Chapter 22

The Lymphatic System and Immunity
Introduction: Lymphatic System and Immunity

- **Pathogens**
  - Microscopic organisms that cause disease
    - Viruses
    - Bacteria
    - Fungi
    - Parasites
  - Each attacks in a specific way
Introduction: Lymphatic System and Immunity

- **Lymphatic system** (lymphoid system)
  - Protects us against disease
  - Lymphatic system cells respond to
    - Environmental pathogens
    - Toxins
    - Abnormal body cells, such as cancers
  - Lymphocytes
    - Part of the immune response
    - Identify, attack, and develop immunity to specific pathogens
Introduction: Lymphatic System and Immunity

- **Immune system**
  - **Immunity**
    - The ability to resist infection and disease
  - All body cells and tissues are involved in production of immunity
    - Not just lymphatic system
Components of Lymphatic System

- **Components of lymphatic system**
  - **Lymph**
    - A fluid similar to plasma but without plasma proteins
  - **Lymphatic vessels**
    - Carry lymph from peripheral tissues to veins
  - **Lymphoid tissues and lymphoid organs**
    - Scattered throughout body
  - **Lymphoid cells**
    - Lymphocytes, phagocytes, and other cells
Figure 22–1 The Components of the Lymphatic System (Part 1 of 2).

**Lymph Nodes and Lymphatic Vessels**
- Cervical lymph nodes
- Thoracic duct
- Right lymphatic duct
- Axillary lymph nodes
- Lymphatics of mammary gland
- Cisterna chyli
- Lymphatics of upper limb
- Lumbar lymph nodes

**Other Lymphoid Tissues and Organs**
- Tonsil
- Thymus
- Spleen
- Mucosa-associated lymphatic tissue (MALT) in digestive, respiratory, urinary, and reproductive tracts
Figure 22–1 The Components of the Lymphatic System (Part 2 of 2).

- Lymph Nodes and Lymphatic Vessels
  - Pelvic lymph nodes
  - Inguinal lymph nodes
  - Lymphatics of lower limb

- Other Lymphoid Tissues and Organs
  - Appendix
  - Red bone marrow

- Lymph
  - Lymphocyte
  - Lymphocyte
22-1 Components of Lymphatic System

- Lymphocytes are produced in
  - Primary lymphoid tissues and organs
  - Red bone marrow and thymus

- Lymphocytes are activated in
  - Secondary lymphoid tissues and organs
  - Tonsils, MALT, lymph nodes, and spleen
22-1 Components of Lymphatic System

- Functions of lymphatic system
  - Produce, maintain, and distribute lymphocytes and other lymphoid cells
  - Return excess fluid to bloodstream
  - Maintain normal blood volume
  - Transport hormones, nutrients, and wastes
22-1 Components of Lymphatic System

- **Lymphatic vessels** (lymphatics)
  - Carry **lymph**—interstitial fluid that has entered lymphatic vessels
    - From peripheral tissues to venous system
22-1 Components of Lymphatic System

- **Lymphatic capillaries**
  - Differ from blood capillaries in several ways
    - Closed at one end rather than forming a tube
    - Have larger luminal diameters
    - Have thinner walls
    - Have flat or irregular outline in sectional view
  - Endothelial cells loosely bound together
  - Overlap of endothelial cells acts as one-way valve
    - Allows fluids, solutes, viruses, and bacteria to enter
    - Prevents their return to intercellular spaces
The interwoven network formed by blood capillaries and lymphatic capillaries. Arrows indicate the movement of fluid out of blood capillaries and the net flow of interstitial fluid and lymph.
A sectional view indicating the movement of fluid from the plasma, through the tissues as interstitial fluid, and into the lymphatic system as lymph.
22-1 Components of Lymphatic System

- Lymph flows
  - From lymphatic capillaries to larger lymphatic vessels containing one-way valves

