SECTION 22-2
Lymphatic vessels, lymphocytes, lymphoid tissues, and lymphoid organs function in body defenses

Lymphatic System

General functions
• With other organ systems, prevents and fights disease
• Returns tissue fluid (ECF) to circulation
• Transports fats in blood

General components
• Lymph = fluid similar to plasma, but fewer proteins
• Lymphatic vessels = run from peripheral tissues to veins
• Lymphoid tissues and organs
• Lymphocytes and supporting cells
Components of Lymphatic System

Lymphatic Vessels

Lymph Capillaries - a.k.a. terminal lymphatics

**Different than blood capillaries** because these:
- Begin as a blind end
- Have larger diameters
- Have thinner walls
- Have flattened cross-section
- Have an incomplete basement membrane or none at all
- Composed of epithelial cells that are not tightly bound together - act as one-way valves
Lymphatic Vessels - 2

Large Lymphatics
- Larger ones have valves, prevent backflow of lymph
- Merge to form lymphatic trunks

Largest:
- Thoracic duct empties into left subclavian vein
- Right lymphatic duct empties into right subclavian vein

See Figure 22-4 for drainage pattern.
Lymphocytes

Total about 1 trillion = 1 kg = 2.2 pounds

1. T cells (Thymus-dependent)
   - Cell-mediated immunity
   - 80% of circulating lymphocytes
   A. Cytotoxic T cells (T<sub>C</sub> cells)
      - Attack foreign cells, virus-infected and cancerous cells
   B. Helper T (T<sub>H</sub> cells)
      - Coordinate cell- and antibody-mediated immunity
   C. Suppressor T cells
      - Inhibit T and B cells

2. B cells (Bone marrow-derived)
   - Antibody-mediated (humoral) immunity
   - 10–15% of circulating lymphocytes
   - Differentiate into plasma cells which secrete antibodies (immunoglobulins)

   Antibody/antigen effects
   - Neutralize toxins
   - Agglutinate and precipitate antigens
   - Activate complement proteins
   - Attract phagocytes

3. NK cells (Natural Killer cells)
   - Immunological surveillance
   - 5–10% of circulating lymphocytes
   - Kill foreign, virus-infected and cancerous cells
Classes of Lymphocytes

- T cells: 80% live 4 years, some live 20+ years, replenish populations via cell division
- B cells: most in circulation are T cells, T cells: 30 min in blood; 5–6 h in spleen; 15–20 h in lymph node, B cells: 30 h in lymph node; circulation for a relatively short time

Circulation
- T cells: 30 min in blood; 5–6 h in spleen; 15–20 h in lymph node
- B cells: 30 h in lymph node; circulation for a relatively short time
Lymphoid Tissues
CT dominated by lymphocytes
- No capsule present
- Germinal center contains dividing cells
1. MALT (Mucosa-associated Lymphoid Tissue)
   - In digestive system - e.g. Peyer’s patches
2. Tonsils
   Large lymph nodules
   e.g. palatine tonsils (2)
   e.g. pharyngeal tonsil (1, a.k.a. adenoids)
   e.g. lingual tonsils

Lymphoid Nodules

Lymphoid Organs
Lymph organs have a capsule separating organ from other tissues
1. Lymph nodes
   - Afferent lymphatics: carry lymph into node
   - Efferent lymphatics: carry lymph away from node
   - Hilus: Blood vessels, nerves enter here
     Efferent vessels exit here
   - Lymph flow: sinuses → outer cortex → deep cortex → medulla → efferent lymphatics
Structure of a Lymph Node

Lymph Node Function

1. Filter (purify) lymph before its return to circulation
   - Antigen = a substance capable of triggering an immune response
   - Node removes 99% of antigens that enter
   - Antigen-presenting cells found here
   - Antigens presented to lymphocytes by macrophages, dendritic cells
2. "Early warning system"
   - Activity in one node triggers activity in nearby nodes
3. In axillae, groin, base of neck, throat, gut, lungs

