

## 4b. Innate (nonspecific) Immunity

# Chapter 16: Innate (nonspecific) Immunity

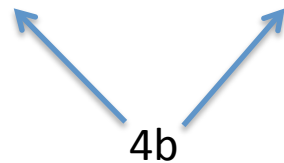
Some terms:

- Susceptibility: Lack of immunity to a disease.
- Immunity: Ability to ward off disease.
- Innate immunity: Defenses against any pathogen.
  - Does not involve specific recognition of a microbe
  - No memory response
- Adaptive immunity
  - Specific response to a specific microbe once a microbe has breached the innate immunity defenses!
  - Slower to respond but develops memory

# 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
<ul style="list-style-type: none"><li>• Intact skin</li><li>• Mucous membranes and their secretions</li><li>• Normal microbiota</li></ul>	<ul style="list-style-type: none"><li>• Phagocytes, such as neutrophils, eosinophils, dendritic cells, and macrophages</li><li>• Inflammation</li><li>• Fever</li><li>• Antimicrobial substances</li></ul>	<ul style="list-style-type: none"><li>• Specialized lymphocytes: T cells and B cells</li><li>• Antibodies</li></ul>

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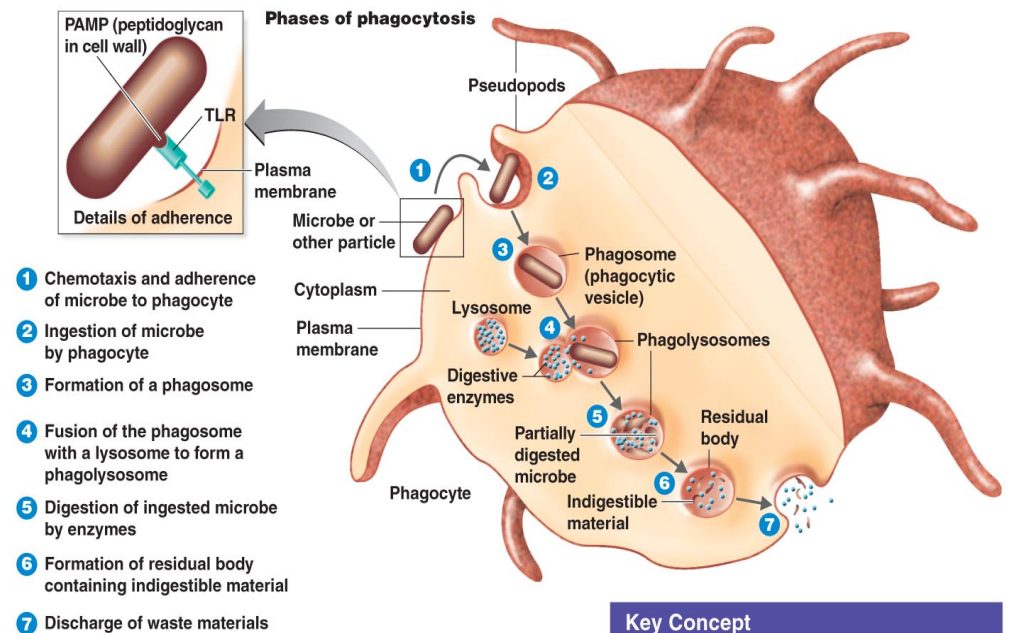


# The Concept of Innate Immunity

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

On Your Cells!

On Pathogen!



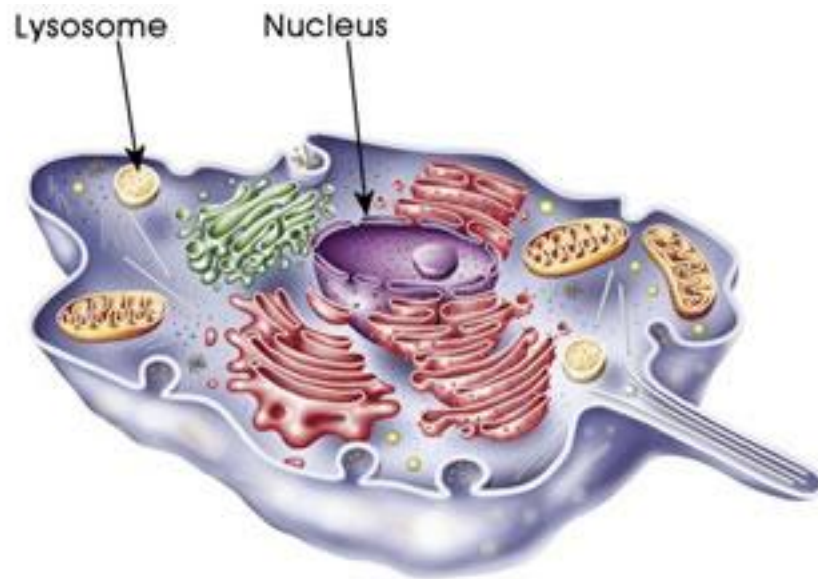
## A. Physical barriers (first line of defense)

- skin, mucous membranes = prevent entry to most pathogens
- Epidermis consists of tightly packed cells with
  - **Keratin**, a protective protein



