocytosis, and include the stages of adherence and ingestion.
- 16-11 Identify six mechanisms of avoiding destruction by phagocytosis.

# Phagocytosis

- *Phago*: from Greek, meaning eat
- *Cyte*: from Greek, meaning cell
- Ingestion of microbes or particles by a cell, performed by phagocytes

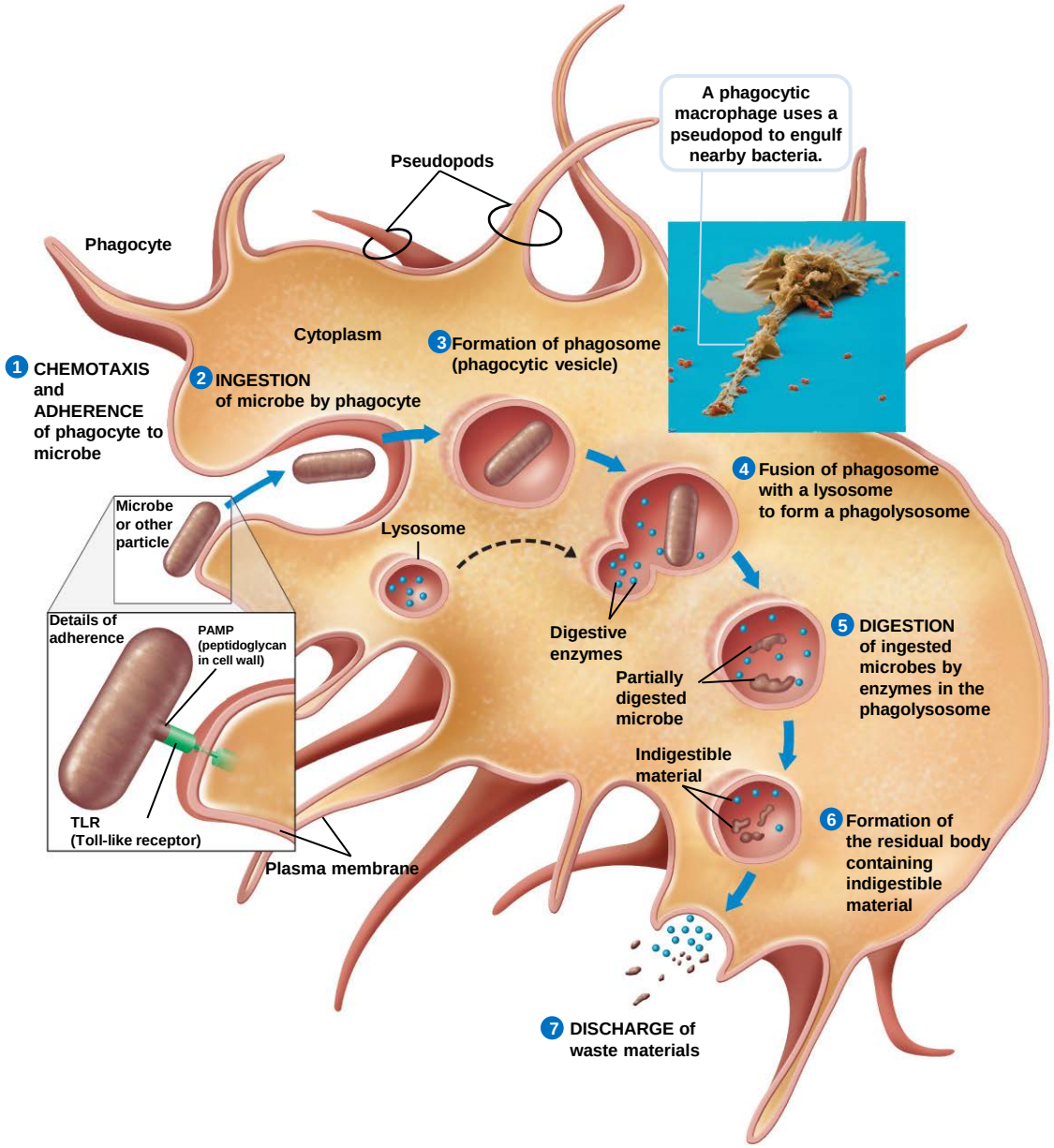
**Figure 16.6 A macrophage engulfing rod-shaped bacteria.**



