Body Defenses Against Infection

Diseases-causing agents, pathogens, can produce infections within the body.

Two lines of defense vs. pathogens:

a. Nonspecific defenses:
   guard against any pathogen.

b. Specific defenses:
   mount a response against a very specific target.
   carried out by lymphocytes that recognize a specific invader.
NON-SPECIFIC DEFENSES

01. Species Resistance
    based upon unique chemical environment or temperature that fails to provide the conditions required by the pathogens of another species.

02. Mechanical Barriers
    unbroken skin and mucous membranes prevent the entry of certain pathogens.

NON-SPECIFIC DEFENSES

03. Chemical Barriers
    a. *Examples:* highly acidic and caustic environment(s) found in gastric juice or lysozyme (tears), which kill many pathogens.
    b. *Interferons:*
       - hormone-like peptides that serve as anti-viral substances.
       - produced by virus-infected cells.
       - interfere with viral transcription etc.
       - may induce nearby cells to produce anti-viral enzymes.
NON - SPECIFIC DEFENSES

04. Fever
protection vs. infection by interfering with bacterial growth conditions

During fever, reduced amount of iron in the blood:
- fewer available nutrients

Phagocytic cells attack with greater vigor when the temperature rises.

05. Natural Killer (NK) Cells (lymphocyte)
responsible for recognizing and destroying abnormal cells when they appear.
defend the body by releasing perforins which cause the cell membrane to disintegrate, destroying the infected cell.

Abnormal cells are: cells infected by viruses & cancer cells

NON - SPECIFIC DEFENSES

06. Inflammation
tissue response to a pathogen.
characterized by:
redness, swelling, heat, and pain.

Major inflammatory responses include:
dilation of blood vessels.
increase in capillary/venule permeability.
invasion of WBCs into affected area.
increase in body fluids and fibrin.
fibroblast appearance: sac production.
active phagocytosis, cell replacement.
NON - SPECIFIC DEFENSES

07. Phagocytosis

a. most active phagocytes: 
   neutrophils (small particles)
   monocytes (large particles)
   leave the bloodstream via dialedesisis.

b. Monocytes >>>>> macrophages,
   become fixed in various tissues.

c. Monocytes + macrophages + neutrophils: 
   mononuclear phagocytic system.

d. Phagocytosis also removes foreign 
   particles from the lymph.
SPECIFIC DEFENSES (Immunity)

01. Immunity
   the response mounted by the body against specific, recognized foreign antigens (non-self molecules).

02. Antigens (agglutinogens)
   Before birth, the body makes an inventory of "self" proteins, polysaccharides, glycoproteins, or glycolipids that are capable of eliciting (prompting) an immune response.

   Sometimes, small molecules called *haptens* combine with larger molecules and become *antigenic* (i.e., capable of eliciting an immune response).
SPECIFIC DEFENSES (Immunity)

03. Lymphocyte Origins

During fetal development, red bone marrow releases lymphocytes into circulation:
70-80% become T lymphocytes (T cells).
Remainder: become B lymphocytes (B cells).

Undifferentiated lymphocytes that reach the thymus become T cells.
B cells are thought to mature in the bone marrow.

Both B and T cells reside in lymphatic organs.
SPECIFIC DEFENSES (Immunity)

04. T cells and Cell - Mediated Immunity

T cells attack foreign, antigen-bearing cells, (i.e., bacteria) by direct cell-to-cell contact, providing cell-mediated immunity.

also secrete cytokines (lymphokines) that enhance cellular response to antigens.

- may also secrete toxins that kill target cells.
- may produce growth-inhibiting factors.
- may make interferon to interfere with viruses and tumor cells.