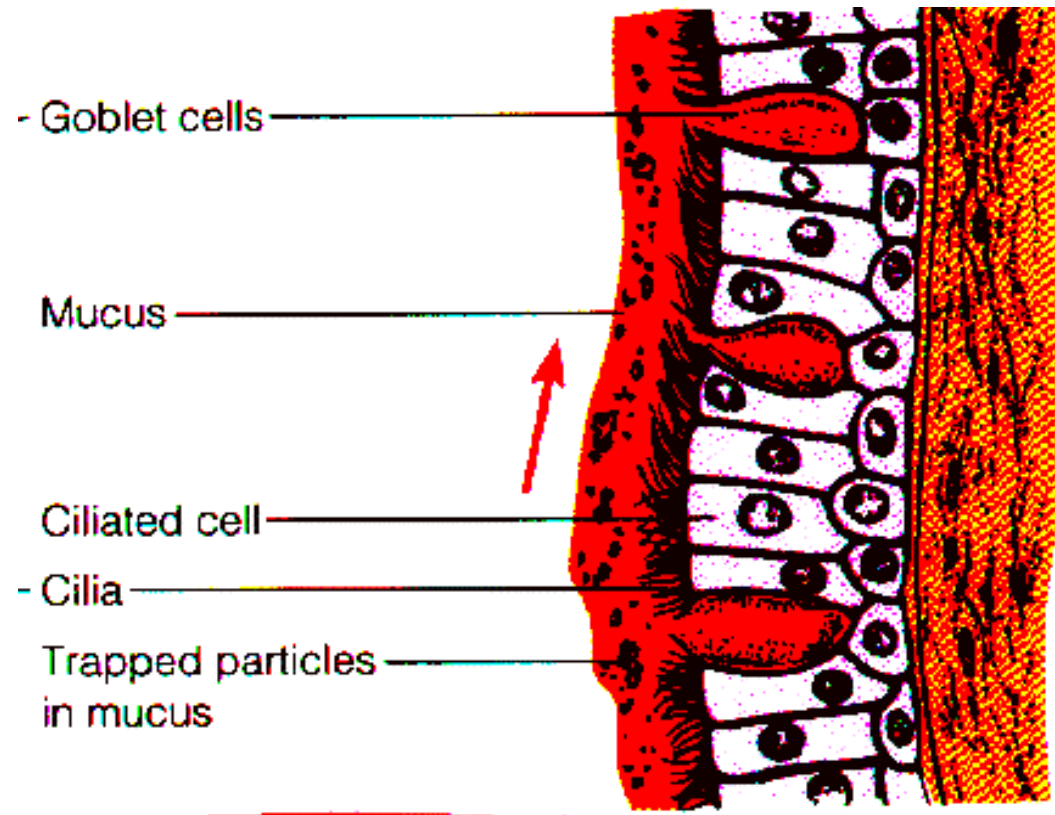
## B. Lysozyme

- enzyme in tears, sweat, saliva, etc that dissolves bacterial cell walls (digests peptidoglycan)