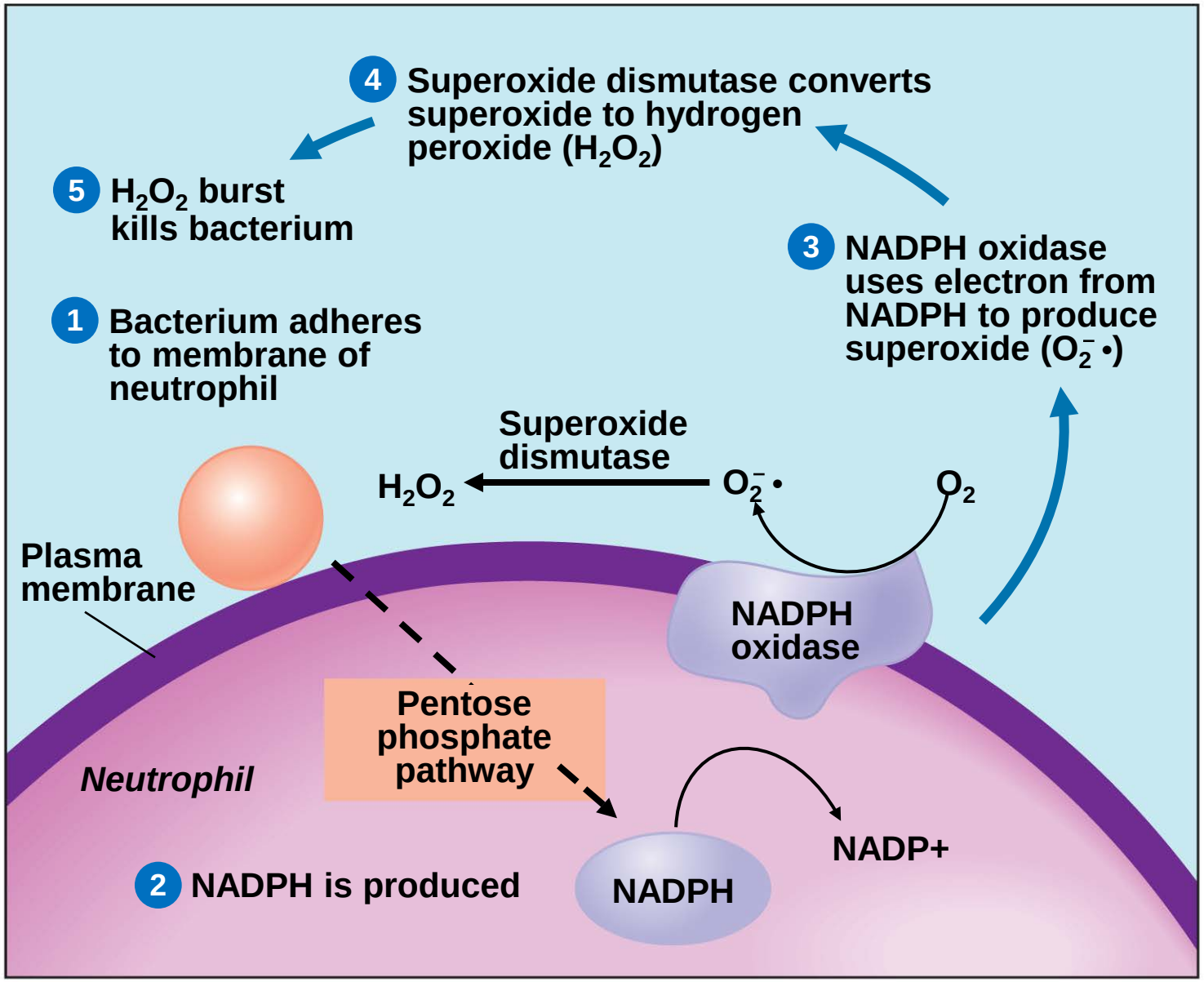
# Phagocytosis

- **Neutrophils**
- **Fixed macrophages**
- **Wandering macrophages**

# Figure 16.7 The Phases of Phagocytosis.



# Oxidative Burst



# Phagocytosis


ANIMATION Phagocytosis: Overview


ANIMATION Phagocytosis: Mechanism

# Microbial Evasion of Phagocytosis

| | |
|---|---|
| Inhibit adherence:<br>M protein, capsules | *Streptococcus pyogenes, S. pneumoniae* |
| Kill phagocytes: Leukocidins | *Staphylococcus aureus* |
| Lyse phagocytes:<br>Membrane attack complex | *Listeria monocytogenes* |
| Escape phagosome | *Shigella*, *Rickettsia* |
| Prevent phagosome–lysosome fusion | HIV, *Mycobacterium tuberculosis* |
| Survive in phagolysosome | *Coxiella burnettii* |

# Microbial Evasion of Phagocytosis


ANIMATION Virulence Factors: Hiding from Host Defenses


ANIMATION Virulence Factors: Inactivating Host Defenses


ANIMATION Phagocytosis: Microbes that Evade It

- What do fixed and wandering macrophages do? 16-9
- What is the role of TLRs in phagocytosis? 16-10
- How does each of these bacteria avoid destruction by phagocytes? *Streptococcus pneumoniae, Staphylococcus aureus, Listeria monocytogenes, Mycobacterium tuberculosis, Rickettsia* 16-11

# Second Line of Defense

- 16-12 List the stages of inflammation.
- 16-13 Describe the roles of vasodilation, kinins, prostaglandins, and leukotrienes in inflammation.
- 16-14 Describe phagocyte migration.
- 16-15 Describe the cause and effects of fever.

# Inflammation

- Activation of **acute-phase proteins** (complement, cytokine, and kinins)
- **Vasodilation** (histamine, kinins, prostaglandins, and leukotrienes)
- Redness
- Swelling (**edema**)
- Pain
- Heat

# Chemicals Released by Damaged Cells

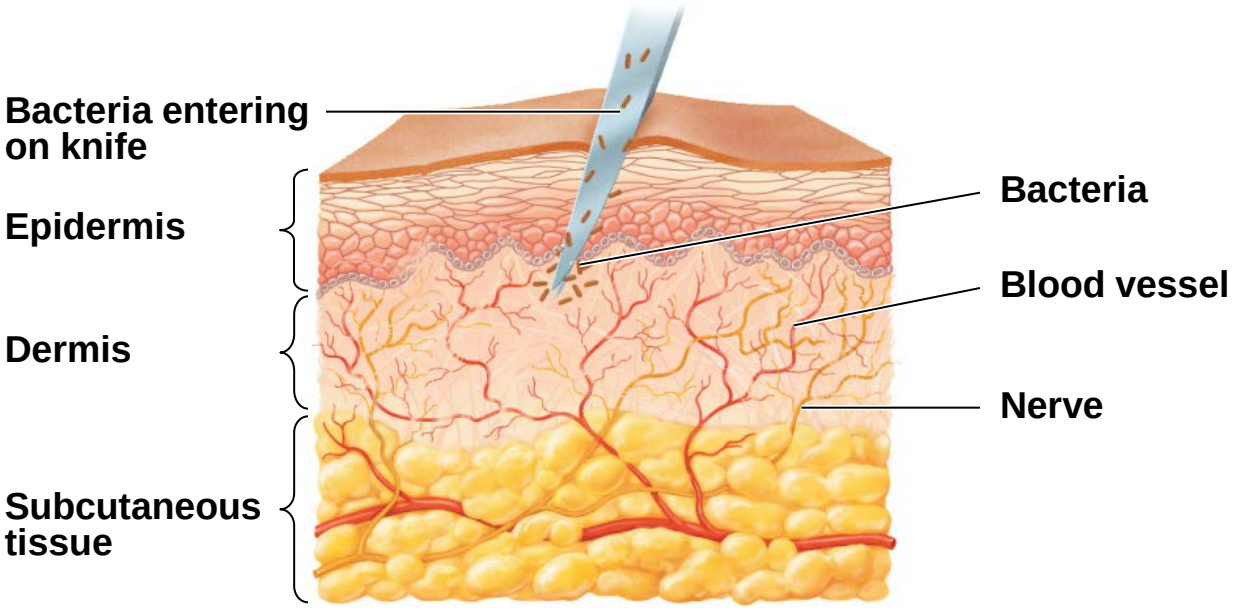
| | |
|---|---|
| **Histamine** | Vasodilation, increased permeability of blood vessels |
| **Kinins** | Vasodilation, increased permeability of blood vessels |
| **Prostaglandins** | Intensify histamine and kinin effect |
| **Leukotrienes** | Increased permeability of blood vessels, phagocytic attachment |