SPECIFIC DEFENSES (Immunity)

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colony stimulating factors</td>
<td>Stimulate bone marrow to produce lymphocytes</td>
</tr>
<tr>
<td>Interferons</td>
<td>Block viral replication, stimulate macrophages to engulf viruses, stimulate B cells to produce antibodies, attack cancer cells</td>
</tr>
<tr>
<td>Interleukins</td>
<td>Control lymphocyte differentiation and growth</td>
</tr>
<tr>
<td>Tumor necrosis factor</td>
<td>Stops tumor growth, releases growth factors, causes fever that accompanies bacterial infection, stimulates lymphocyte differentiation</td>
</tr>
</tbody>
</table>
05. **T cells types and Activation**

*T cell activation* requires the presence of an antigen-bearing cell, (i.e., macrophage or B cell) that has *already encountered* the antigen.

Some major types of T cells:

- helper T cells
- memory T cells
- cytotoxic T cells

REFERENCE ONLY:

Helper T cells bearing a CD4 antigen are the specific targets for HIV, the virus causing AIDS.

*** You will soon learn that B cell lymphocytes can also make *memory* B cells! *

---

**Helper T Cells:**

*Activation:* must first encounter a macrophage displaying the antigen.

If the antigen fits the helper T cell's antigen receptor, it becomes activated. Activated T cells release cytokines which may then activate B cells that have already encountered an antigen and cause the B cells to proliferate.

**Memory T Cells:**

provide a *no-delay response* to any future exposure to the same antigen.

**Cytotoxic T Cells:**

also continually *monitor* the body's own cells, recognizing and eliminating tumor cells and virus-infected cells by release of *perforin* and other means.
06. **B cells** and *Antibody - Mediated Immunity*

**Summary:** B cells attack pathogens by differentiating into **plasma cells** that secrete **antibodies** (immunoglobulins). A small number will become **B memory cells**.

*Body fluids* aid in attacking and destroying specific antigens or antigen-bearing particles through *antibody-mediated immunity*. 
**SPECIFIC DEFENSES (Immunity)**

**06. B cells and Antibody - Mediated Immunity**

**B cell Activation:**

1. When an *activated* helper T cell encounters a B cell (which has itself encountered an antigen), the helper T cell releases *cytokines*. This may activate the B cell so that it can divide and form a *clone (copies)*. See slide 20.

2. Some of the B cells become *plasma cells*, producing and secreting *antibodies*. Some become *B memory cells*: waiting for the encounter with the same antigen in the future. See slide 21.

---

**SPECIFIC DEFENSES (Immunity)**

**B-Cell Proliferation**

- Proliferation: Multiplying or increasing in number

Different B cells respond to different antigens on the surface of a given pathogen, leading to a polyclonal response.

Sometimes the Anamnestic response is referred to as the secondary response i.e., follow the first exposure! Swiftly and more powerfully…
SPECIFIC DEFENSES (Immunity)

Antibody Formation

06. B cells and Antibody - Mediated Immunity

Antibody Molecules:

a. Antibodies (immunoglobulins):
   \textit{gamma globulin fraction} of plasma.

b. Each immunoglobulin molecule is composed of \textit{two light chains} and \textit{two heavy chains} of amino acids.

c. Variable regions at the ends of the chains serve as unique antigen-binding sites.
### Table 16.5 Steps in Antibody Production

<table>
<thead>
<tr>
<th>B Cell Activity</th>
<th>T Cell Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Antigen-bearing agents enter tissues.</td>
<td>1. Antigen-bearing agents enter tissues.</td>
</tr>
<tr>
<td>2. B cell becomes activated when it encounters an antigen that fits its antigen receptors, either alone or more often in conjunction with helper T cells.</td>
<td>2. Accessory cell, such as a macrophage, phagocytizes antigen-bearing agent, and the macrophage’s lysosomes digest the agent.</td>
</tr>
<tr>
<td>3. Activated B cell proliferates, enlarging its clone.</td>
<td>3. Antigens from the digested antigen-bearing agents are displayed on the surface membrane of the accessory cell.</td>
</tr>
<tr>
<td>4. Some of the newly formed B cells differentiate further to become plasma cells.</td>
<td>4. Helper T cell becomes activated when it encounters a displayed antigen that fits its antigen receptors.</td>
</tr>
<tr>
<td>5. Plasma cells synthesize and secrete antibodies whose molecular structure is similar to the activated B cell’s antigen receptors.</td>
<td>5. Activated helper T cell releases cytokines when it encounters a B cell that has previously combined with an identical antigen-bearing agent.</td>
</tr>
<tr>
<td>6. Antibodies combine with antigen-bearing agents, helping to destroy them.</td>
<td>6. Cytokines stimulate the B cell to proliferate.</td>
</tr>
<tr>
<td>7. Some of the newly formed B cells differentiate into antibody-secreting plasma cells.</td>
<td>7. Some of the newly formed B cells differentiate into antibody-secreting plasma cells.</td>
</tr>
<tr>
<td>8. Antibodies combine with antigen-bearing agents, helping to destroy them.</td>
<td>8. Antibodies combine with antigen-bearing agents, helping to destroy them.</td>
</tr>
</tbody>
</table>