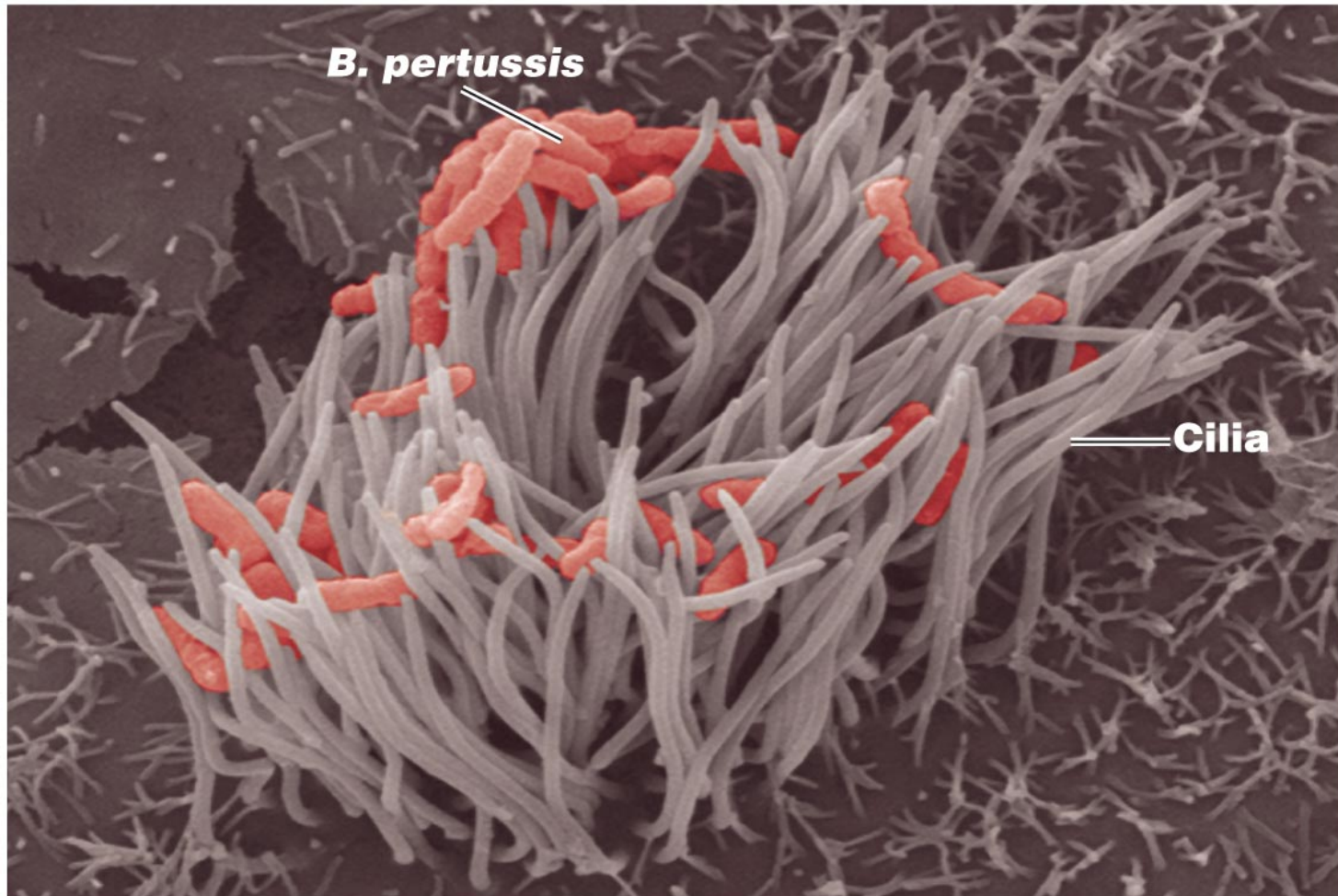


# C. Respiratory cilia

- carry pathogens out of lungs

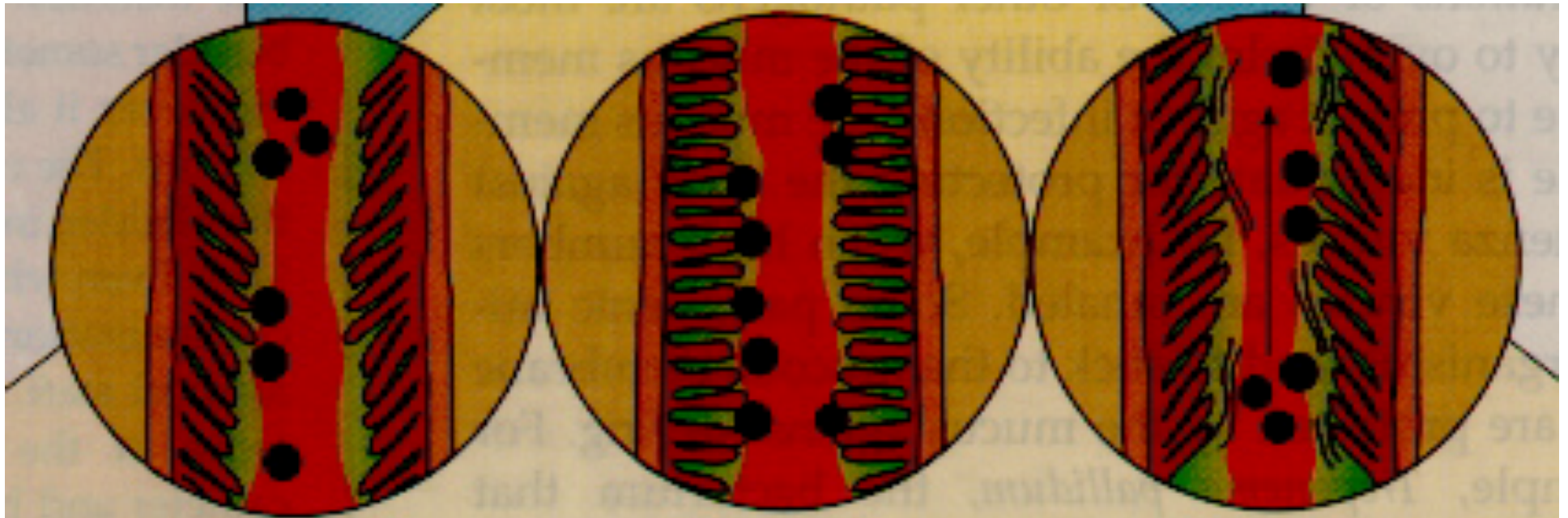


# Respiratory cilia



SEM | 2  $\mu$ m





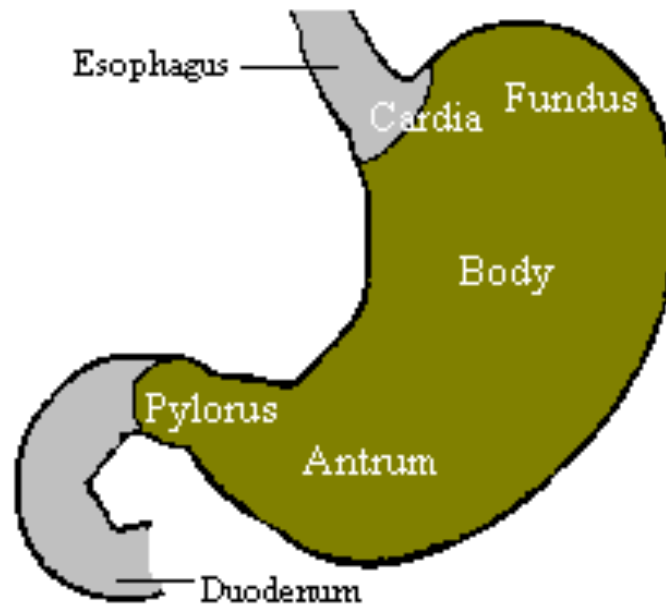
Microorganisms enter  
respiratory tract

Microorganisms attach  
to mucous membrane

Wave-like motion of cilia  
drives microorganisms  
upward

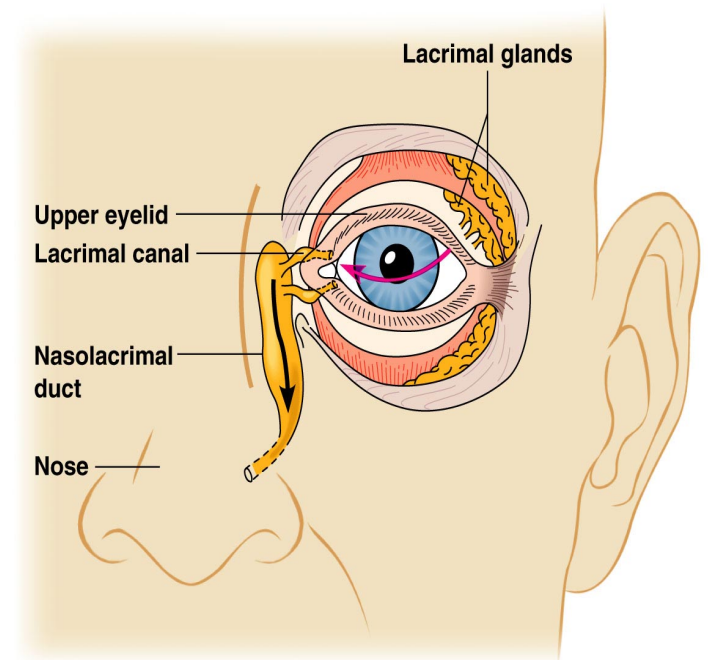
## D. Stomach acid

- HCl at pH 1-2
- kills many, but not all pathogens



# Physical factors

- Mucous membranes
- Ciliary escalator:  
Microbes trapped in mucus  
are transported away from  
the lungs.
- Lacrimal apparatus:  
Washes eye.
- Saliva: Washes microbes off.
- Urine: Flows out.
- Vaginal secretions: Flow out.



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# 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

## **Innate (Nonspecific) Immunity**

### **First line of defense**

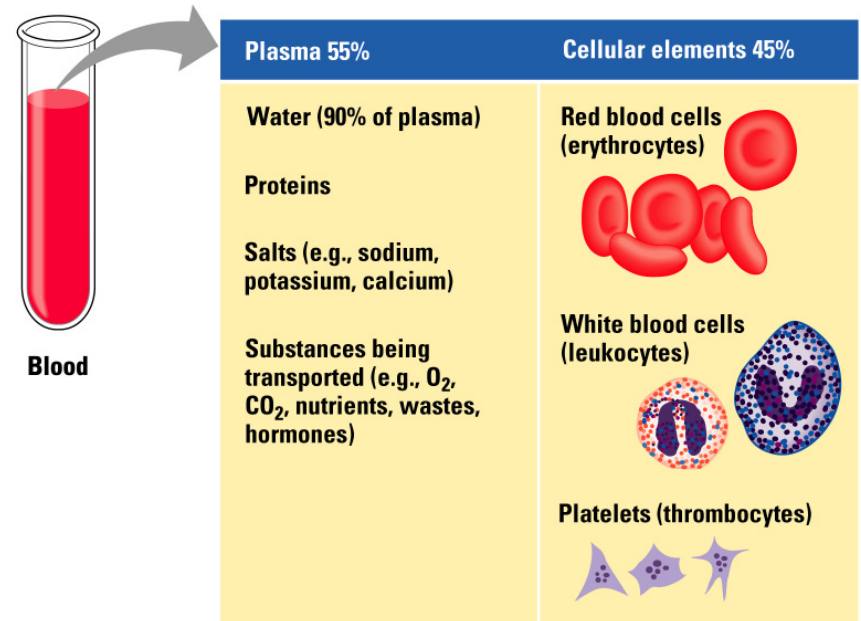
- Intact skin
- Mucous membranes and their secretions
- Normal microbiota