# Phagocyte Migration and Phagocytosis

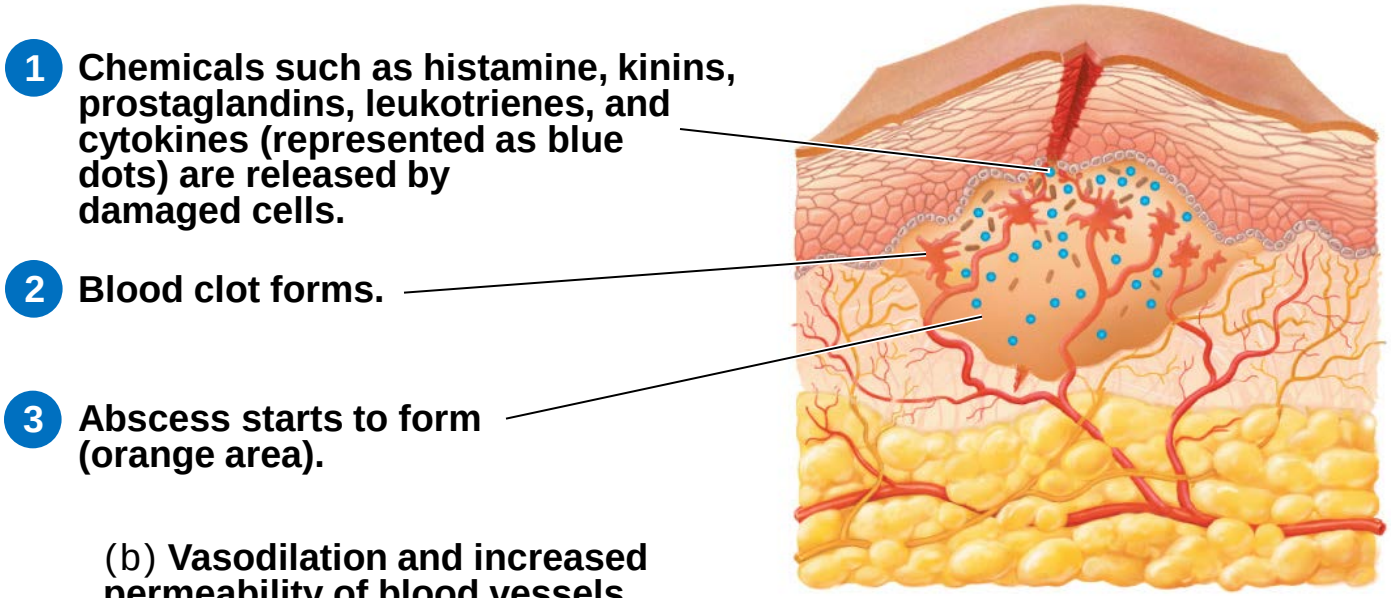

ANIMATION Inflammation: Overview


ANIMATION Inflammation: Steps

**Figure 16.8a-b The process of inflammation.**




(a) **Tissue damage**




(b) **Vasodilation and increased permeability of blood vessels**

Figure 16.8c The process of inflammation.

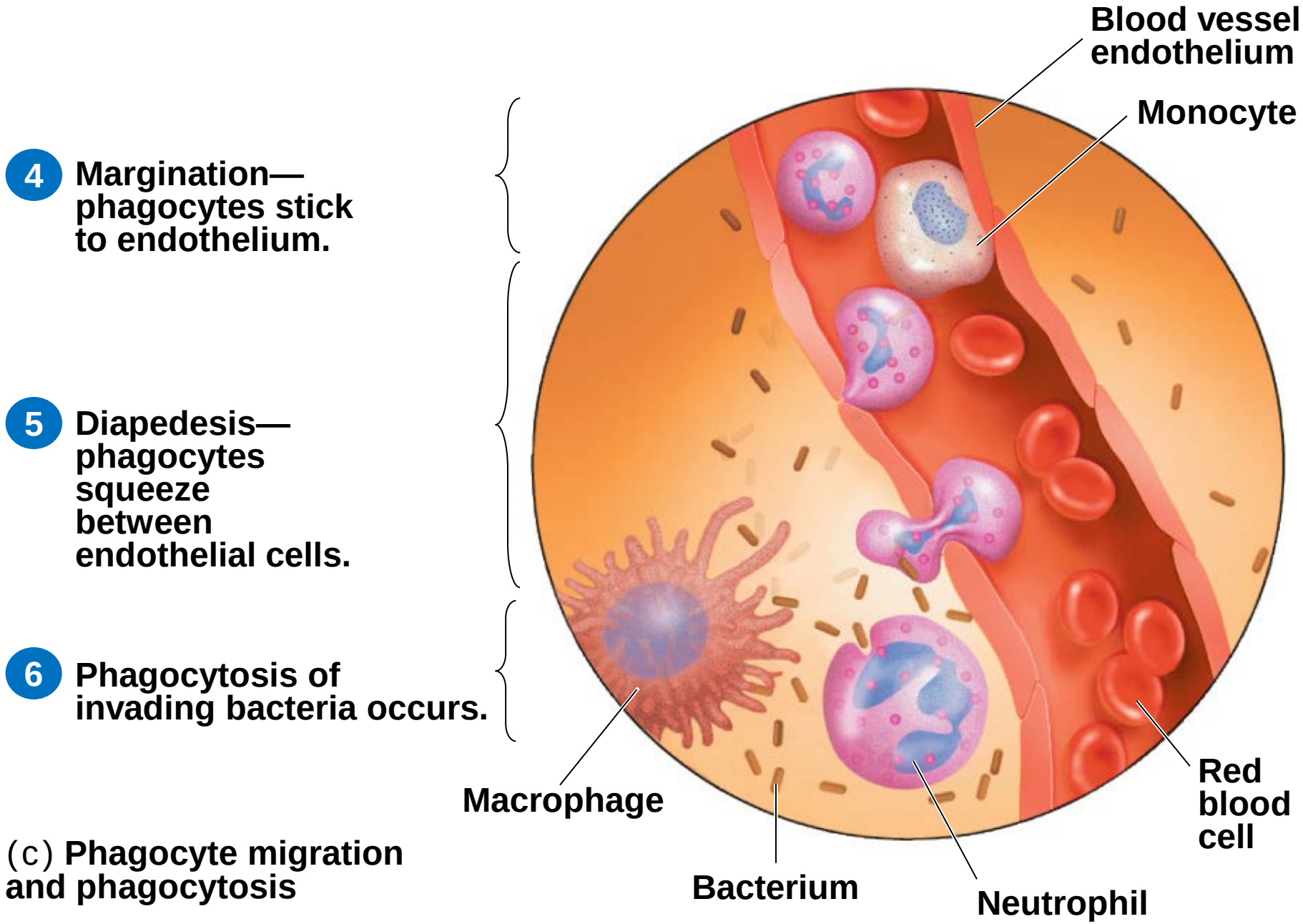
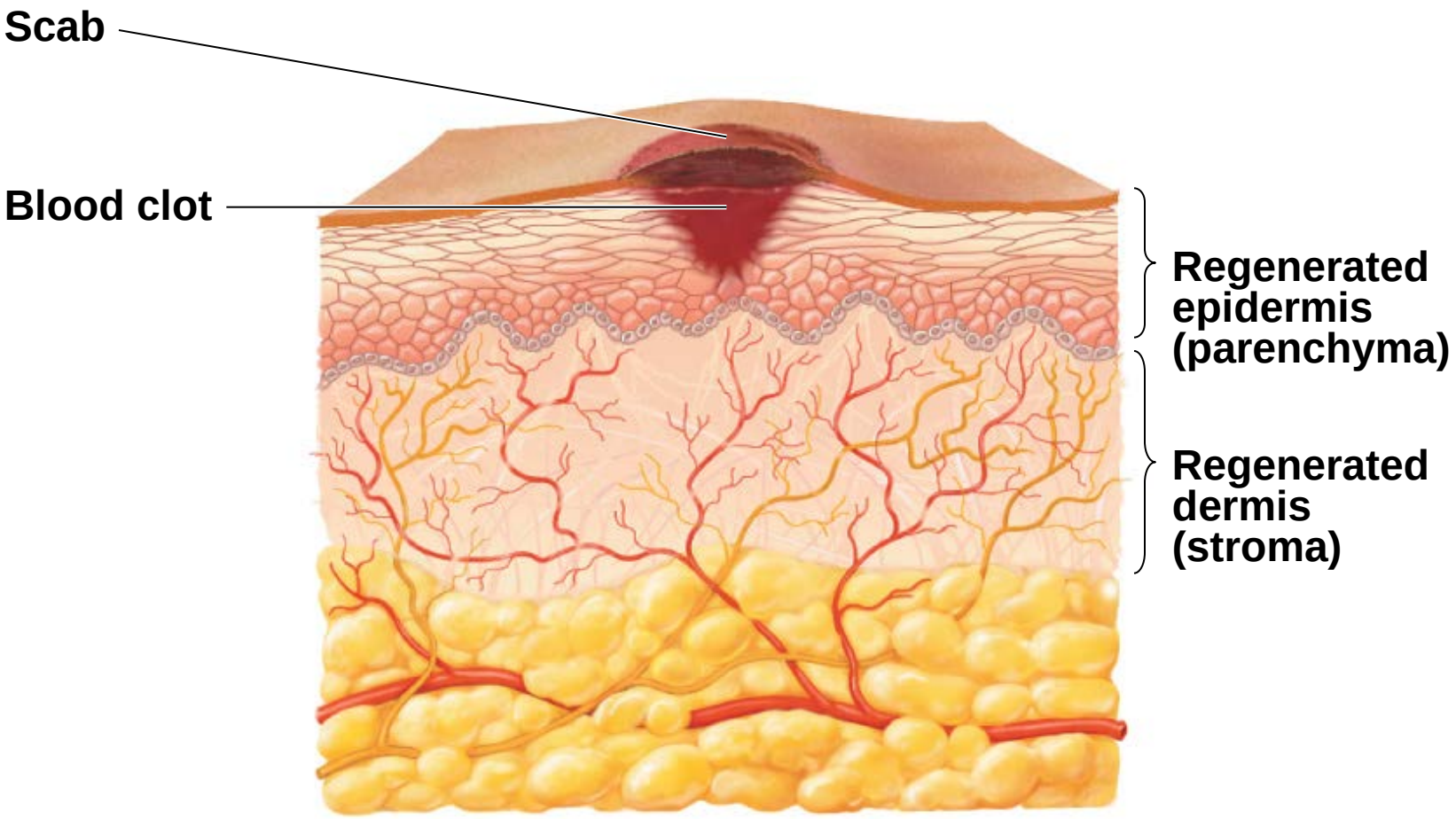