The Thymus
<table>
<thead>
<tr>
<th>Thymus – 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divided into lobes</td>
</tr>
<tr>
<td>Located in mediastinum</td>
</tr>
<tr>
<td>Lymphoid stem cells differentiate into T cells here</td>
</tr>
<tr>
<td>• T cells mature here (thymosins)</td>
</tr>
<tr>
<td>Maximum <strong>relative size</strong> (% body wt.) in first 1–2 yrs. of life</td>
</tr>
<tr>
<td>Maximum <strong>absolute size</strong> just before puberty</td>
</tr>
<tr>
<td>Involutes (deteriorates) thereafter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thymus – 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytes are surrounded by reticular epithelial cells which</td>
</tr>
<tr>
<td>• Maintain blood-thymus barrier in cortex</td>
</tr>
<tr>
<td>• Secrete thymic hormones</td>
</tr>
<tr>
<td>✓ Promote stem cell division</td>
</tr>
<tr>
<td>✓ Promote T cell maturation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thymic (Hassall’s) Corpuscles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymic corpuscles produce chemical signals that cause <strong>dendritic cells</strong> in the thymus to induce development of regulatory (CD4+CD25+) T cells</td>
</tr>
<tr>
<td>These cells then patrol the body looking for “rogue” T cells that could cause autoimmune diseases. (<a href="http://www.ncbi.nlm.nih.gov/pubmed/16121185">http://www.ncbi.nlm.nih.gov/pubmed/16121185</a>)</td>
</tr>
</tbody>
</table>
The Spleen is the Largest Lymphoid Organ

Functions
- Removes abnormal, worn out blood cells and platelets
- Stores iron and platelets
- Initiates immune responses to antigens in blood (T and B cells)

Red pulp
- Many RBCs

White pulp
- Many lymphocytes

Types of Defense Mechanisms

1. **Nonspecific defenses = Nonspecific Resistance (to Disease)**
   - Response is the same *regardless of the invader*
   - Present at birth

2. **Specific Defenses = Specific Resistance (to Disease)**
   - Response is specific to a particular antigen
   - May also develop after birth
   - Requires activity of lymphocytes

SECTION 22-3
Nonspecific defenses do not discriminate between potential threats and respond the same regardless of the invader

1. Physical barriers
2. Phagocytes
3. Immunological surveillance
4. Interferons
5. Complement
6. Inflammation
7. Fever
### 1. Physical (Mechanical/Chemical) Barriers

<table>
<thead>
<tr>
<th>A. Epithelial modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Often stratified (thick), keratinized</td>
</tr>
<tr>
<td>• Contain desmosomes or tight junctions</td>
</tr>
<tr>
<td>• Have dense, fibrous basement membrane</td>
</tr>
<tr>
<td>• Acidic pH in skin, stomach, vagina</td>
</tr>
<tr>
<td>- Inhibits pathogen growth</td>
</tr>
<tr>
<td>- Good for “friendly” bacteria</td>
</tr>
<tr>
<td>• Lysozyme in tears, saliva = antimicrobial</td>
</tr>
<tr>
<td>• Unsaturated fats in sebum = antimicrobial</td>
</tr>
</tbody>
</table>

### 1. Physical Barriers – 2

<table>
<thead>
<tr>
<th>A. Epithelial modifications (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mucous membranes and cilia</td>
</tr>
<tr>
<td>- Mucus traps pathogens</td>
</tr>
<tr>
<td>- Some mucus is acidic</td>
</tr>
<tr>
<td>- Transported to removal site by cilia</td>
</tr>
<tr>
<td>- Name of this epithelium?</td>
</tr>
<tr>
<td>B. Tears, saliva, urine, mucus</td>
</tr>
<tr>
<td>- Wash away pathogens</td>
</tr>
<tr>
<td>C. Vomiting, diarrhea</td>
</tr>
<tr>
<td>- Removes pathogens</td>
</tr>
</tbody>
</table>

### 2. Phagocytes/Phagocytosis

<table>
<thead>
<tr>
<th>A. Microphages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Neutrophils</td>
</tr>
<tr>
<td>- Cellular debris, bacteria</td>
</tr>
<tr>
<td>• Eosinophils</td>
</tr>
<tr>
<td>- Antigen-antibody complexes</td>
</tr>
<tr>
<td>B. Macrophages</td>
</tr>
<tr>
<td>- a.k.a. monocyte-macrophage system</td>
</tr>
<tr>
<td>- a.k.a. reticuloendothelial system</td>
</tr>
<tr>
<td>- Engulf pathogens</td>
</tr>
<tr>
<td>- Act as antigen-presenting cells</td>
</tr>
</tbody>
</table>
2. Phagocytes/Phagocytosis – 2

B. Macrophages (continued)

- Release toxins
  - \( \text{H}_2\text{O}_2 \), NO, tumor necrosis factor
- Types derived from monocytes
  a) Fixed macrophages (histiocytes)
     - Reside in specific tissues
     - E.g. microglia, Kupffer cells (liver)
  b) Free (wandering) macrophages
     - a.k.a. mobile macrophages
     - Travel throughout tissues

