Chapter 16: Nonspecific Host Defenses

Introduction

Resistance: Ability to ward off disease.
- Nonspecific Resistance: Defenses that protect against *all* pathogens.
- Specific Resistance: Protection against *specific* pathogens.

Susceptibility: Vulnerability or lack of resistance.

Protection Against Invading Pathogens

   Examples: Skin and mucous membranes.

2. Second Line of Defense: Innate non-specific immune defenses provide rapid local response to pathogen after it has entered host.
   Examples: Fever, phagocytes (macrophages and neutrophils), inflammation, and interferon.

3. Third line of defense: Antigen-specific immune responses, specifically target and attack invaders that get past first two lines of defense.
   Examples: Antibodies and lymphocytes.

Three Lines of Defense Against Infection

First Line of Defense: Skin and Mucous Membranes

I. Mechanical Defenses
1. Skin has two Layers:
   A. Epidermis: Thin outer layer of epithelial tissue. Contains Langerhans cells, dead cells, and keratin (waterproof).
   B. Dermis: Thick inner layer of connective tissue. Infections are rare in intact skin. Exceptions:
      - Hookworms can penetrate intact skin
      - Dermatophytes: “Skin loving” fungi

Intact Skin is an Effective Barrier Against Most Pathogens
I. Mechanical Defenses

   - Two layers: Outer epithelial and inner connective layer.
   - Epithelial layer secretes mucus which maintains moist surfaces.
   - Although they inhibit microbial entry, they offer less protection than skin.
   - Several microorganisms are capable of penetrating mucous membranes:
     - Papillomavirus
     - Treponema pallidum
     - Enteroinvasive E. coli
     - Entamoeba histolytica

3. Lacrimal apparatus: Continual washing and blinking prevents microbes from settling on the eye surface.
4. Saliva: Washes microbes from teeth and mouth mucous membranes.
5. Mucus: Thick secretion that traps many microbes.
6. Nose Hair: Coated with mucus filter dust, pollen, and microbes.
7. Ciliary Escalator: Cilia on mucous membranes of lower respiratory tract move upwards towards throat at 1-3 cm/hour.

10. Urination: Cleanses urethra.
11. Vaginal Secretions: Remove microbes from genital tract.

Epiglottis Protects Respiratory System from Infection During Swallowing

B. Chemical Defenses:
   - Sebum: Oily substance produced by sebaceous glands that forms a protective layer over skin. Contains unsaturated fatty acids which inhibit growth of certain pathogenic bacteria and fungi.
   - pH: Low, skin pH usually between 3 and 5. Caused by lactic acid and fatty acids.
   - Perspiration: Produced by sweat glands. Contains lysozyme and acids.
   - Lysozyme: Enzyme that breaks down gram-positive cell walls. Found in nasal secretions, saliva, and tears.

B. Chemical Defenses (Continued)
   - Gastric Juice: Mixture of hydrochloric acid, enzymes, and mucus. pH between 1.2 to 3 kills many microbes and destroys most toxins. Many enteric bacteria are protected by food particles.
     - Helicobacter pylori neutralizes stomach acid and can grow in the stomach, causing gastritis and ulcers.
   - Transferrins: Iron-binding proteins in blood which inhibit bacterial growth by reducing available iron.
### Cellular Elements of Blood

<table>
<thead>
<tr>
<th>Cell Type (WBC)</th>
<th># Cells/mm³</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (RBC)</td>
<td>4.8-5.4 million</td>
<td>Transport O₂ and CO₂</td>
</tr>
<tr>
<td>Leukocytes (WBC)</td>
<td>5000-9000</td>
<td>Various</td>
</tr>
<tr>
<td>A. Granulocytes</td>
<td>1. Neutrophils (70% of WBC)</td>
<td>Phagocytosis</td>
</tr>
<tr>
<td></td>
<td>2. Basophils (1%)</td>
<td>Produce histamine</td>
</tr>
<tr>
<td></td>
<td>3. Eosinophils (4%)</td>
<td>Toxins against parasites; some phagocytosis</td>
</tr>
<tr>
<td>B. Monocytes/Macrophages (5%)</td>
<td></td>
<td>Phagocytosis</td>
</tr>
<tr>
<td>C. Lymphocytes (20%)</td>
<td></td>
<td>Antibody production (B cells); cell-mediated immunity (T cells)</td>
</tr>
</tbody>
</table>

| Platelets | 300,000 | Blood clotting |

### Composition of Human Blood

#### Platelets Form Blood Clots

1. **Phagocytosis**
   - Derived from the Greek words “Eat and cell”.
   - Phagocytosis is carried out by white blood cells: macrophages, neutrophils, and occasionally eosinophils.
   - Neutrophils predominate early in infection.
   - Wandering macrophages: Originate from monocytes that leave blood and enter infected tissue, and develop into phagocytic cells.
   - Fixed Macrophages (Histiocytes): Located in liver, nervous system, lungs, lymph nodes, bone marrow, and several other tissues.