**Figure 16.8d The process of inflammation.**




(d) **Tissue repair**

# Fever

- Abnormally high body temperature
- Hypothalamus is normally set at 37° C
- Gram-negative endotoxins cause phagocytes to release interleukin-1 (IL-1)
- Hypothalamus releases prostaglandins that reset the hypothalamus to a high temperature
- Body increases rate of metabolism, and **shivering** occurs, which raise temperature
- Vasodilation and sweating: body temperature falls (**crisis**)

- What purposes does inflammation serve? 16-12
- What causes the redness, swelling, and pain associated with inflammation? 16-13
- What is margination? 16-14
- Why does a chill indicate that a fever is about to occur? 16-15

# Antimicrobial Substances

- 16-16 List the major components of the complement system.
- 16-17 Describe three pathways of activating complement.
- 16-18 Describe three consequences of complement activation.

# The Complement System

- Serum proteins activated in a cascade
- Activated by
  - Antigen–antibody reaction
  - Proteins C3, B, D, P and a pathogen


ANIMATION Complement: Overview

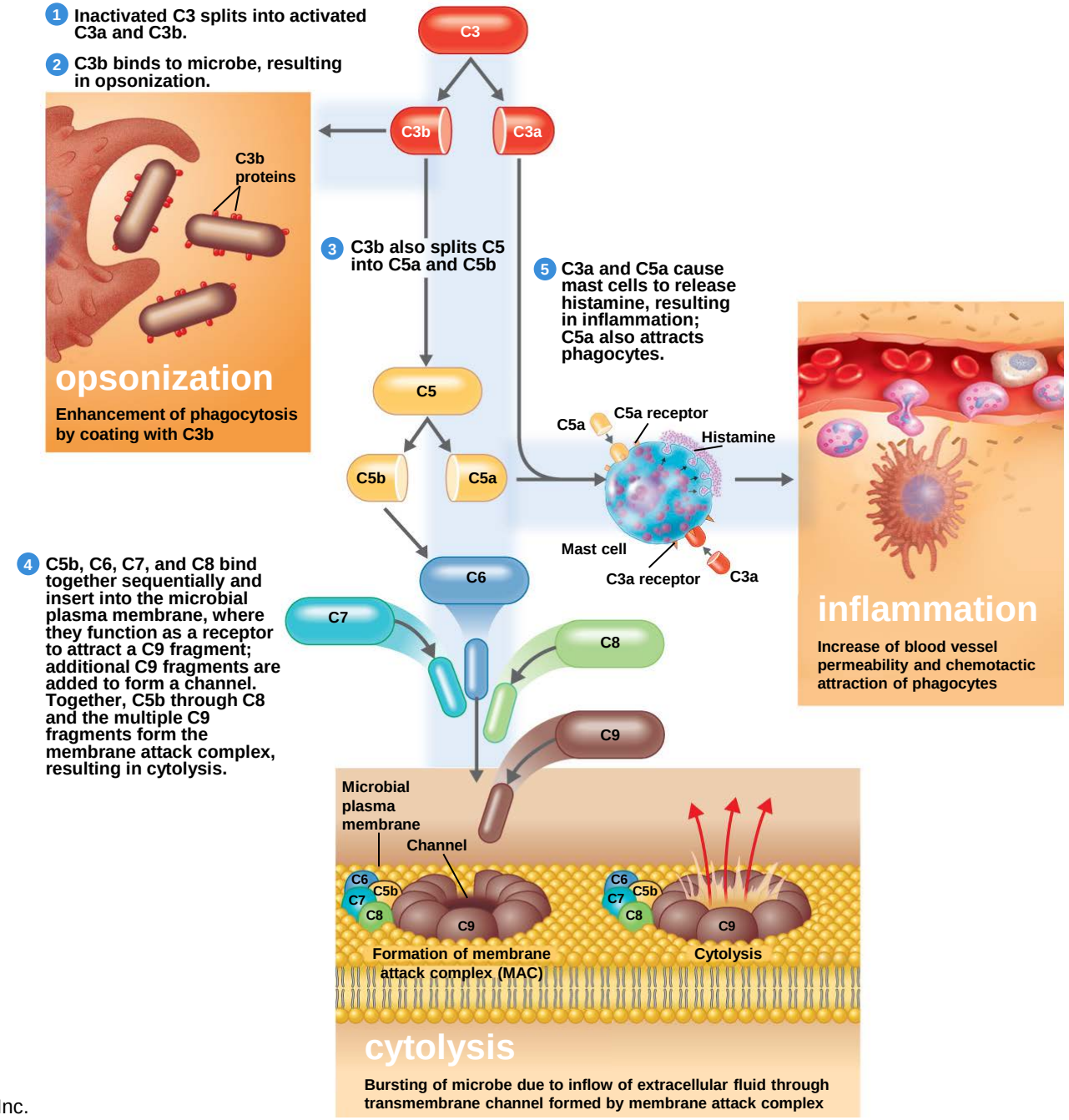

ANIMATION Complement: Activation

# The Complement System

- C3b causes opsonization
- C3a + C5a cause inflammation
- C5b + C6 + C7 + C8 + C9 cause cell lysis


ANIMATION Complement: Results

# Figure 16.9 Outcomes of Complement Activation.



# Effects of Complement Activation

- Opsonization, or immune adherence: enhanced phagocytosis
- Membrane attack complex: cytolysis
- Attract phagocytes