- Lacteals
  - Special lymphatic capillaries in small intestine
  - Transport lipids from digestive tract
A diagrammatic view of areolar connective tissue containing blood vessels and a lymphatic vessel. The cross-sectional view at right emphasizes their structural differences.
Like valves in veins, each lymphatic valve consists of a pair of flaps that permit movement of fluid in only one direction.
22-1 Components of Lymphatic System

- Lymphatic vessels
  - **Superficial lymphatics**
  - **Deep lymphatics**
    - Larger vessels that accompany arteries and veins
    - Located in skin, mucous membranes, and serous membranes lining body cavities
  - Join to form large **lymphatic trunks** that empty into two major collecting vessels
    - **Thoracic duct**
    - **Right lymphatic duct**
22-1 Components of Lymphatic System

- Thoracic duct
  - Base expands to form **cisterna chyli**, which receives lymph from
    - Right and left lumbar trunks
    - Intestinal trunk
  - Inferior segment collects lymph from
    - Left bronchomediastinal trunk
    - Left subclavian trunk
    - Left jugular trunk
  - Empties into left subclavian vein
Right lymphatic duct
  - Collects lymph from
    • Right jugular trunk
    • Right subclavian trunk
    • Right bronchomediastinal trunk
  - Empties into right subclavian vein
The thoracic duct carries lymph from tissues inferior to the diaphragm and from the left side of the upper body. The smaller right lymphatic duct carries lymph from the rest of the body.
The thoracic duct empties into the left subclavian vein. The right lymphatic duct empties into the right subclavian vein.
The thoracic duct empties into the left subclavian vein. The right lymphatic duct empties into the right subclavian vein.
22-1 Components of Lymphatic System

- **Lymphedema**
  - Blockage of lymph drainage from a limb
  - Causes severe swelling
  - Interferes with immune system function

- **Lymphoid cells**
  - Immune system cells and supportive cells in lymphoid tissues
  - **Lymphocytes**
    - Make up 20–40 percent of circulating leukocytes
    - Most are stored, not circulating
22-1 Components of Lymphatic System

- Types of lymphocytes
  - T cells
    - Thymus-dependent
  - B cells
    - Bone marrow–derived
  - NK cells
    - Natural killer cells
22-1 Components of Lymphatic System

- **Lymphoid tissues**
  - Connective tissues dominated by lymphocytes

- **Lymphoid nodules** (lymphatic nodules)
  - Areolar tissue with densely packed lymphocytes
  - **Germinal center** contains dividing lymphocytes
  - Distributed in
    - Lymph nodes
    - Spleen
    - Respiratory tract (tonsils)
    - Along digestive, urinary, and reproductive tracts
Figure 22–5b Lymphoid Nodules (Part 1 of 2).

- Intestinal lumen
- Mucous membrane of intestinal wall
- Aggregated lymphoid nodule in intestinal mucosa
- Germinal center
- Underlying connective tissue

**b** Aggregated lymphoid nodules in the intestine
Figure 22–5b Lymphoid Nodules (Part 2 of 2).

Intestinal lumen

Germinal center

Aggregated lymphoid nodule in intestinal mucosa

Underlying connective tissue

Aggregated lymphoid nodules

LM × 20

b Aggregated lymphoid nodules in the intestine
22-1 Components of Lymphatic System

- Five **tonsils** in wall of pharynx
  - Pharyngeal tonsil (adenoid)
  - Left and right **palatine tonsils**
  - Two **lingual tonsils**

- **Tonsillitis**
  - Inflammation of tonsils, especially palatine tonsils
The locations of the tonsils

Pharyngeal tonsil

Palate

Palatine tonsil

Lingual tonsil

Figure 22–5a Lymphoid Nodules (Part 1 of 2).
Figure 22–5a Lymphoid Nodules (Part 2 of 2).