---

### SPECIFIC DEFENSES (Immunity)

#### 06. B cells and Antibody-Mediated Immunity (Humoral)

<table>
<thead>
<tr>
<th>Antibody isotypes of mammals</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA</td>
<td>Found in mucosal areas, such as the gut, respiratory tract and urogenital tract, and prevents colonization by pathogens. Also found in saliva, tears, and breast milk.</td>
</tr>
<tr>
<td>IgD</td>
<td>Functions mainly as an antigen receptor on B cells that have not been exposed to antigens. It has been shown to activate basophils and mast cells to produce antimicrobial factors.</td>
</tr>
<tr>
<td>IgE</td>
<td>Binds to allergens and triggers histamine release from mast cells and basophils, and is involved in allergy. Also protects against parasitic worms.</td>
</tr>
<tr>
<td>IgG</td>
<td>In its four forms, provides the majority of antibody-based immunity against invading pathogens. The only antibody capable of crossing the placenta to give passive immunity to fetus.</td>
</tr>
<tr>
<td>IgM</td>
<td>Expressed on the surface of B cells and in a secreted form with very high avidity. Eliminates pathogens in the early stages of B cell mediated (humoral) immunity before there is sufficient IgG.</td>
</tr>
</tbody>
</table>


---

Not Required: Monomer Dimer Pentamer arrangements.

Also Not required: number of types of each immunoglobulin class.
SPECIFIC DEFENSES (Immunity)

06. B cells and *Antibody-Mediated Immunity*

**Antibody Actions:**

a. react to antigens in *three* ways:

1. **direct attack:**
   - agglutination, precipitation, and neutralization of antigens.

2. **activation of complement:**
   - can produce opsonization, chemotaxis, inflammation, or lysis in target cells or antigens.

3. **stimulation of changes** in areas that prevent pathogen spreading.

---

**SPECIFIC DEFENSES (Immunity)**

06. B cells and *Antibody-Mediated Immunity*

- **Complement system**
- **Presence of antibodies combined with antigens**
- **Activation of complement proteins**
  - **Opsonization:** enhancing phagocytosis of antigens
  - **Chemotaxis:** attracting macrophages and neutrophils
  - **Lysis:** rupturing membranes of foreign cells
  - **Clumping:** of antigen-bearing agents
  - **Altering the molecular structure of viruses**
SPECIFIC DEFENSES (Immunity)

06. Immune Response

When B or T cells become activated the first time, their actions constitute a **primary immune response**, after which some cells remain as memory cells.

If the same antigen is encountered again, the more numerous memory cells can mount a more rapid response, known as the **secondary immune response**.