**Figure 16.10 Cytolysis caused by complement.**

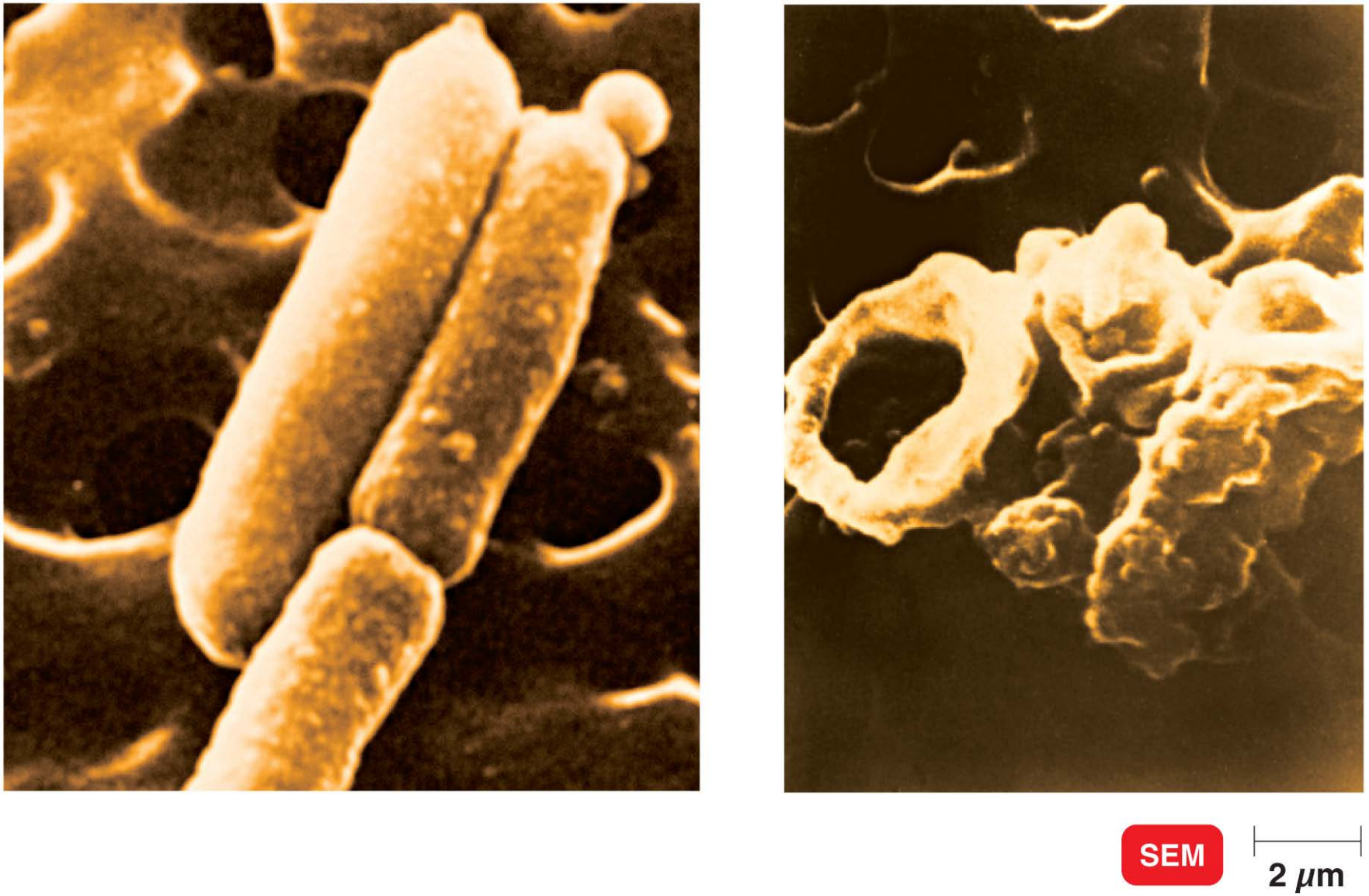


**Figure 16.11 Inflammation stimulated by complement.