Immune System
Immune System surveillance: Seek and destroy mission

Immune system is designed to detect and destroy pathogens including:

**Viruses:**
- Chickenpox
- HIV-causes AIDS
- Hepatitis
- Herpes Simplex—cold sores
- Mononucleosis
- Influenza
- SARS
- Smallpox
- West Nile Fever

**Bacteria**

**Fungi**

**Worms**

**Cells that are not behaving (cancer)**

A. Polio virus (paralysis) B. Cholera bacterium (diarrhea) C. Protozoan parasite (Toxoplasma gondii) D. Ascaris (nematodes - removed from 2 year old intestinal obstruction)
Legionnaire’s disease: pneumonia-like disease first observed at American Legion convention. Death in 5-30% of cases, but treated with antibiotics. Spread through water.
Body is Constantly Challenged by Pathogens

Bacteria:

- *Bacillus anthracis* causes anthrax
- *Escherichia coli* (a.k.a. *E. coli*) lives in the gut, where it helps digest food and produces Vitamin K. The "bad" strain of *E. coli* O157:H7 causes severe foodborne sickness.
- *Mycobacterium tuberculosis* causes tuberculosis, a major killer from the past that has recently resurged with the advent of AIDS.
- *Staphylococcus* (a.k.a. *staph*) can cause serious infections and is one of the most drug-resistant bacteria.
- *Streptococcus pneumoniae* causes strep throat, meningitis, and pneumonia.
Are there complex, membrane-bound organelles?

(a) Prokaryotic Cell
Exponential Growth of Bacteria

Figure 11.1  Exponential growth of bacteria. *Salmonella*, the bacterium that causes food poisoning, reproduces every 20 minutes. If a sandwich with two bacteria is left out for 20 minutes, each bacterial cell will make a copy of itself, yielding four bacteria. After 40 minutes there will be eight bacteria; within eight hours there will be 33 million bacteria.
What are viruses?

- Viruses are not cells. They contain RNA or DNA, protein and a coat but are totally dependent on other organisms for their survival.
- Some form crystals when dried.

HIV can replicate to produce several billion virus copies per day.
HIV animation

• Which part of HIV enters the host cell?
• Is HIV made of DNA or RNA?
• What is the role of reverse transcriptase?
• Which enzyme splices the viral DNA into the host DNA?
• What is made from the DNA that is spliced into the host cell’s nucleus?
World-wide distribution of some major parasitic diseases

The figures show the total number of infections worldwide (some individuals may have more than one infection) and the number of infection-related deaths per year.

<table>
<thead>
<tr>
<th>Type of Disease</th>
<th>Estimated Human Infections</th>
<th>Estimated Deaths Per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All helminths</td>
<td>4.5 billion</td>
<td>&gt;500,000</td>
</tr>
<tr>
<td>Ascaris</td>
<td>1 billion</td>
<td>20 thousand</td>
</tr>
<tr>
<td>Hookworms</td>
<td>900 million</td>
<td>50-60 thousand</td>
</tr>
<tr>
<td>Trichuris</td>
<td>750 million</td>
<td>?</td>
</tr>
<tr>
<td>Filarial worms</td>
<td>657 million</td>
<td>20-50 thousand</td>
</tr>
<tr>
<td>Schistosomes</td>
<td>200 million</td>
<td>0.5-1.0 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>489 million</td>
<td>1-2 million</td>
</tr>
</tbody>
</table>
Example: Flesh-eating bacteria (necrotizing fasciitis)

Transmission: Group A strep infection in minor wound

- Treatment: Antibiotics,
  - protein synthesis
  - inhibitors, amputation

Mechanisms:
- Release of toxins
Three Lines of Defense

First line of defense (nonspecific): Skin and mucous membranes

Second line of defense (nonspecific): Phagocytosis by macrophages

Third line of defense (specific): Immune response

Innate immunity

Adaptive immunity

Pathogens
Non-specific: Block or attack any potential infectious organism. Cannot distinguish one attack from another. Always works the same way. Directed against any type of invading agent.

