First Line of Defense

- Nonspecific defense
- Purpose: prevent entry
- Two components:
  - Physical
  - Chemical
- Primary players = skin and mucous membranes
  - respiratory, digestive, urinary, and reproductive systems
Skin – physical
- Two major layers
  - Epidermis
    - Epidermal dendritic cells
  - Dermis

Skin – chemical
- Dermicidins
- Perspiration
  - Salt
  - Lysozyme
- Sebum
  - pH

Mucous membranes
- Two distinct layers
  - Epithelium
  - Deeper connective layer
    - supports epithelium
Epithelium

- Thin, outer covering of mucous membranes
- Tightly packed
- Continuous shedding
- Goblet cells → secrete mucous
- Ciliated cells → propel mucous

Microbial Antagonism

- How?
  - Secrete antimicrobial substances
  - Consume nutrients
    - makes them unavailable to pathogens
  - Alter pH
  - Helps stimulate second line of defense
  - Provide vitamins to host

Other Components of First Line

- Chemical secretions
  - Lysozyme
    - Tears, saliva, urine, sweat
  - Acidity
    - Stomach, urine, vaginal secretions
  - Iron-binding chemicals
    - Gastroferritin, transferrin, vaginal and prostate secretions
Table 15.2: Sensors and Activators That Contribute to the First Line of Defense

<table>
<thead>
<tr>
<th>Sensor/Activator</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal surfaces</td>
<td>Sodium bicarbonate, saliva, tears, and other secretions (e.g., mucus, tears)</td>
</tr>
<tr>
<td>Tip of the nose</td>
<td>Lysosome in macrophages and other phagocytes</td>
</tr>
<tr>
<td>Skin barriers</td>
<td>Normal flora</td>
</tr>
<tr>
<td>Nasal mucosa</td>
<td>Skin microflora</td>
</tr>
<tr>
<td>Epithelial lining</td>
<td>Nonspecific defense</td>
</tr>
</tbody>
</table>

First Line of Defense

- **Nonspecific defense**
  - First line of defense is breached
- **Cells, antimicrobial chemicals, and processes**

Second line of defense
Blood

- Formed elements \(\rightarrow\) cells & cell fragment
- Plasma \(\rightarrow\) mostly water + electrolytes, dissolved gases, nutrients, & proteins
  - Complement proteins
  - Antibodies
  - Clotting factors
    - Remove clotting factors \(\rightarrow\) serum

Formed elements

- Erythrocytes
- Platelets
- Leukocytes
  - Granulocytes
  - Agranulocytes

Granulocytes

- Contain large granules
- 3 types
  - Basophils- stain with basic dyes
    - methylene blue
  - Eosinophils- stain with acidic dyes
    - eosin
  - Neutrophils- stain with a mixture of acidic and basic dyes
### Agranulocytes

- Do not contain granules in cytoplasm
- 2 types
  - Lymphocytes
  - Monocytes

### Granulocytes

<table>
<thead>
<tr>
<th>Type</th>
<th>%</th>
<th>Functions</th>
</tr>
</thead>
</table>
| Basophils| 0.5 – 1% | Release histamine  
Mediate inflammation |
| Eosinophils| 2 – 4% | Phagocytic cells capable of diapedesis  
↑ during allergic rxns, parasitic worm infections |
| Neutrophils| 60 – 70% | Phagocytic cells capable of diapedesis  
↑ during bacterial infections  
Mediate inflammation |

### Agranulocytes

<table>
<thead>
<tr>
<th>Type</th>
<th>%</th>
<th>Functions</th>
</tr>
</thead>
</table>
| Lymphocytes| 20 – 25% | Mostly involved in specific immunity (T-cells, B-cells)  
[NK cells → non-specific]  
↑ in response to viral infection |
| Monocytes| 3 – 8% | Mature into macrophages |
Macrophages
- Professional Phagocytes
  - Wandering macrophages
  - Fixed macrophages
- Mononuclear phagocytic system
  - Macrophages + monocytes

Second Line of Defense
- Phagocytosis
- Extracellular killing
- Nonspecific chemical defenses
- Inflammation
- Fever
Phagocytosis: 5 Steps

Extracellular Killing

- Eosinophils
  - Attach to parasitic helminths (worms)
    - Secrete toxins
      - Eosinophilia → helminth infection

Extracellular Killing

- Neutrophils
  - Secrete toxic chemicals
  - NETs
- Natural killer lymphocytes (NK cells)
  - Secrete toxins
    - Virally infected cells and cancerous cells
Nonspecific Chemical Defenses

- Lysozyme
- Complement
- Interferon
- Defensins

Complement System

- Set of serum proteins
  - Numbered by order of discovery
- Complement activation → lysis of foreign cell
  - Classical Pathway
    - Ag-Ab activate
  - Alternate Pathway
    - Pathogens / products activate

Classical pathway
Alternate Pathway

- Antibody independent
- Useful during early stages of infection

Results of Complement Activation

- MAC attack
  - c5b, c6, c7, c8, c9
- Opsonization
  - c3b
- ↑ Permeability of capillaries
  - c3a, c5a
- Recruitment of phagocytes
  - c3a, c5a

Opsonization
Interferons

- Proteins released by host cells
- Inhibit viral spreading
- Most effective against ds RNA viruses
- Cause many symptoms associated with viral infections
- 3 Classes
  - Alpha & Beta – early stages of infection
  - Gamma – later stages of infection
  - Activates macrophages

Defensins

- Small peptides
- Mechanisms of action
  - Punch holes in cytoplasmic membranes
  - Interfere with internal signaling, other metabolic processes
  - Interfere with bacterial heat shock proteins
- Inflammation ↑ defensin production
Inflammation

- Nonspecific response to tissue damage
- Characterized by:
  - redness, heat, swelling, and pain
- Two types
  - Acute
  - Chronic

Fever

- Body temp > 37°C
- Pyrogens → hypothalamus
- Various types of pyrogens
  - Bacterial toxins
  - Components of lysed bacteria
  - Antibody-antigen complexes
  - Interleukin-1 (IL-1)

Fever production

- Hypothalamus → prostaglandin
  - Resets “thermostat”
- Result: muscle contractions, ↑ metabolic activity, constriction of blood vessels
- Decrease in IL-1 production
  - Body temp returns to normal
Benefits of Fever

- Enhances effects of interferons
- Inhibits growth of some microorganisms
- May enhance:
  - phagocytes
  - cells of specific immunity
  - tissue repair