Immunity

- The ability to ward off disease caused by microbes or their products and to protect against environmental agents such as pollen, chemicals, and pet dander
- Innate vs. adaptive immunity

Innate Immunity

Chapter 16
BIO 220

• Innate vs. adaptive immunity
  - Innate immunity
    - Immunity that you are born with
    - “Early warning system” – designed to keep pathogens out of the body and eliminate those that gain access to the body
    - Rapid response, but not specific
  - Adaptive immunity
    - Immunity that develops as a consequence of exposure to specific pathogens
    - Slower response, but tailored to specific pathogen
    - Body retains a memory of the pathogen

Lines of defense
First line of defense: Skin and mucous membranes

Mucous membranes
- Line cavities and passageways exposed to the external environment
- Secrete mucus, a slightly viscous glycoprotein that acts as a sticky trap
Lacrimal apparatus

Physical factors cont.

- Saliva
- Epiglottis
- Earwax
- Urine
- Vaginal secretions
- Gastric motility (i.e. peristalsis)

Sneezing, coughing, vomiting, etc.

Diarrhea

At the old tapeworms house
Lysozyme
...in Sweat
...in Tears
...in Saliva

Other chemical factors
- Sebum
- Earwax
- Saliva
- Gastric juice
- Vaginal secretions
- Urine

Normal microbiota
- Help prevent overgrowth of pathogens
  - Compete with pathogens for nutrients
  - Produce substances harmful to pathogens
    - Bacteriocins
  - Can alter environmental conditions which can impact the survival of pathogens
    - pH
- Probiotics?

Second line of defense
Defensive cells & proteins
Formed elements

Fig. 16.4

Granulocyte “-philis” vs. Agranulocyte “-cytes”

Neutrophil

Basophil

Eosinophil

Monocyte

Lymphocyte

Neutrophil

Fxn: Phagocytosis

Basophil
Eosinophil

Monocytes give rise to Macrophages

Fxn: Phagocytosis

Lymphocytes
**Natural Killer Cells**

- **Perforins & granzymes**

**Lymphatic System components:**
- Lymph
- Lymphatic vessels
- Lymphatic tissues & organs

**Functions of the Lymphatic System**
- Drains excess interstitial fluid
- Transports dietary lipids & lipid-soluble vitamins absorbed by the GI tract
- Carries out immune responses
Lymph is derived from plasma

Lymph nodes
- Are biological filters
- Lymphocytes
- Phagocytes

Lymphoid tissues and organs
- Red bone marrow
- Thymus
- Tonsils
- Peyer's patches
- Spleen
Phagocytes

- Phagocytosis is the ingestion of a microbe or other substance by a cell.
- Examples of phagocytes include neutrophils, macrophages, eosinophils, dendritic cells
- Macrophages may be “fixed” or “free” (wandering)
- Mononuclear phagocytic (reticuloendothelial) system – various macrophages of the body

Phagocytosis

- Phagocytes are activated when various components commonly found on pathogens (pathogen-associated molecular patterns or PAMPs) bind to protein receptors (i.e. Toll-like receptors or TLRs) on the plasma membranes of the defensive cells.

Phases of phagocytosis

**Chemotaxis**
- Can be microbial products, cytokines, components of damaged cells, etc.

**Adherence**
- Binding of PAMPs and TLRs
- Binding initiates phagocytosis and recruitment
- Opsonization
Phases of phagocytosis

Ingestion
• Pseudopodia engulf microbe
• Formation of phagosome

Digestion
• Phagosome fuses with lysosome to form phagolysosome
• Lysosomal enzymes attack microbial cells
• Formation of residual body
• Discharge of wastes

Microbial evasion of phagocytes
• M proteins and capsules inhibit attachment of microbe to phagocytes (S. pyogenes, S. pneumoniae)
• Microbes may release leukocidins, which can kill phagocytes (S. aureus)
• Some pathogens secrete pore-forming toxins that lyse phagocyte cell membranes once inside the phagocyte (T. cruzi, L. monocytogenes)
• Some can survive (and even thrive) within the phagocyte (C. burnetti)

Microbial evasion of phagocytes
• Some microbes can escape from phagosome before it combines with lysosome
  — Shigella, Rickettsia
• Others prevent fusion of phagosomes and lysosomes and the acidification of digestive enzymes
  — Plasmodium, M. tuberculosis, Chlamydia
• Biofilms can impede phagocytosis
**Inflammation**

- Redness
- Pain
- Heat
- Swelling
- Loss of function*

**Functions of inflammation**

- Destroy injurious agent and remove it and its by-products from the body
- If destruction not possible, confine or wall off agent and its by-products
- Repair or replace damaged tissue
Vasodilation/increased permeability of blood vessels

- Vasodilation and increased permeability occur, leading to edema
- Blood clot helps prevent spread of microbe or its toxins
- Pus!