Two TYPES:

1. **External**
   - Barriers
   - Secretions

2. **Internal**
   - Anti-microbial proteins
     - Interferons
     - Complement system
   - Phagocytic white blood cells
   - Inflammatory response
   - Fever

Specific/Adaptive (Immune System): Protect against specific pathogens. Depends on activities of lymphocytes. Specific resistance (immunity) since it develops after exposure to environmental hazards.

Two types:

1. **Humoral (antibodies)**
2. **Cell mediated (lymphocytes)**
The 7 Nonspecific Defenses

1. Physical barriers
2. Phagocytic cells
3. Immunological surveillance
4. Interferons
5. Complement
6. Inflammation
7. Fever
1. Physical Barriers and their secretions

Physical barriers, Secretions and Accessory structures (hair, cilia)

- Skin (stratified squamous epithelia)
  - Secretions (acidic)
    - Oil
    - Sweat
- Mucous membranes
  - Digestive
    - Secretions:
      - Acidic
      - Mucus (e.g. stomach)
  - Respiratory (nose and airways)
    - Cilia
    - Secretions:
      - Lysosyme (enzyme that digest cell walls of bacteria)
      - Mucous
  - Genitourinary tract
    - Cilia
    - Secretions
2. Phagocytes: Nonspecific Immune Responses

Phagocytes
- Microphages:
  - Neutrophils and Eosinophils
  - Leave blood to enter tissues
- Monocytes > Macrophages (reticulo-endothelial system)
  - Migratory
  - Residential (e.g. Kupffer cells in liver, microglia in the brain)

Natural killer cells: kill by lysing with perforins not by phagocytosis

**PHAGOCYTES**
Remove debris and pathogens

<table>
<thead>
<tr>
<th>Fixed macrophage</th>
<th>Neutrophil</th>
<th>Free macrophage</th>
<th>Eosinophil</th>
<th>Monocyte</th>
</tr>
</thead>
</table>

**IMMUNOLOGICAL SURVEILLANCE**
Destroys abnormal cells

Natural killer cell → Lysed abnormal cell

**INTERFERONS**
Increase resistance of cells to viral infection; slow the spread of disease

Interferons released by activated lymphocytes, macrophages, or virus-infected cells

PERFORINS
Activated Phagocytes:
- engulf pathogen and destroy it with lysosomal enzymes
- bind to pathogen so other cells can destroy it
- destroy pathogen by releasing toxic chemicals into interstitial fluid

Phagocyte Chemotaxis

1. Microbe adheres to phagocyte.
2. Phagocyte forms pseudopods that eventually engulf the particle.
3. Phagocytic vesicle is fused with a lysosome.
4. Microbe in fused vesicle is killed and digested by lysosomal enzymes within the phagolysosome, leaving a residual body.
5. Indigestible and residual material is removed by exocytosis.
3. Immunological Surveillance: NK cells quickly attack cells that “look” abnormal

Natural killer cells survey cells in the body – looking for abnormal antigens. If strange antigens appear on cell surface (cancer cells with tumor specific antigens, cells infected with viruses (display abnormal proteins), they bind, attack by secreting perforin (that forms a big leaky channel), a protein that pokes holes in the abnormal cell membrane. Abnormal cell swells and dies.
4. Interferons

Interferons: chemicals released by lymphocytes, macrophages and cells infected with virus. Interferons bind to surface receptors to stimulate production of antiviral proteins and thus protects the target cell from viral infection (they do not kill viruses).

Three types of interferons (alpha, beta, gamma)
Use clinically to treat viral infections (hepatitis, herpes) and some cancers

http://pathmicro.med.sc.edu/mayer/vir-host2000.htm
Innate defenses → Internal defenses

1. Virus enters cell.
2. Interferon genes turned on.
3. Interferon molecules produced.
4. Interferon binding stimulates cell to turn on genes for antiviral proteins.
5. Antiviral proteins block viral reproduction.