Pharyngeal epithelium

Germinal centers within nodules

Pharyngeal tonsil  LM × 40

The locations of the tonsils
22-1 Components of Lymphatic System

- Mucosa-associated lymphoid tissue (MALT)
  - Lymphoid tissues associated with digestive system
  - Aggregated lymphoid nodules
    - Clustered deep to intestinal epithelial lining

- Appendix (vermiform appendix)
  - Contains a mass of fused lymphoid nodules
Components of Lymphatic System

- Lymphoid organs
  - Include
    - Lymph nodes
    - Thymus
    - Spleen
  - Separated from surrounding tissues by a fibrous connective tissue capsule
22-1 Components of Lymphatic System

- **Lymph nodes**
  - **Trabeculae**
    - Bundles of collagen fibers
    - Extend from capsule into interior of lymph node
  - **Hilum**
    - Shallow indentation where blood vessels and nerves reach lymph node
22-1 Components of Lymphatic System

- Lymph nodes
  - **Afferent lymphatics**
    - Carry lymph from peripheral tissues to lymph node
  - **Efferent lymphatics**
    - Leave lymph node at hilum
    - Carry lymph to venous circulation
Figure 22–6 The Structure of a Lymph Node (Part 1 of 2).

- Lymphatic vessel
- Lymph nodes
- Efferent vessel
- Trabeculae
- Medulla (B cells and macrophages)
- Medullary sinus
- Cortex (B cells)
- Subcapsular space
- Paracortex (T cells)
- Capsule
- Medullary cord
- Afferent vessel
- Hilum
- Lymph node artery and vein
- Dividing
- Lymph nodes
22-1 Components of Lymphatic System

- Lymph flow through nodes
  - From subcapsular space
    - Contains macrophages and dendritic cells
  - Through outer cortex
    - Contains B cells within germinal centers
  - Through paracortex (dominated by T cells)
  - Through the core (medulla)
    - Organized into medullary cords
      - Contains B cells and macrophages
  - Finally, into efferent lymphatics at hilum
Figure 22–6 The Structure of a Lymph Node (Part 2 of 2).

- Subcapsular space
- Germinal center
- Cortex
- Capsule
- Dividing B cell
- Dendritic cells
- Nuclei of B cells
- Capillary
Components of Lymphatic System

- **Lymph node function**
  - Purify lymph before return to venous circulation
    - Remove 99 percent of antigens
  - Antigens released due to infection
    - Enter lymph and stimulate macrophages and lymphocytes in lymph nodes
    - Are also carried by dendritic cells to lymph nodes

- **Lymphoid tissues and lymph nodes**
  - Monitor peripheral infections
  - Respond before infections reach vital organs
22-1 Components of Lymphatic System

- Lymph nodes of gut, trachea, lungs, thoracic duct
  - Protect against pathogens in digestive and respiratory systems

- Largest lymph nodes
  - In groin, axillae, and base of neck
  - Swell in response to infection

- Lymphadenopathy
  - Chronic or excessive enlargement of lymph nodes
  - May indicate infections or cancer
22-1 Components of Lymphatic System

- **Thymus**
  - Located in mediastinum
  - Atrophies after puberty
    - Diminishing effectiveness of immune system
  - Divided into two thymic *lobes*
  - **Septa** divide lobes into smaller *lobules*
22-1 Components of Lymphatic System

- Thymic lobule
  - Dense outer cortex
  - Pale central medulla

- Lymphocytes
  - Divide in cortex
  - Migrate into medulla
  - Mature T cells leave thymus by medullary blood vessels
22-1 Components of Lymphatic System

- **Epithelial reticular cells**
  - Surround lymphocytes in cortex
  - Form layered structures in medulla known as *thymic (Hassall’s) corpuscles*
  - Maintain **blood thymus barrier** in cortex
    - Absent in medulla

- **Thymic hormones**
  - Thymosin—an extract from thymus containing several hormones
    - Promotes development and maturation of T cells
The appearance and position of the thymus in relation to other organs in the chest.
Anatomical landmarks on the thymus.
Fibrous septa divide the tissue of the thymus into lobules resembling interconnected lymphoid nodules.
Higher magnification reveals the unusual structure of thymic corpuscles. The small cells are lymphocytes in various stages of development.
Functions of the **spleen**