#### Phagocytic Cells: Macrophages (Monocytes), Neutrophils, and Eosinophils

1. **Chemotaxis**: Phagocytes are chemically attracted to site of infection.
2. **Adherence**: Phagocyte plasma membrane attaches to surface of pathogen or foreign material.
   - Adherence can be inhibited by capsules (S. pneumoniae) or M protein (S. pyogenes).
   - Opsonization: Coating process with opsonins that facilitates attachment.
   - Opsonins include antibodies and complement proteins.

#### II. Second Line of Defense

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Phagocytes are Attracted to Site of Infection by Chemotaxis

Phagocytes are attracted to the site of infection by chemotaxis. This process involves the release of chemical signals by damaged cells, which attract phagocytes. Phagocytes then move towards the site of infection, where they engulf microorganisms.

Stages of Phagocytosis (Continued)

3. Ingestion: The plasma membrane of phagocytes extends projections (pseudopods) which engulf the microbe. The microbe is enclosed in a sac called the phagosome.

4. Digestion: Inside the cell, the phagosome fuses with a lysosome to form a phagolysosome. Lysosomal enzymes kill most bacteria within 30 minutes and include:
   - Lysozyme: Destroys cell wall peptidoglycan
   - Lipases and Proteases
   - RNase and DNase

After digestion, residual body with undigestable material is discharged.

Process of Phagocytosis

The process of phagocytosis involves several stages:

1. Chemotaxis and adherence of microbe to phagocyte
2. Ingestion of microbe by phagocyte
3. Fusion of phagosome with a lysosome to form a phagolysosome
4. Digestion of ingested material by enzymes
5. Formation of residual body containing undigestable material
6. Discharge of residual material

Inflammation

Inflammation is triggered by tissue damage due to infection, heat, wound, etc.

Four Major Symptoms of Inflammation:
1. Redness
2. Pain
3. Heat
4. Swelling

May also observe:
5. Loss of function

Functions of Inflammation

1. Destroy and remove pathogens
2. If destruction is not possible, to limit effects by confining the pathogen and its products.
3. Repair and replace tissue damaged by pathogen and its products.

Stages of Inflammation

1. Vasodilation: Increase in diameter of blood vessels.
   Triggered by chemicals released by damaged cells: histamine, kinins, prostaglandins, and leukotrienes.
2. Phagocyte Migration and Margination:
   Margination is the process in which phagocytes stick to lining of blood vessels.
   Diapedesis (Emigration): Phagocytes squeeze between endothelial cells of blood vessels and enter surrounding tissue.
**Process of Inflammation**

**Stages of Inflammation (Continued)**

Phagocytes are attracted to site of infection through chemotaxis.

Phagocytes destroy microbes, as well as dead and damaged host cells.

3. **Tissue Repair**: Dead and damaged cells are replaced.

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**Antimicrobial Substances:**

I. **Complement System**: Large group of serum proteins that participate in the lysis of foreign cells, inflammation, and phagocytosis.

Two mechanisms of complement activation:

1. **Classical Pathway**: Initiated by an immune reaction of antibodies.

2. **Alternative Pathway**: Initiated by direct interaction of complement proteins with **microbial polysaccharides**.

Both pathways cleave a complement protein called C3, which triggers a series of events.

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**Consequences of Complement Activation:**

1. **Cytolysis**: Due to the formation of a membrane attack complex (MAC) which produces lesions in microbial membranes.

2. **Inflammation**: Complement components (C3a) trigger the release of histamine, which increases vascular permeability.

3. **Opsonization**: Complement components (C3b) bind to microbial surface and promote phagocytosis.

4. **Inactivation of Complement**: Regulatory proteins limit damage to host cells that may be caused by complement.
II. Interferons: Antiviral proteins that interfere with viral multiplication.
- Small proteins (15,000 to 30,000 kDa)
- Heat stable and resistant to low pH
- Important in acute and short term infections.
- Have no effect on infected cells.
- Host specific, but not virus specific

Interferon alpha and beta: Produced by virus infected cells and diffuse to neighboring cells. Cause uninfected cells to produce antiviral proteins (AVPs).

Interferon gamma: Produced by lymphocytes. Causes neutrophils to kill bacteria.