### **Second line of defense**

- Natural killer cells and phagocytic white blood cells
- Inflammation
- Fever
- Antimicrobial substances

# Mammalian Blood Composition

- Plasma (55%)
  - Water
  - Ions
  - Plasma Proteins
  - Nutrients
  - Waste
  - Gases
  - Hormones
- Cellular Elements (45%)
  - Erythrocytes
  - Leukocytes
  - Thrombocytes



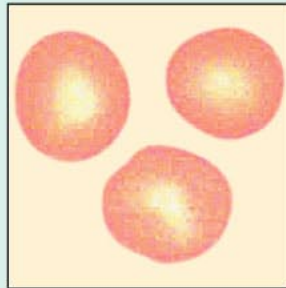
# Formed Elements in Blood

TABLE 16.1

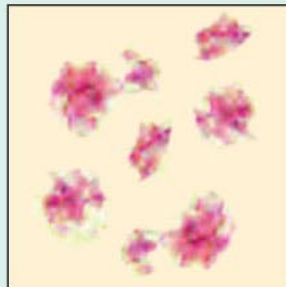
Formed Elements in Blood

Type of Cell

**Erythrocytes (Red Blood Cells)**



**Platelets**



Type of Cell

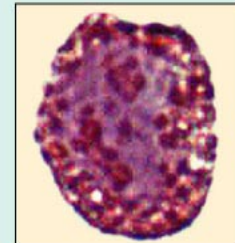
**Leukocytes (White Blood Cells)**

A. Granulocytes (stained)

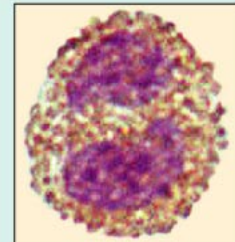
1. Neutrophils (PMNs)  
(60–70% of leukocytes)



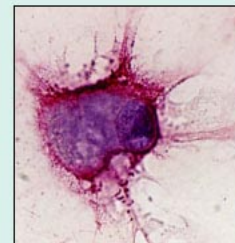
2. Basophils (0.5–1%)



3. Eosinophils (2–4%)


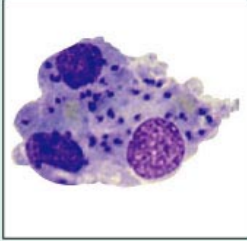
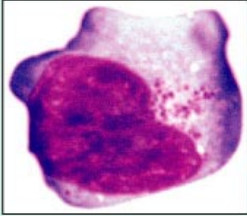

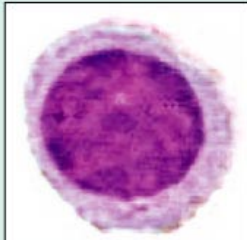


4. Dendritic cells





**TABLE 16.1****Formed Elements in Blood** (continued)

Type of Cell	Numbers per Microliter ( $\mu\text{L}$ ) or Cubic mm ( $\text{mm}^3$ )
B. Agranulocytes (stained) 1. Monocytes (3–8%)	 
2. Lymphocytes (20–25%) <ul style="list-style-type: none"><li>• Natural killer (NK) cells</li><li>• T cells</li><li>• B cells</li></ul>	  

\*Discussed in Chapter 17.

# Differential White Cell Count

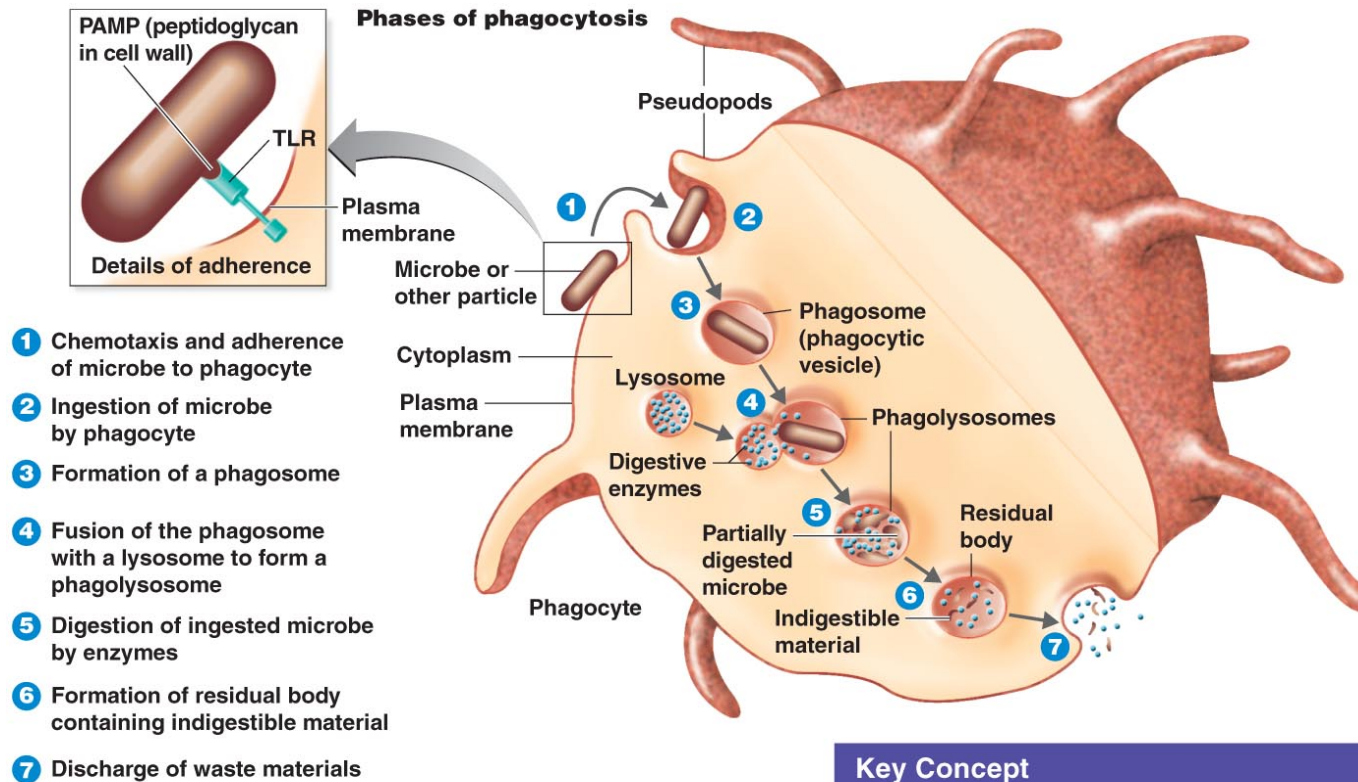
- Percentage of each type of white cell in a sample of 100 white blood cells

<b>Neutrophils</b>	60–70%
<b>Basophils</b>	0.5–1%
<b>Eosinophils</b>	2–4%
<b>Monocytes</b>	3–8%
<b>Lymphocytes</b>	20–25%

# White Blood Cells

- **Neutrophils**: Phagocytic (most abundant)
- **Basophils**: Produce histamine
- **Eosinophils**: Toxic to parasites and some phagocytosis (worm infections)
- **Dendritic cells**: Initiate adaptive immune response
- **Monocytes**: Phagocytic as mature macrophages
  - Fixed macrophages in lungs, liver, and bronchi
  - Wandering macrophages roam tissues.
- **Lymphocytes**: Involved in specific immunity.