1. Removal of abnormal blood cells and other blood components by phagocytosis
2. Storage of iron recycled from red blood cells
3. Initiation of immune responses by B cells and T cells
   - In response to antigens in circulating blood
22-1 Components of Lymphatic System

- Anatomy of the spleen
  - Attached to stomach by gastrosplenic ligament
  - Contacts diaphragm and left kidney
  - Splenic veins, arteries, and lymphatic vessels
    - Communicate with spleen at hilum

- Histology of the spleen
  - Cellular components within capsule make up pulp
    - Red pulp contains many red blood cells
    - White pulp resembles lymphoid nodules
22-1 Components of Lymphatic System

- **Trabecular arteries**
  - Branch and radiate toward capsule
  - Finer branches surrounded by white pulp
  - Capillaries discharge red blood cells into red pulp

- **Red pulp**
  - Contains elements of circulating blood
    - Plus fixed and free macrophages
22-1 Components of Lymphatic System

- Splenic circulation
  - Blood passes through network of reticular fibers
  - Then enters large sinusoids lined by macrophages
    - Which empty into trabecular veins
A transverse section through the trunk, showing the typical position of the spleen projecting into the peritoneal cavity. The shape of the spleen conforms to the shapes of adjacent organs.
A posterior view of the surface of an intact spleen, showing major anatomical landmarks.
White pulp is dominated by lymphocytes; it appears purple because the nuclei of lymphocytes stain very darkly. Red pulp contains large numbers of red blood cells.
22-1 Components of Lymphatic System

- Spleen function
  - Phagocytes and other lymphocytes in spleen
    • Identify and attack damaged and infected cells in circulating blood

- Splenectomy
  - Removal of a severely ruptured spleen
22-2 Innate and Adaptive Immunity

- **Immunity**
  - Ability to resist and defend against infectious organisms and other damaging substances
  - **Resistance**
    - Ability of body to maintain immunity

- **Immune response**
  - Body’s reaction to infectious agents and other abnormal substances
Two types of immunity

- **Innate (nonspecific) immunity**
  - Always works the same way
  - Against any type of invading agent

- **Adaptive (specific) immunity**
  - Protects against specific pathogens
  - Depends on activities of lymphocytes
  - Develops after exposure to environmental hazards
22-2 Innate and Adaptive Immunity

- Lymphocytes
  - **B cells, T cells, and NK cells**

- Lymphocyte distribution
  - Tissues maintain different T cell and B cell populations
  - Lymphocytes wander through tissues
    - Enter blood vessels or lymphatics for transport
    - Can survive many years
Lymphocyte production

- Also called lymphocytopoiesis, involves
  - Bone marrow
  - Thymus
  - Peripheral lymphoid tissues
- Hemocytoblasts in bone marrow
  - Divide into two types of lymphoid stem cells
Lymphoid stem cells

- **Group 1**
  - Remain in bone marrow and develop with help of stromal cells
  - Produce B cells and NK cells
  - B cells differentiate with exposure to interleukin-7

- **Group 2**
  - Migrate to thymus
  - Develop in environment isolated from blood
  - T cells differentiate with exposure to hormones
One group of stem cells remains in the red bone marrow, producing daughter cells that mature into NK cells and B cells.
Thymus

The second group of stem cells migrates to the thymus, where subsequent divisions produce daughter cells that mature into T cells.

Migrate to thymus

Lymphoid stem cells

Production, selection, and differentiation of T cells

Mature T cells

Thymic hormones
All three types of lymphocytes circulate throughout the body in the bloodstream, establishing immunity.

### Peripheral Tissues

**Immune surveillance**

**NK cells** attack foreign cells, body cells infected by viruses, and cancer cells. They secrete chemicals that lyse the plasma membrane of the abnormal cells.