**Host Cell 1**
Infected by virus; makes interferon; is killed by virus

**Host Cell 2**
Binds interferon from cell 1; interferon induces changes that protect it

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5. **Complement**

Group of 20 proteins in plasma that are activated by antibodies bound to antigen (CLASSIC) or by complement protein path stimulated (Alternative - slower). Both lead to the same final common pathway which stimulates inflammation, attracts phagocytes, enhances phagocytosis by opsonization.

Complement proteins in blood (factor P, factor B, and factor D) interact in plasma to form C3 to C3b.

In the presence of C3b, 5 complement proteins join to form membrane attack complex (MAC) that forms a pore and causes cell lysis - DEATH!

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**Opsonization:** coats bacterial surfaces, which enhances phagocytosis.

**MAC** causes inflammation:
- stimulates histamine release, increased blood vessel permeability, chemotactic attraction of phagocytes, etc.

**Insertion of MAC and cell lysis** (holes in target cell’s membrane)

**Complement proteins** insert themselves into the membrane of pathogens, creating a pore.

**Pore**
- Complement proteins (C5b-C9)
- H2O and ions
- Pathogen
- Water and ions enter cell.
- Cell swells and lyses.

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Fig. 24-8
6. Inflammatory Response

A localized response triggered by any stimulus that kills cells or injures tissue generates 4 cardinal signs and symptoms: Swelling, redness, heat, pain.

Inflammatory Response prevents the spread of damaging agents to nearby tissues, disposes of cell debris and pathogens and sets the stage for repair processes.
Inflammation

**Steps of the Inflammatory Response**

- The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?

1. Damaged tissues release histamines, increasing blood flow to the area.
2. Histamines cause capillaries to leak, releasing phagocytes and clotting factors into the wound.
3. Phagocytes engulf bacteria, dead cells, and cellular debris.
4. Platelets move out of the capillary to seal the wounded area.
6. DETAILS: Inflammation and Tissue Repair

Injured cells release: prostaglandins, proteins, & potassium ions
Changes interstitial environment and stimulates mast cells that release:
- histamine (increases capillary permeability)
- heparin (inhibits clotting)

Increased blood flow:
- raises local temperature
- causes area to swell, redden, and become painful

Blood clot forms around damaged area, isolating it

Complement:
- breaks down bacteria
- attracts phagocytes

Activated phagocytes secrete cytokines to generate positive feedback > neutrophils attack debris and bacteria and can stimulate production of more neutrophils

Phagocytes and foreign proteins activate body's specific defense system
Macrophages clean up pathogens and cell debris
Fibroblasts form scar tissue
Pathogens and active macrophages can secrete pyrogens that reset the body's thermostat and lead to fever (defense mechanism due to growth inhibition, increase phagocytosis)

- Necrosis: local tissue destruction in area of injury
- Pus: mixture of debris and necrotic tissue
- Abscess: pus accumulated in an enclosed space
7. Fever

- **Body temperature above 37°C (99°F)**
  - increases body metabolism
  - accelerates defenses
  - inhibits some viruses and bacteria
- **Pyrogens** Any material that causes the hypothalamus to raise body temperature:
  - circulating pathogens, toxins, or antibody complexes
- **Interleukin-1 (IL-1):**
  - cytokine that acts as an *endogenous pyrogen*
  - released by active macrophages
ADAPTIVE/SPECIFIC IMMUNE RESPONSE

Humoral - B cells (+THelper): antibodies

Cell Mediated - T cells (Cytotoxic and T helper): Cell killing
# Compare B Cells & T Cells

<table>
<thead>
<tr>
<th></th>
<th>B cells</th>
<th>T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where are they produced?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Where do they mature?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which react to bacteria?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which react to cells containing viruses or larger organisms like parasitic worms?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which produce antibodies?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which have receptors?</td>
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