# Figure 16.7



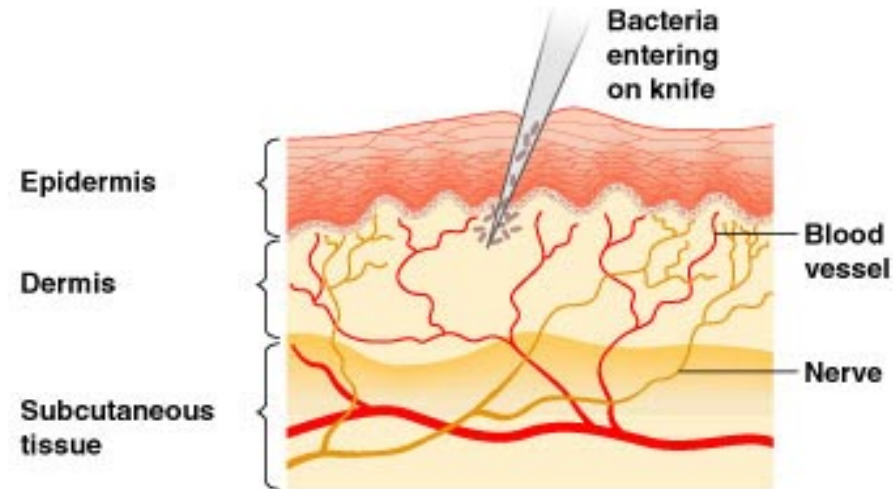
## Key Concept

Phagocytes migrate to a site of infection and can destroy the infecting bacteria. The phases of phagocytosis are chemotaxis, adherence, ingestion, and digestion.

# Microbial Evasion of Phagocytosis

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

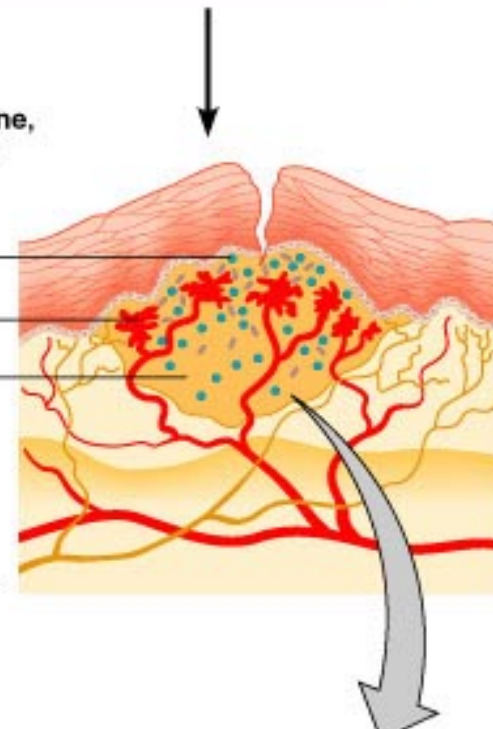
# Inflammation



**(a) Tissue damage**

- 1** Chemicals such as histamine, kinins, prostaglandins, and leukotrienes (represented as blue dots) are released by damaged cells.
- 2** Blood clot forms.
- 3** Abscess starts to form (dark yellow area).