- **NK cells**
- **Abnormal cell**
- **Cell destroyed**

**Antibody-mediated immunity**

When stimulated, **B cells** can differentiate into **plasma cells**, which produce and secrete antibodies. These antibodies attach to pathogens. This starts a chain reaction that leads to the destruction of the pathogen.

- **NK cells**
- **B cell**
- **Plasma cell**
- **Antibodies**
- **Cell destroyed**

**Cell-mediated immunity**

One type of mature **T cell**, called **cytotoxic T cells**, plays a role in cell-mediated immunity. These cells attack and destroy foreign cells or body cells infected by viruses.

- **Cytotoxic T cell**
- **Abnormal cell**
- **Antibodies**
- **Cell destroyed**
22-2 Innate and Adaptive Immunity

- T cells and B cells
  - Migrate throughout body
    - To defend peripheral tissues
  - Retain their ability to divide
    - Essential to immune system function
22-3 Innate Defenses

- Innate (nonspecific) defenses
  - Block or attack any foreign substance or pathogen
  - Cannot distinguish one pathogen from another
22-3 Innate Defenses

- Innate defenses
  - Physical barriers
  - Phagocytes
  - Immune surveillance
  - Interferons
  - Complement
  - Inflammation
  - Fever
<table>
<thead>
<tr>
<th>Innate Defenses</th>
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<tr>
<td><strong>Physical barriers</strong></td>
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<td>keep hazardous organisms and materials outside the body.</td>
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<tr>
<td><img src="image" alt="Diagram of physical barriers" /></td>
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<tr>
<td><strong>Phagocytes</strong></td>
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<tr>
<td>engulf pathogens and cell debris.</td>
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<tr>
<td><img src="image" alt="Diagram of phagocytes" /></td>
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<tr>
<td><strong>Immune surveillance</strong></td>
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<tr>
<td>is the destruction of abnormal cells by NK cells in peripheral tissues.</td>
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<tr>
<td><img src="image" alt="Diagram of immune surveillance" /></td>
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<td><strong>Interferons</strong></td>
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<tr>
<td>are chemical messengers that coordinate the defenses against viral infections.</td>
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<td><img src="image" alt="Diagram of interferons" /></td>
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### Innate Defenses

<table>
<thead>
<tr>
<th><strong>Complement</strong></th>
<th><strong>Inflammation</strong></th>
<th><strong>Fever</strong></th>
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</thead>
<tbody>
<tr>
<td>is a system of circulating proteins that assist antibodies in the destruction of pathogens. It also lyses cells, and enhances phagocytosis and inflammation.</td>
<td>is a localized, tissue-level response that tends to limit the spread of an injury or infection.</td>
<td>is an elevation of body temperature that speeds up tissue metabolism and the activity of defenses.</td>
</tr>
</tbody>
</table>

#### Complement

- Lysed pathogen

#### Inflammation

- Mast cell

1. Increases blood flow
2. Activates macrophages
3. Increases capillary permeability
4. Activates complement
5. Stimulates regional clotting reaction
6. Increases regional temperature
7. Activates adaptive defenses

#### Fever

- Body temperature rises above 37.2°C in response to pyrogens

- Chart showing body temperature range from 0 to 100 with an arrow pointing to 100.
22-3 Innate Defenses

- Physical barriers
  - Outer layer of skin
  - Hair
  - Epithelial layers of internal passageways
  - Secretions that flush away materials
    - Sweat, mucus, and urine
  - Secretions that kill or inhibit microorganisms
    - Containing enzymes, antibodies, or stomach acid
22-3 Innate Defenses

- **Phagocytes**
  - Attack and remove dangerous microorganisms
  - **Microphages**
    - Neutrophils and eosinophils
    - Enter peripheral tissues to fight infections
  - **Macrophages**
    - Large phagocytic cells derived from monocytes
    - Distributed throughout body
    - Make up *monocyte–macrophage system* (reticuloendothelial system)
22-3 Innate Defenses