Fig. 16.9

Phagocyte migration & phagocytosis

- As flow of blood decreases, phagocytes stick to the inner lining of blood vessels (margination)
- Diapedesis
- Phagocytosis by neutrophils and then macrophages

Fig. 16.9

Pus Formation

- Pocket of dead phagocytes and damaged tissue
- Common with inflammation
- Continues until infection gone
Inflammation – Tissue repair

- Repair is not complete until all harmful substances have been removed or neutralized
- During repair, the stroma or parenchyma produce new cells

Endotoxins and the pyrogenic response

To adjust to higher temperature, the body responds by constricting blood vessels, increasing metabolic rate, and shivering. This higher temperature is maintained until the cytokines are eliminated. As the infection subsides, vasodilation and sweating occur.

Fever

- IL-1 increases T cell production
- Intensifies affects of interferons
- Increases production of transferrins
- Speeds up repair

Complement system

- Consists of more than 30 proteins produced by the liver circulating in the blood and within tissues
- Proteins inactive until split into fragments
- C1-9, activated fragments a and b
- Complements action of other immune responses in destroying microbes entering the body
- Destroy microbes by cytolysis, opsonization, and inflammation
Complement activation

- Classical pathway
- Alternative pathway
- Lectin pathway

Inflammation stimulated by complement

CSa also attracts phagocytes to site of infection
Regulation of complement

- Once complement is activated, its destructive capabilities usually cease very quickly to minimize destruction of host cells
- This regulation is due to proteins in host blood and on certain cells, which are present in higher concentrations than the complement proteins
- Bring about the breakdown or inhibition of activated complement

Evading the complement system

- Capsules can prevent complement activation
  - Inhibition of MAC formation
  - Discourage opsonization
  - Inhibit the formation or function or cause the destruction of certain complement proteins
- Alterations to O polysaccharide
  - Inhibition of MAC formation
- etc.

Interferons (IFNs)

- Produced by lymphocytes and induce neutrophils and macrophages to kill bacteria
- Causes macrophages to produce NO that kills bacteria and tumor cells by inhibiting ATP synthesis
- Increases antigen presentation
Iron-binding proteins

- Transferrin – blood and tissue fluids
- Lactoferrin – milk, saliva, mucus
- Ferritin – liver, spleen, red bone marrow
- Hemoglobin – erythrocytes

- Many pathogenic bacteria obtain iron by secreting proteins called siderophores

Antimicrobial peptides (AMPs)

- Peptides of about 12 – 50 amino acids
- Broad spectrum of activity
- Inhibition of cell wall synthesis, form pores in the plasma membrane, destruction of nucleic acids
- Dermcidin – sweat glands
- Defensins and cathelicidins – neutrophils, macrophages and epithelium
- Thrombicidin – platelets

Antimicrobial peptides

- Work synergistically with other antimicrobials
- Stable over a wide range of pH
- Microbes do not seem to become resistant
- Participate in other immune functions
  - Sequester LPS shed from gram neg. bacteria
  - Attract dendritic cells
  - Recruit mast cells