The ability to produce a secondary immune response may be long-lasting.
SPECIFIC DEFENSES (Immunity)

06. Immune Response

### Table 16.8 Practical Classification of Immunity

<table>
<thead>
<tr>
<th>Type</th>
<th>Mechanism</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naturally acquired active immunity</td>
<td>Exposure to live pathogens</td>
<td>Symptoms of a disease and stimulation of an immune response</td>
</tr>
<tr>
<td>Artificially acquired active immunity</td>
<td>Exposure to a vaccine containing weakened or dead pathogens or their components</td>
<td>Stimulation of an immune response without the severe symptoms of a disease</td>
</tr>
<tr>
<td>Artificially acquired passive immunity</td>
<td>Injection of antibodies of antitoxin</td>
<td>Immunity for a short time without stimulating an immune response</td>
</tr>
<tr>
<td>Naturally acquired passive immunity</td>
<td>Antibodies passed to fetus from pregnant woman with active immunity</td>
<td>Short-term immunity for infant without stimulating an immune response</td>
</tr>
</tbody>
</table>
Allergic or hypersensitivity reactions are excessive immune responses that may lead to tissue damage.

Delayed-reaction allergy results from repeated exposure to substances that cause inflammatory reactions in the skin.

Antibody-dependent cytotoxic reactions occur when blood transfusions are mismatched.

Immune complex allergic reactions involve autoimmunity.

During allergic reactions, mast cells release histamine and serotonin:

Allergy mediators sometimes flood the body, resulting in anaphylactic shock, a severe form of immediate-reaction allergy: next slide. (i.e. penicillin)
07. Allergic Reactions

08. Transplantations

Table 16.9 Transplant Types

<table>
<thead>
<tr>
<th>Type</th>
<th>Donor</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isograft</td>
<td>Identical twin</td>
<td>Bone marrow transplant from a healthy twin to a twin who has leukemia</td>
</tr>
<tr>
<td>Autograft</td>
<td>Self</td>
<td>Skin graft from one part of body to replace burned skin</td>
</tr>
<tr>
<td>Allograft</td>
<td>Same species</td>
<td>Kidney transplant from relative or closely matched donor</td>
</tr>
<tr>
<td>Xenograft</td>
<td>Different species</td>
<td>Heart valves from a pig</td>
</tr>
</tbody>
</table>
### Table 16.10 Autoimmune Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Symptoms</th>
<th>Antibodies Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerulonephritis</td>
<td>Lower back pain</td>
<td>Kidney cell antigens that resemble streptococcal bacteria antigens</td>
</tr>
<tr>
<td>Graves disease</td>
<td>Restlessness, weight loss, irritability, in-</td>
<td>Thyroid gland antigens near thyroid-stimulating hormone receptor, causing overactivity</td>
</tr>
<tr>
<td></td>
<td>creased heart rate and blood pressure</td>
<td></td>
</tr>
<tr>
<td>Juvenile diabetes</td>
<td>Thirst, hunger, weakness, emaciation</td>
<td>Pancreatic beta cells</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>Fatigue and weakness</td>
<td>Red blood cells</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>Muscle weakness</td>
<td>Receptors for neurotransmitters on skeletal muscle</td>
</tr>
<tr>
<td>Pernicious anemia</td>
<td>Fatigue and weakness</td>
<td>Binding site for vitamin B on cells lining stomach</td>
</tr>
<tr>
<td>Rheumatic fever</td>
<td>Weakness, shortness of breath</td>
<td>Heart valve cell antigens that resemble streptococcal bacteria antigens</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Joint pain and deformity</td>
<td>Cells lining joints</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Red rash on face, prolonged fever, weakness, kidney damage</td>
<td>DNA, neurons, blood cells</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Lower abdominal pain</td>
<td>Colon cells</td>
</tr>
</tbody>
</table>

*
Antigen Presentation

dendritic cell

1. A phagocyte "eats" a bacteria.
2. Parts of the bacteria (antigen) goes to the surface of the phagocyte

activated helper T cell

3. The phagocyte presents the antigen to a helper T cell

helper T cell

4. The helper T cell is activated.
1. The B-cell finds an antigen which matches its receptors.
2. It waits until it is activated by a T-helper cell.
3. Then the B-cell divides to produce plasma and memory cells.
4. Plasma cells produce antibodies that attach to the current type of invader.
5. "Eater cells," prefer intruders marked with antibodies and "eats" loads of them.
6. If the same intruder invades again, memory cells help to activate the immune system to activate much faster.