**

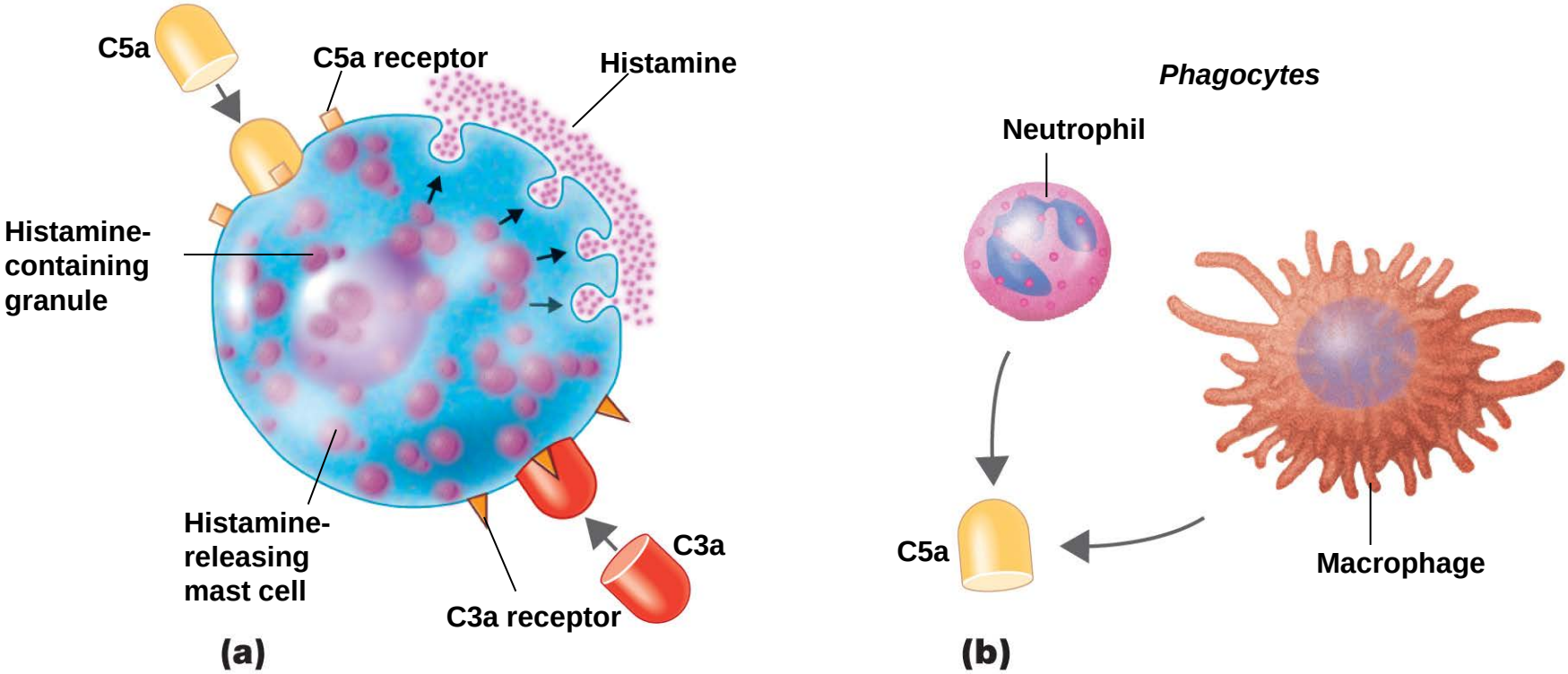


**Figure 16.12 Classical pathway of complement activation.**

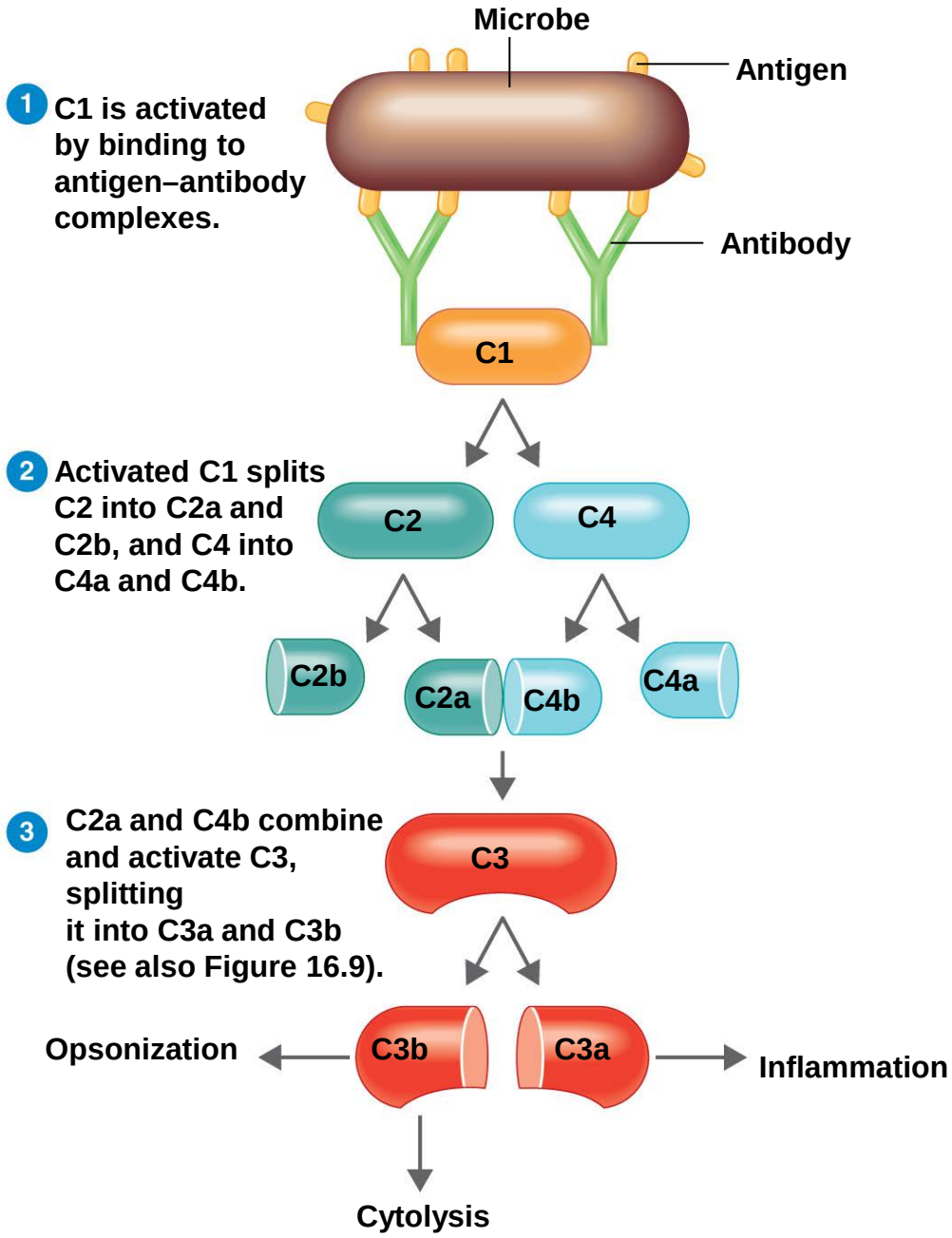