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



# Inflammation

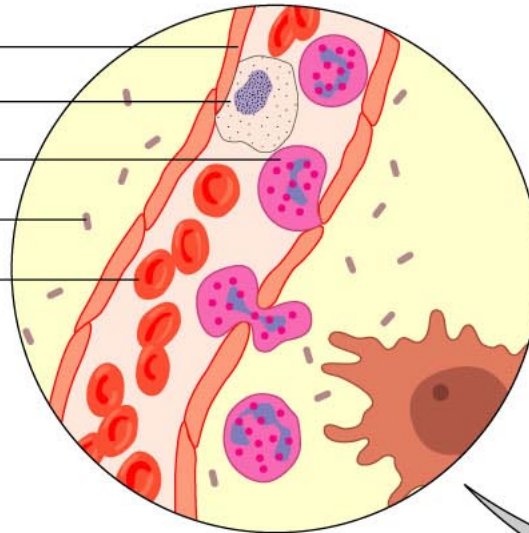
Blood vessel  
endothelium

Monocyte

Neutrophil

Bacterium

Erythrocyte



**4** Margination—  
phagocytes  
stick to  
endothelium.

**5** Emigration—  
phagocytes  
squeeze between  
endothelial cells.

**6** Phagocytosis  
of invading  
bacteria.

**(c)** Phagocyte migration and phagocytosis

Bacterium

Neutrophil

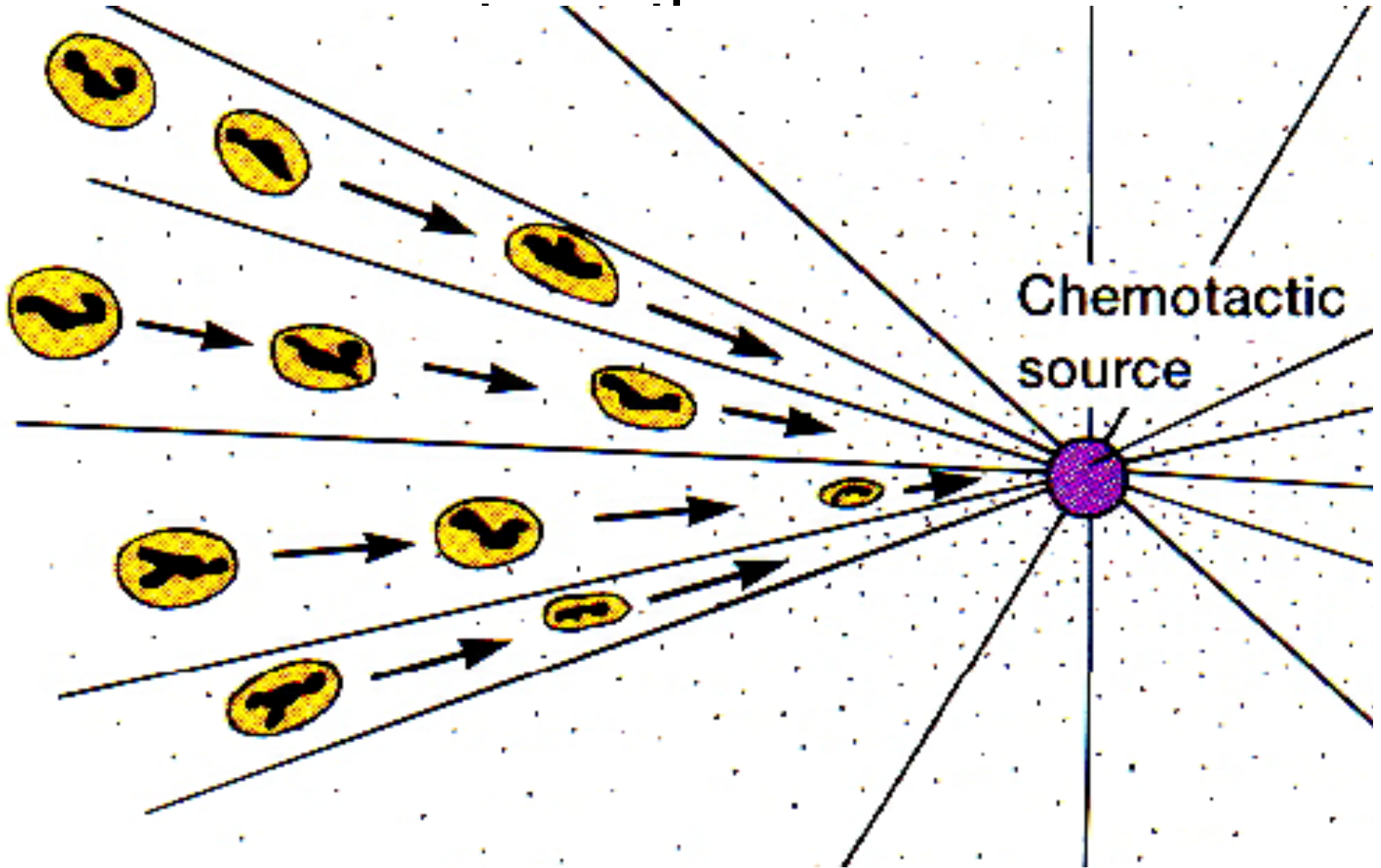
Macrophage

# Inflammation

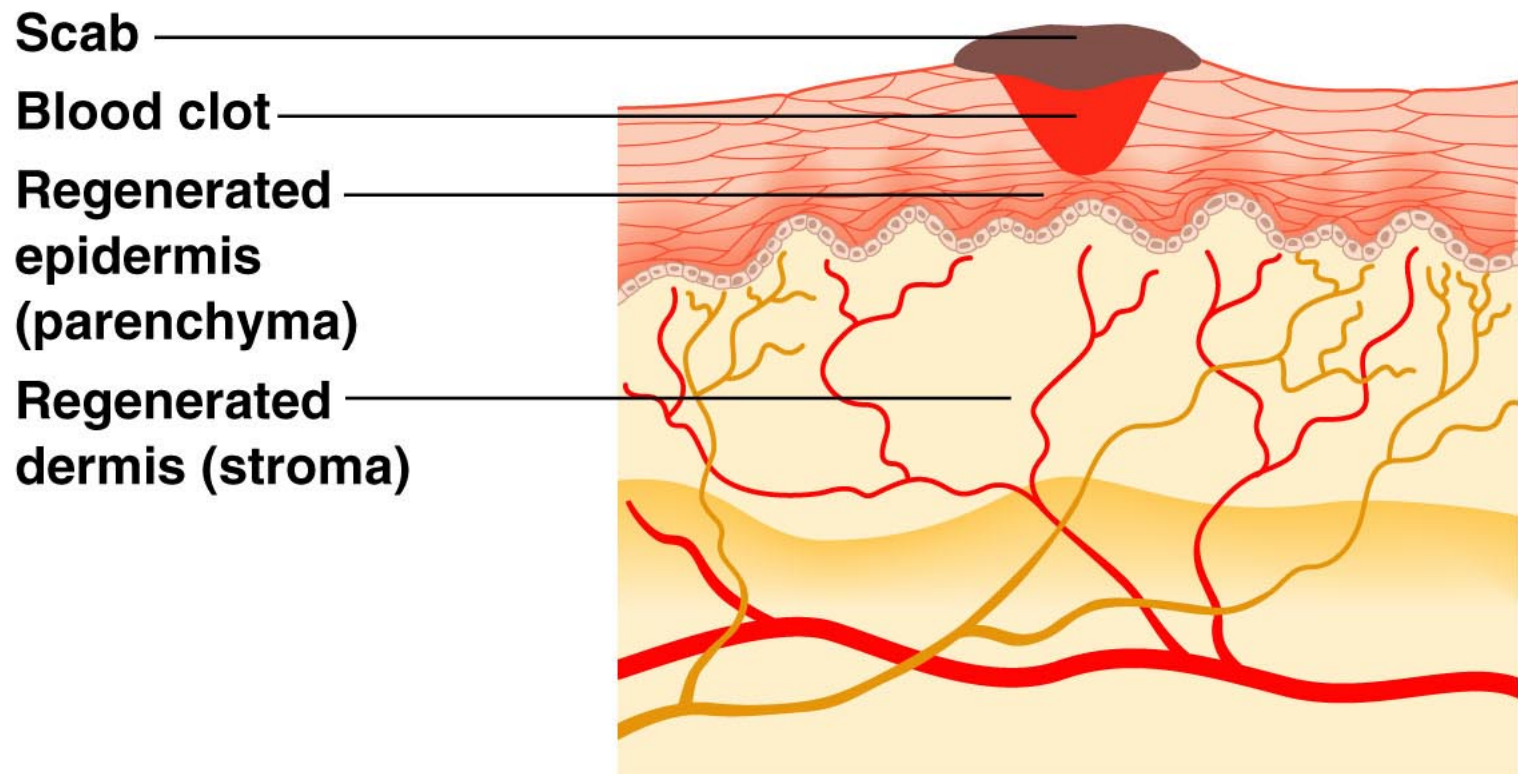
- Redness
- Pain
- Heat
- Swelling (edema)
- Acute-phase proteins activated (complement, cytokine, and kinins)
- Vasodilation (histamine, kinins, prostaglandins, and leukotrienes)
- Margination and emigration of WBCs
- Tissue repair