**Table 16.2** Summary of Innate Immunity Defenses

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIRST LINE OF DEFENSE: SKIN AND MUCOUS MEMBRANES</strong></td>
<td></td>
</tr>
<tr>
<td>Saliva</td>
<td>Moistens skin, promotes desquamation, provides nutrients and growth factors for bacteria, enhances immune response</td>
</tr>
<tr>
<td>Nasal mucus</td>
<td>Promotes rapid mucus removal, dilutes and neutralizes toxins, provides nutrients for bacteria</td>
</tr>
<tr>
<td>Tears</td>
<td>Moistens skin, promotes desquamation, provides nutrients and growth factors for bacteria, enhances immune response</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Moistens skin, promotes desquamation, provides nutrients and growth factors for bacteria, enhances immune response</td>
</tr>
<tr>
<td><strong>CHALLENGE FACTORS</strong></td>
<td></td>
</tr>
<tr>
<td>Intact skin</td>
<td>Functions as a barrier to entry of pathogens</td>
</tr>
<tr>
<td><strong>IMMUNE RESPONSE</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Phagocytic cells</strong></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Phagocytose and kill bacteria</td>
</tr>
<tr>
<td>Macrophages</td>
<td>Phagocytose and kill bacteria</td>
</tr>
<tr>
<td><strong>Antimicrobial peptides</strong></td>
<td></td>
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<td>Dermcidin</td>
<td>Secreted by sweat glands, inhibits bacterial growth</td>
</tr>
<tr>
<td>Defensins and cathelicidins</td>
<td>Secreted by neutrophils, macrophages, and epithelial cells, inhibit bacterial and viral replication</td>
</tr>
<tr>
<td>Thrombicidin</td>
<td>Secreted by platelets, inhibits bacterial and viral replication</td>
</tr>
<tr>
<td><strong>Chemical factors</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sweat</strong></td>
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</tr>
<tr>
<td>Lactoferrin</td>
<td>Secreted by sweat glands, inhibits bacterial growth</td>
</tr>
<tr>
<td><strong>Saliva</strong></td>
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</tr>
<tr>
<td>Bacteriocins</td>
<td>Secreted by oral bacteria, inhibits bacterial growth</td>
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<tr>
<td><strong>Tears</strong></td>
<td></td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Secreted by tears, inhibits bacterial growth</td>
</tr>
<tr>
<td><strong>Mucous membranes</strong></td>
<td></td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Secreted by mucous membranes, inhibits bacterial growth</td>
</tr>
<tr>
<td><strong>Chemical defense</strong></td>
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</tr>
<tr>
<td><strong>Skin</strong></td>
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<tr>
<td>Lysozyme</td>
<td>Secreted by skin, inhibits bacterial growth</td>
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<tr>
<td><strong>Nasal mucus</strong></td>
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</tr>
<tr>
<td>Lysozyme</td>
<td>Secreted by nasal mucus, inhibits bacterial growth</td>
</tr>
</tbody>
</table>

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![Iron-binding proteins](image1.png)

![Antimicrobial peptides (AMPs)](image2.png)


## 16.2 Summary of Innate Immunity Defenses (Continued)

<table>
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<tr>
<th>Component</th>
<th>Function</th>
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</thead>
<tbody>
<tr>
<td><strong>SECRETORY DEFENSES</strong></td>
<td></td>
</tr>
<tr>
<td>Phagocytes</td>
<td>Phagocytes by cells such as macrophages, eosinophils, dendritic cells, and microphages</td>
</tr>
<tr>
<td>Natural Killer (NK) cells</td>
<td>Kill infected cells by releasing granules of perforin and granzymes; Phagocytes then kill the cells.</td>
</tr>
<tr>
<td>Innate Lymphocytes</td>
<td>Cytotoxic and antibody-producing cells that initiate an immune response.</td>
</tr>
<tr>
<td>Fever</td>
<td>Inhibit the effects of pathogens; induce secretion of antimicrobial agents; and speed up body reactions that aid recovery.</td>
</tr>
<tr>
<td><strong>ANTIMICROBIAL SUBSTANCES</strong></td>
<td></td>
</tr>
<tr>
<td>Complement system</td>
<td>Causes lysis of inclusion, prevents phagocytosis, and contributes to inflammation.</td>
</tr>
<tr>
<td>Interferon</td>
<td>Inhibits viral replication, blocks viral infection, and decreases phagocytosis.</td>
</tr>
<tr>
<td>Interleukin (IL)</td>
<td>Induces growth of certain factors by enhancing the presence of available free ribosomes.</td>
</tr>
<tr>
<td>Antimicrobial peptide (AMPs)</td>
<td>A variety of short peptides, bacteria to antibiotics, and participate in reactive oxygen species (ROS).</td>
</tr>
</tbody>
</table>

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