**Figure 16.13 Alternative pathway of complement activation.**

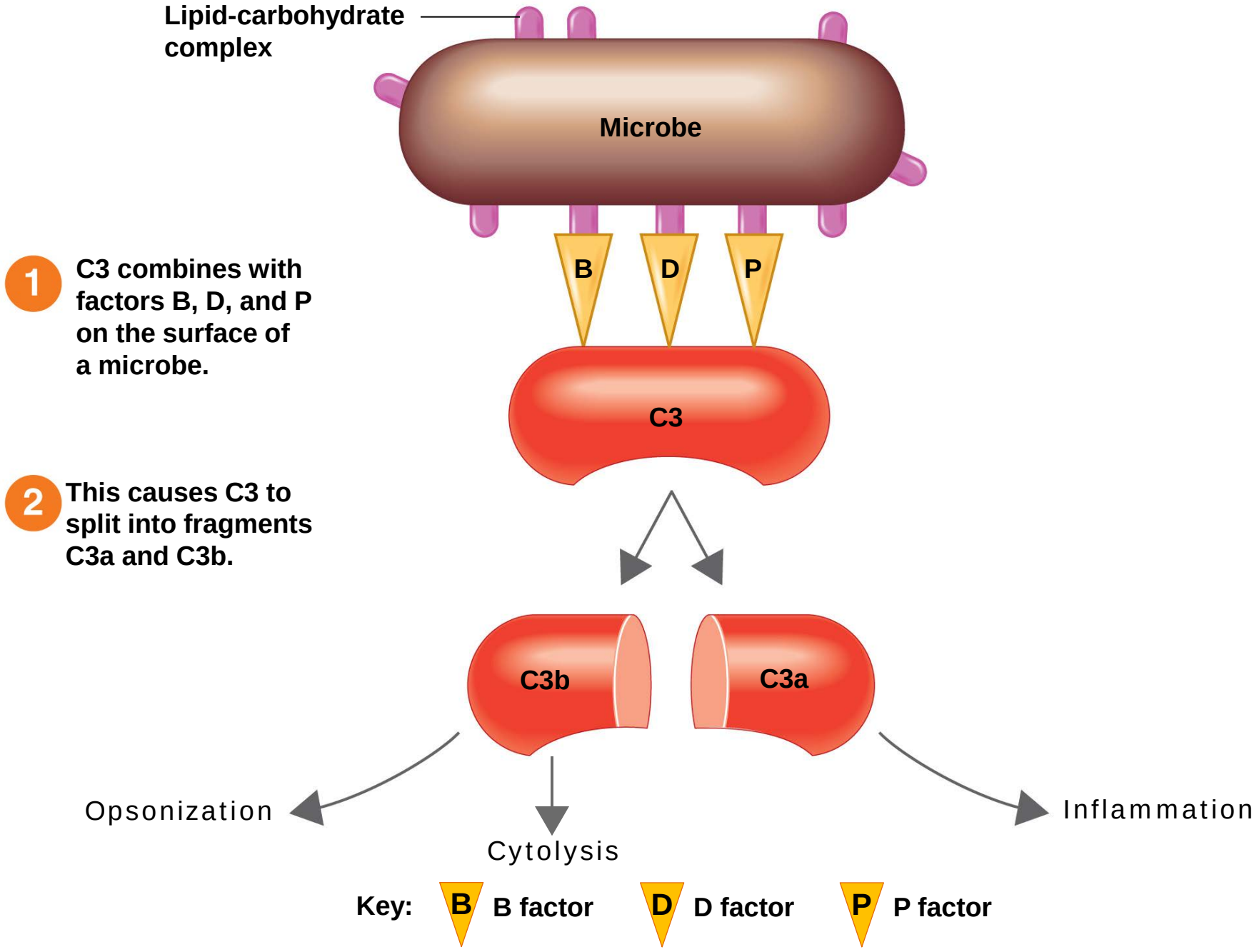
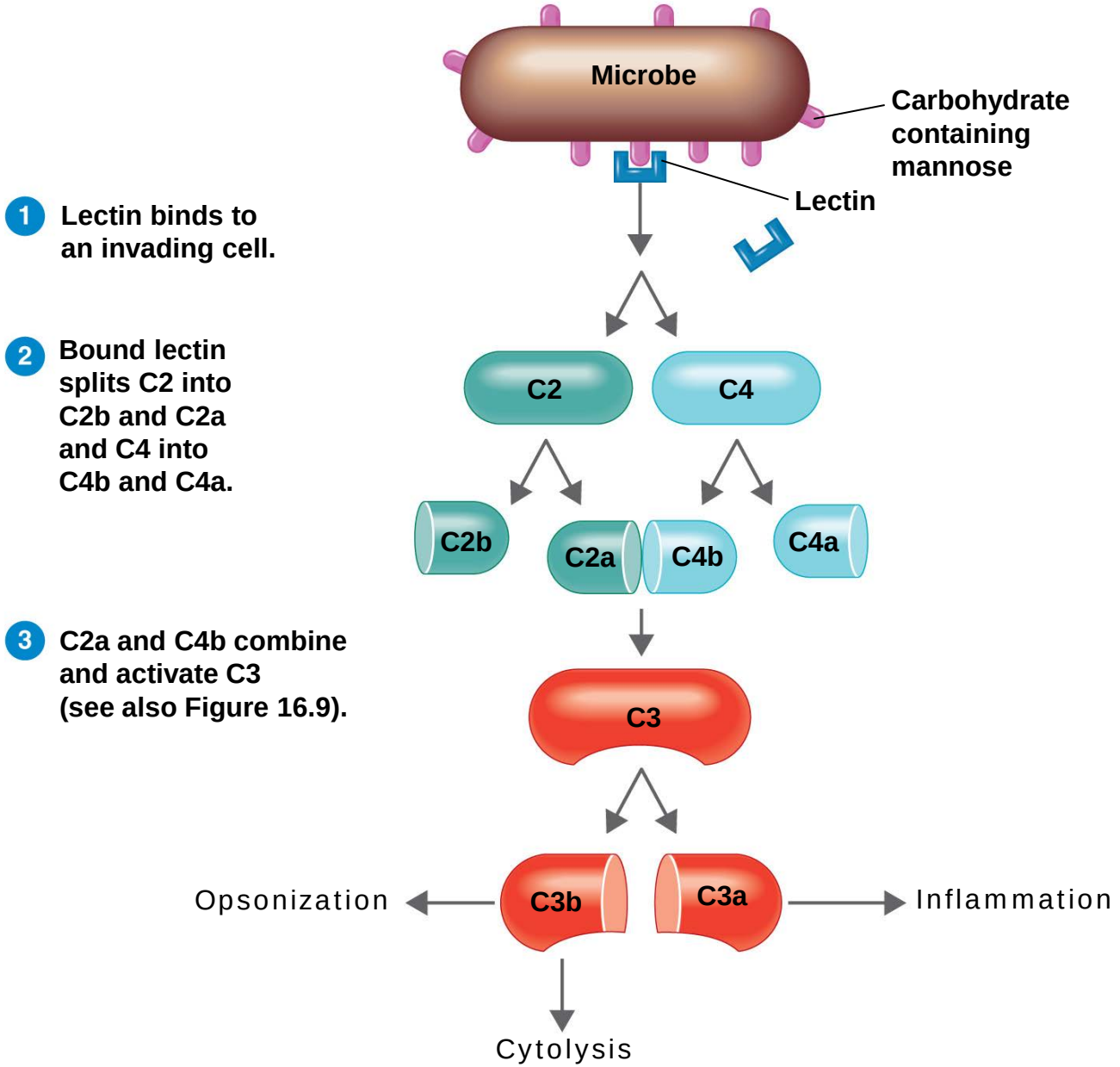