# chemotaxis: phagocytes attracted



# Tissue Repair



## (d) Tissue repair

<b>Innate Immunity</b>		<b>Adaptive Immunity (Chapter 17)</b>
<b>First line of defense</b>	<b>Second line of defense</b>	<b>Third line of defense</b>
<ul style="list-style-type: none"> <li>• Intact skin</li> <li>• Mucous membranes and their secretions</li> <li>• Normal microbiota</li> </ul>	<ul style="list-style-type: none"> <li>• Phagocytes, such as neutrophils, eosinophils, dendritic cells, and macrophages</li> <li>• Inflammation</li> <li>• Fever</li> <li>• Antimicrobial substances</li> </ul>	<ul style="list-style-type: none"> <li>• Specialized lymphocytes: T cells and B cells</li> <li>• Antibodies</li> </ul>

# Fever

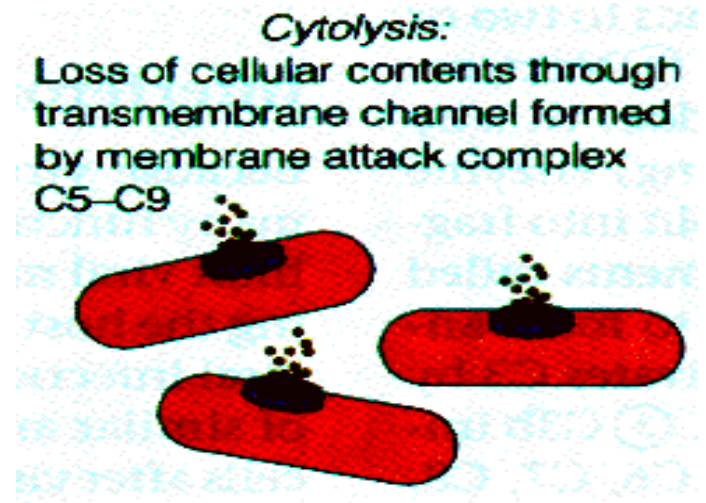
- Abnormally high body temperature
- Hypothalamus normally set at **37°C**
- **Gram-negative** endotoxin cause phagocytes to release **interleukin-1 (IL-1)**
- **Hypothalamus** releases **prostaglandins** that reset the hypothalamus to a high temperature
- Body increases rate of metabolism and shivering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

# Fever

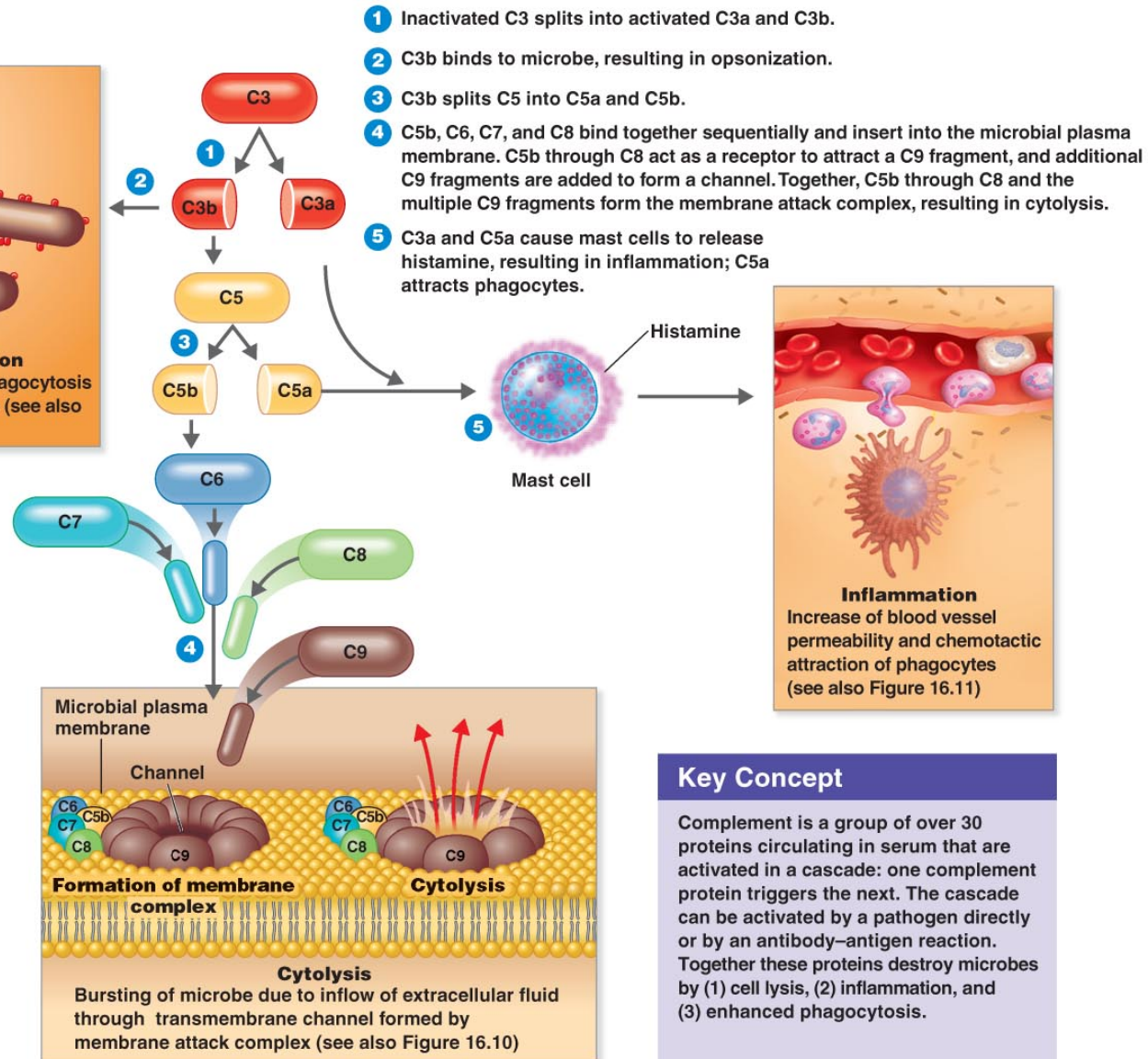
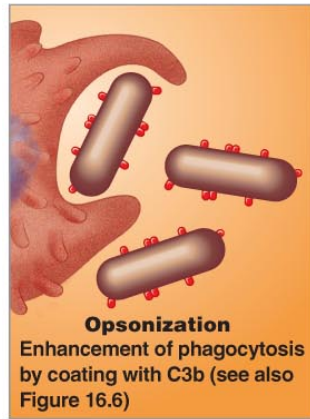
- A moderate fever is beneficial to host defenses
- speeds up body defenses; slows down growth of pathogens
- Fever producing *pyrogens* are produced by activated macrophages as well as bacteria, viruses, and other microbes
  - Stimulate hypothalamus to raise body temp.
  - Thus cell metabolism increases and blood vessels constrict keeping heat within (cold skin/chills with fever)
  - But, above **105° F**, convulsions and death may result
    - Infants >100°F and older children >102°F need medical attention!