2. Phagocytes/Phagocytosis – 3

B. Macrophages (continued)

- Movement
  - Diapedesis
    - Exit capillary walls
  - Chemotaxis
    - Attracted to chemical signals
  - Adhesion
    - Receptors allow attachment to target

3. Immunological Surveillance

- Carried out by Natural Killer (NK) cells
- Cells recognize a variety of abnormal antigens
  - On bacteria
  - On cancerous cells (tumor-specific antigens)
  - On virus-infected cells (viral antigens)

- NK cell activation - see Figure 22-12
  - Release perforins
4. Interferons are Cytokines

Released by:
- Activated lymphocytes
- Macrophages, fibroblasts
- Virus-infected cells

Effects:
- Cause production of antiviral proteins
- Interfere with viral reproduction in cells
- Stimulate NK cells and macrophages
- Decrease inflammation, slow spread of infection

5. Complement (Proteins) – 1

- Are plasma proteins that complement antibody function
- Function through a cascade of reactions
- Involved in both specific (classical pathway) and nonspecific (alternative pathway) defenses

Synthesized by many cell types:
- Liver, neutrophils, fibroblasts, epithelial cells (e.g. in gut), endothelial cells, adipocytes, kidney tubular cells, myocytes, etc.

(JE Volanakis and MM Frank, 1998)
5. Complement Proteins – 2

A. Classical pathway
Faster, more effective than alternative pathway
- $C_1$ binds to antibody on antigen (specific defense)
- Cascade (chain reaction) initiated
- Eventually, $C_3$ (inactive) $\rightarrow$ $C_{3b}$ (active)
- $C_{3b}$ attaches $\rightarrow$ rest of cascade and effects

5. Complement (Proteins) – 3

B. Alternative pathway
Slower, less effective
Does not involve antibodies (non-specific defense)
- Factors P (properdin), B and D interact with bacterial membrane (not antibody)
- $C_{3b}$ is formed, attaches to invader
- Cascade and complement effects follow
5. Complement (Proteins) - 4

Complement cascade effects:
- Membrane attack complexes formed → lysis of target cell
- Stimulates inflammation
  - ↑ histamine release
- Attracts phagocytes (chemotaxis)
- Enhances phagocytosis
  - Opsonization ("to make tasty")
  - Phagocyte receptors recognize complement

6. Inflammation

Response to cell damage or infection

Symptoms:
- Swelling (edema)
- Redness
- Heat
- Pain

Know why each of these symptoms appears.
Chapter 22 – Part 1

6. Inflammation – 2

Tissue damage causes changes in interstitial fluid
Damaged cells release:
• Prostaglandins
• Proteins
• K⁺ (causes vasodilation)
Pathogens/antigens are also present in a damaged area
Area is red, swollen, warm and painful.
Why?

6. Inflammation Response

A. Mast cells/basophils respond to chemical changes

Release:
• Histamine
  ↑ vasodilation → ↑ blood flow
  ↑ capillary permeability
  (plasma proteins, antibodies, and complement can leak into injury)
• Heparin
  Anticoagulant (local area doesn't clot)
• Prostaglandins
  Increase histamine effects

6. Inflammation Response – 2

B. Clotting Factors and complement enter tissues

• Region isolated from surroundings
• Slows spread of pathogens
• Bacteria attacked (complement)
C. Increased temperature (due to ↑ blood flow)
• ↑ chemical reaction rates
• ↑ phagocyte activity
• Denature foreign proteins
6. Inflammation Response – 3

D. Neutrophils attracted to site
   • First line of (cellular) defense
   • Phagocytosis, cytokine release

E. Pain: Stop doing that!
   • e.g. substance P, chemicals from mast cells

F. Leukocyte secretions (cytokines) activate specific defenses

7. Fever

Fever is a regulated increase in body temperature
Pyrogen = a substance that causes fever
   • Can be a pathogen, toxin, antibody-antigen complex or chemical released by macrophage
   • E.g. macrophage releases interleukin 1 → hypothalamus releases prostaglandins → hypothalamic thermostat set to higher value
### 7. Fever – Benefits of Fever

Leads to:
- Overall increase in metabolic rate
- Increased phagocyte activity
- Increased activity of T and B cells
- Intensifies effects of interferon
- Inhibits growth of some bacteria