Chapter 14
Topics
- Defense Mechanisms
- Non-specific immunity

Defense Mechanisms
- **Innate** - Non specific
  - First line of defense
  - Second line of defense
- **Acquired** - Specific
  - Third line of defense

Summary of the major components of the host defenses.

First line of defense
- **Barriers**
  - Anatomical
  - Chemical

Anatomical barriers
- **Skin**
  - Outermost layer
  - Hair follicles
  - Skin glands
  - Dequamation
- **Mucous membrane**
  - Digestive
  - Urinary
  - Respiratory
  - Eye

The trachea contain cilia that entrap and propel particles out of the respiratory tract
Chemical barriers
• Sebaceous secretions
• Tears and saliva – lysozyme
• Acidic pH
  – Sweat
  – Stomach
  – Skin
  – Semen
  – Vagina - mediated by presence of Lactobacillus

Immunology
• Study of the development of resistance to infectious agents by the body
  – Surveillance of the body
  – Recognition of foreign material
  – Destruction of foreign material or agent
• Involve nonspecific (Second line) and specific (Third line) immune defense systems
• White blood cells (WBC) or leukocytes are involved

WBC
• WBC recognize "self" markers on the host cell
  – Do not attack or do not respond to host cell
• WBC recognize non-self markers on the invading microbe
  – Attack or respond to microbe

Search, recognize, and destroy is the mandate of the immune system

Blood
• Stem cells precursors
• Hemopoiesis
• Components

Hemopoiesis
• Production of blood
  – Starts at the embryonic stage
    • Yolk sac and liver
  – Continues during adult stage
    – Hematopoietic stem cells in bone marrow
**White blood cells**

- **Leukocytes**
  - **Granulocytes** (large cytoplasmic granules)
    - Neutrophils
    - Basophils
    - Eosinophils
  - **Agranulocytes**
    - T cells
    - B cells
    - Monocytes

**Neutrophils**

- Present in high numbers in blood and tissue
- Phagocytizes bacteria – granules contain digestive enzymes
- First to arrive during an immune response (inflammation)

**Eosinophils**

- Contain granules with hydrolytic enzymes
- Attach and destroy large eucaryotic pathogens (worms)
- Associated with inflammation and allergies

**Basophils**

- Present in low in number in the body
- Function is similar to eosinophils. Involved in allergic reactions due to cytoplasmic granules
- Localized basophils are called mast cells
**Lymphocytes**

- **Specific immunity**
  - T cells → cellular immunity
  - B cells → humoral/antibody immunity
- Third line of defense
- Present throughout the body

**Monocytes**

- Agranulocyte
- Differentiate into macrophages (circulation and lymphatics) and dendritic cells (tissue associated)
- Phagocytosis

**Lymphatic system**

- Network of vessels, cells, and tissues that extend to most body areas
- Connected to the blood system
- Provides an auxiliary route for the return of extracellular fluid to the circulatory system
- “Drain off” system for inflammatory response
- Contains lymphocytes, phagocytes and antibodies

**Lymphatic system**

- Fluids
- Vessels
- Nodes
- Spleen
- Thymus
- Miscellaneous (GALT)

**Gut-associated lymphoid tissue (GALT)**

- Recognized incoming microbes from food
- Supply lymphocytes for antibody response
- Ex. Appendix, lacteals, Peyer’s patches
**Non-specific Immunity**

*Second Line of Defense*

- Inflammation
- Phagocytosis
- Interferon
- Complement

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**Inflammation**

- Four major symptoms
  - Redness
  - Warmth
  - Swelling
  - Pain
  That result in **Cellular Damage**

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**Inflammation - 1**

- Injury
- Rubor, calor
- Tumor, calor
- Dolor

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**Causes**

- Trauma
- Tissue injury due to physical or chemical agents
- Reaction to foreign pathogens or bodies (i.e., medical implants)

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**Function**

- Mobilize and attract immune components to the site of injury
- Localized and remove harmful substances
- Destroy microbes and block their invasion
- Aid in the repair of tissue damage
1. Vascular changes

- Blood cells, tissue cells, and platelets release chemical mediators and cytokines
- Chemical mediators
  - Vasoactive
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines)
    - Affect WBC

2. Edema

- Leakage of vascular fluid (exudate) into tissue
- Exudate - plasma proteins, blood cells (WBC), debris, and pus
- Migration of WBC is called diapedesis or transmigration
  - Chemotaxis

3. Fever

- Caused by pyrogens
  - reset the hypothalamic thermostat (increase temperature)
- Pyrogens
  - Microbes and their products (ex. LPS)
  - Leukocyte products (ex. Interleukins)
  - IL-1 resets the thermostat
- Inhibits microbe and viral multiplication, reduces nutrient availability, increases immune reactions