## Antimicrobial substances: The Complement System

- Complement (complement system): a series of over 30 blood proteins (produced by the liver) that circulate in the bloodstream and sequentially bond together to causes lysis of pathogens, inflammation and help phagocytosis
- “complements” the cells of the immune system in destroying microbes
- can be a specific or nonspecific defense



# Compliment Sysmtem

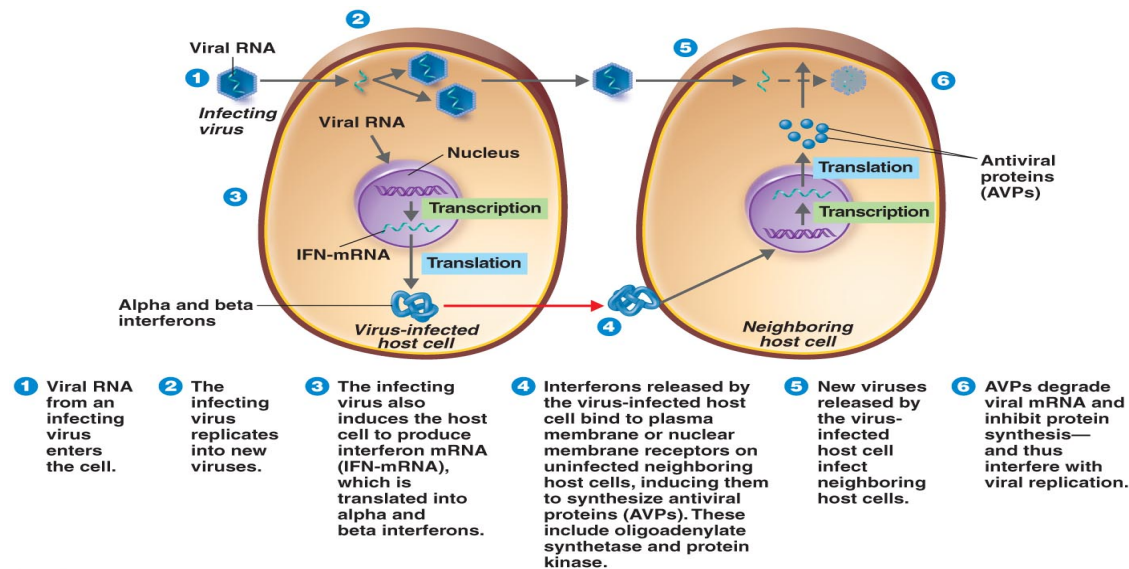


## Key Concept

Complement is a group of over 30 proteins circulating in serum that are activated in a cascade: one complement protein triggers the next. The cascade can be activated by a pathogen directly or by an antibody-antigen reaction. Together these proteins destroy microbes by (1) cell lysis, (2) inflammation, and (3) enhanced phagocytosis.

# Interferons (IFNs)

- messenger proteins produced by virus-infected cells
- tell surrounding cells to produce anti-viral protein
- also produced by genetic engineered microorganisms for injection as antiviral drugs





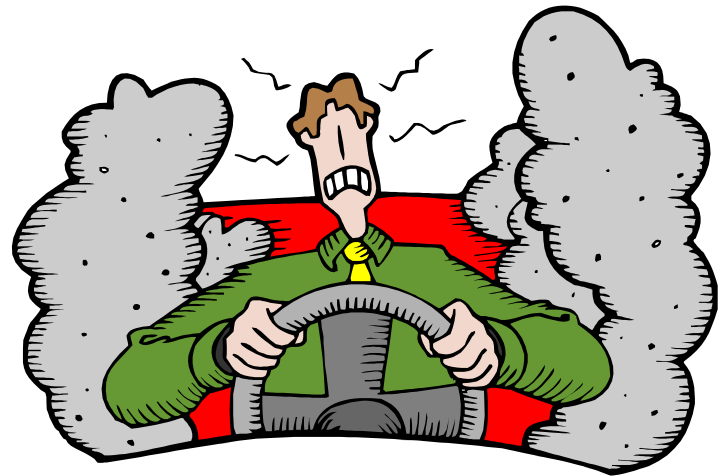
# Summary of Second Line of Defense

**Table 16.2** Summary of Innate Immunity Defenses (continued)

Component	Functions
<b>SECOND LINE OF DEFENSE</b>	
<b>Defensive Cells</b>	
<b>Phagocytes</b>	Phagocytosis by cells such as neutrophils, eosinophils, dendritic cells, and macrophages.
<b>Natural killer (NK) cells</b>	Kill infected target cells by releasing granules that contain perforin and granzymes. Phagocytes then kill the infected microbes.
<b>Inflammation</b>	Confines and destroys microbes and initiates tissue repair.
<b>Fever</b>	Intensifies the effects of interferons, inhibits growth of some microbes, and speeds up body reactions that aid repair.
<b>Antimicrobial Substances</b>	
<b>Complement system</b>	Causes cytolysis of microbes, promotes phagocytosis, and contributes to inflammation.
<b>Interferons</b>	Protect uninfected host cells from viral infection.
<b>Iron-Binding Proteins</b>	Inhibit growth of certain bacteria by reducing the amount of available iron.
<b>Antimicrobial Peptides (AMPs)</b>	Inhibit cell wall synthesis, form pores in the plasma membrane that cause lysis; and destroy DNA and RNA.

# Stress theory of disease

- Hans Selye
- A. Stressor: any force that elicits the stress response
  - invasion by pathogen
  - trauma
  - surgery
  - emotional conflict
  - performance demands
  - difficult relationships
  - life changes (positive or negative)



## B. Stress

- the body's response to any stressor
- includes many measurable physiological changes intended to increase resistance to stressors
- also called the *General Adaptation Syndrome*
- 1. Eustress: beneficial stress; appropriate in degree and duration; produces optimum physical and mental function and resistance to pathogens
- 2. Distress: harmful stress; excessive in degree and/or duration; impairs physical and mental function; reduces resistance to pathogens
- Stress management