**Figure 16.14 The lectin pathway of complement activation.**



# Some Bacteria Evade Complement

- Capsules prevent C activation
- Surface lipid–carbohydrate complexes prevent formation of membrane attack complex (MAC)
- Enzymatic digestion of C5a

- What is complement? 16-16
- List the steps of complementation activation via (1) the classical pathway, (2) the alternative pathway, and (3) the lectin pathway. 16-17
- Summarize the major outcomes of complement activation. 16-18

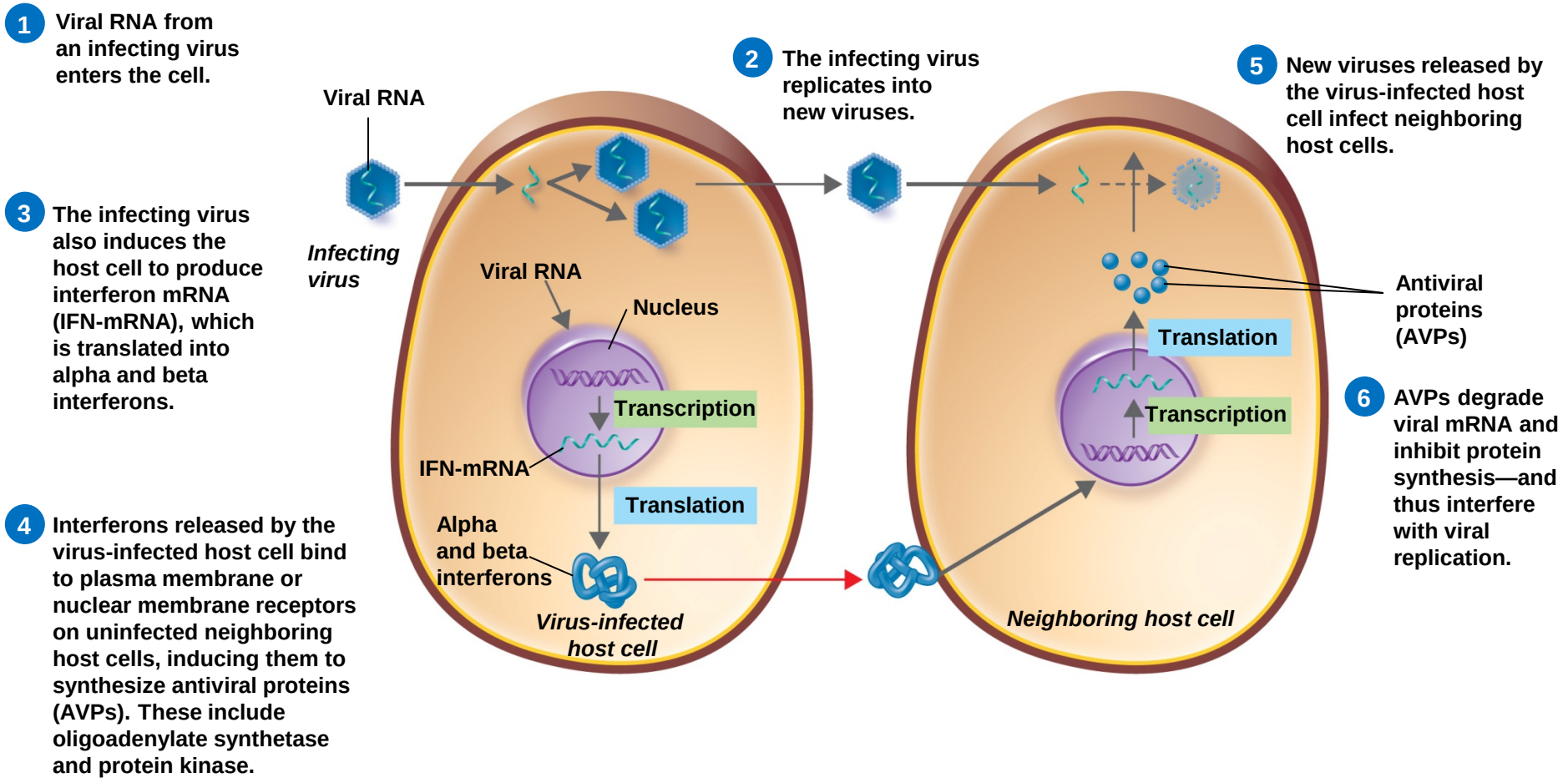
# Antimicrobial Substances

- 16-19 Define *interferons*.
- 16-20 Compare and contrast the actions of IFN-α and IFN-β with IFN-γ.
- 16-21 Describe the role of iron-binding proteins in innate immunity.
- 16-22 Describe the role of antimicrobial peptides in innate immunity.

# Interferons (IFNs)

- IFN-$\alpha$ and IFN-$\beta$: cause cells to produce antiviral proteins that inhibit viral replication
- IFN-$\gamma$: causes neutrophils and macrophages to phagocytize bacteria

# Figure 16.15 Antiviral action of alpha and beta interferons (IFNs).



# Innate Immunity

- **Transferrins**
  - Bind serum iron
- **Antimicrobial peptides**
  - Lyse bacterial cells

- What is interferon? 16-19
- Why do IFN-α and IFN-β share the same receptor on target cells, yet IFN-γ has a different receptor? 16-20
- What is the role of siderophores in infection? 16-21
- Why are scientists interested in AMPs? 16-22