Phagocytosis

Neutrophils and monocytes/macrophages (and dendritic cells) are called professional phagocytes

Eosinophils
Phagocytosis

**Neutrophils** - First to arrive during an immune response (inflammation)
- Neutrophils are primary components of pus

**Monocytes/Macrophages** - Differentiate into macrophages (circulation and lymphatics) and dendritic cells (tissue associated)

Macrophages

- Monocytes/macrophages ➔ motile
- Specialized/Residents:
  - Alveolar ➔ lungs
  - Langerhan cells ➔ skin
  - Kupffer cells ➔ liver
- 1) Responsible for phagocytosis
- 2) Interact with B and T cells

Mechanism of Phagocytosis

- Chemotaxis
- Ingestion
- Phagolysosome
- Destruction

1. Chemotaxis & binding

- Directed by
  - Pathogen-associated molecular patterns (PAMPs)
    - Peptidoglycan
    - LPS
  - Foreign debris

2. Ingestion

- Pseudopods enclose the pathogen or foreign material
- Form a **phagosome** or **phagocytic vacuole**
3. Phagolysosome

- Lysosomes fuse with the phagosome
- Other antimicrobials chemicals are released into the phagolysosome

4. Destruction

- Within the phagolysosome
  - A) Oxygen-dependent mechanisms – Similar to byproducts of respiration
  - B) Oxygen-independent mechanisms – due to numerous hydrolytic enzymes
- Undigestible debris are released

Interferon

- Produced due to viral infections, microbe infections, RNA, immune products, and antigens
**Classes**

- Interferon alpha
  - Product of lymphocytes and macrophages
- Interferon beta
  - Product of fibroblasts and epithelial cells
- Interferon gamma
  - Product of T cells

**Activity**

- Ex. Virus - binds to host cell
- A signal is sent to the nucleus to synthesized (transcription and translation) interferon
- Interferon is secreted
- Binds to other host cells
- Host cells produce antiviral proteins
  - Inhibit viral multiplication or translation
  - Not virus-specific

Interferon is produced, released, and taken-up by a near-by cell, where by original cell is not protected but the recipient cell is protected.

**Other Roles of Interferon**

- Activates and instructs T and B cell development
- Inhibits cancer cells
- Activates macrophages

**Complement**

- Consist of ~26 blood proteins
- **Produced** by liver hepatocytes, lymphocytes, and monocytes
- Pathways
- Cascade reaction
- Stages

**Pathways**

- Classical
  - Activated by the presence of antibody bound to microbes
- Lectin
  - Activated when a host serum protein binds a sugar (mannan) in the wall of fungi and other microbes
- Alternative
  - Activated when complement proteins bind to cell wall or surface components of microbes
The three complement pathways, their activators, and the complement proteins involved.

Table 14.1 Complement Pathways

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Activators</th>
<th>Initial Components (that initially bind)</th>
<th>Complement Proteins Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical (Kemp's effect)</td>
<td>Complement-fixing antibodies (IgG, IgM), serine proteases, surface components</td>
<td>C1 complex, C9</td>
<td>C1 complex, C4, C5, C6, C7, C8, C9, Membrane Attack Complex</td>
</tr>
<tr>
<td>Lectin</td>
<td>Mananases, Mannose-binding lectin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternative (Decoy, leucocyte effect)</td>
<td>Bacterial or fungal cell wall, viruses, Retinal factors</td>
<td>C3</td>
<td>Factor D, Factor H, Properdin</td>
</tr>
</tbody>
</table>

Fig. 14.21a

(a) Initiation. The classical pathway begins when C1 components bind to antibodies bound to a foreign cell.

Fig. 14.21b

(b) Amplification and cascade. The C1 complex is an enzyme that activates a second series of components, C4 and C2. When these have been enzymatically cleaved into separate molecules, they become a second enzyme complex that activates C3. At this same site, C3 binds to C5 and cleaves it to form a product that is tightly bound to the membrane.

Fig. 14.21d

(c) Polymerization. C5a is a reactive site for the final assembly of an attack complex. In series, C6, C7, and C8 aggregate with C5 and become integrated into the membrane. They form a substrate upon which the final component, C9, can bind. Up to 16 of these C9 units ring the central core of the complex.

(d) Membrane attack. The final product of these reactions is a large, donut-shaped enzyme that punctures small pores through the membrane, leading to cell lysis.
Complement does 3 things

• Inflammation $\rightarrow$ C3a, C4a, C5a
• Opsonization $\rightarrow$ C3b
• MAC killing $\rightarrow$ C5-C9