- Activated macrophages
  - Respond to pathogens in several ways
    - 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
22-3 Innate Defenses

- Types of macrophages
  - **Fixed macrophages** (histiocytes)
    - Stay in specific tissues and organs (e.g., dermis and bone marrow)
    - **Microglia** found in central nervous system
    - **Stellate macrophages** found in liver sinusoids
  - **Free macrophages** (wandering macrophages)
    - Travel throughout body
    - **Alveolar macrophages** (phagocytic dust cells)
22-3 Innate Defenses

- Free macrophages and microphages
  - Move through capillary walls (emigration)
  - Are attracted or repelled by chemicals in surrounding fluids (chemotaxis)
  - Phagocytosis begins
    - When phagocyte attaches to target (adhesion)
    - And surrounds it with a vesicle
22-3 Innate Defenses

- **Immune surveillance**
  - Carried out by natural killer (NK) cells
  - Activated NK cells
    1. Identify and adhere to abnormal cells
    2. Golgi apparatus produces vesicles containing **perforins**
    3. Vesicles release perforins by exocytosis
    4. Perforins form pores in abnormal cell’s plasma membrane, causing lysis
Figure 22–11 How Natural Killer Cells Kill Cellular Targets (Part 1 of 4).

1. Recognition and adhesion

NK cell  Golgi apparatus

Antigen  Abnormal cell
Figure 22-11 How Natural Killer Cells Kill Cellular Targets (Part 2 of 4).

2 Realignment of Golgi apparatus
Figure 22–11 How Natural Killer Cells Kill Cellular Targets (Part 3 of 4).

Secretion of perforin

Perforin molecules

Pores formed by perforin complex

NK cell

Abnormal cell
Figure 22–11 How Natural Killer Cells Kill Cellular Targets (Part 4 of 4).

Lysis of abnormal cell
22-3 Innate Defenses

- Immune surveillance
  - **Tumor-specific antigens**
    - On plasma membranes of cancer cells
    - Identified as abnormal by NK cells
    - Some cancer cells avoid detection (*immunological escape*)
  - Cells infected with viruses
    - Present abnormal proteins on plasma membranes
    - Allows NK cells to identify and destroy them
22-3 Innate Defenses

- **Interferons (IFNs)**
  - Small proteins released by activated lymphocytes and macrophages
  - Trigger production of antiviral proteins
  - Antiviral proteins do not kill viruses
    - Block viral replication in the cell
  - IFNs are one type of cytokine
- **Cytokines**
  - Chemical messengers released by tissue cells
  - Important to immune response
## 22-3 Innate Defenses

### Types of interferons

- **Interferon alpha** ($\alpha$)
  - Produced by cells infected with viruses
  - Stimulates NK cells

- **Interferon beta** ($\beta$)
  - Secreted by fibroblasts
  - Slows inflammation

- **Interferon gamma** ($\gamma$)
  - Secreted by T cells and NK cells
  - Stimulates macrophage activity
<table>
<thead>
<tr>
<th><strong>Interferon alpha (α)</strong></th>
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<tr>
<td>is produced by cells infected with viruses. It attracts and stimulates NK cells and enhances resistance to viral infection.</td>
<td><img src="image" alt="Cell" /></td>
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<th><strong>Interferon beta (β)</strong></th>
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<td>is secreted by fibroblasts and slows inflammation in a damaged area.</td>
<td><img src="image" alt="Fibroblast" /></td>
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<th><strong>Interferon gamma (γ)</strong></th>
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<td>is secreted by T cells and NK cells and stimulates macrophage activity.</td>
<td><img src="image" alt="Macrophage" /></td>
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22-3 Innate Defenses

- **Complement system**
  - More than 30 special *complement proteins* in plasma
  - Assists antibodies in destruction of pathogens
  - Complement proteins work together in cascades
  - Three routes of activation of complement
    - Classical pathway
    - Lectin pathway
    - Alternative pathway
22-3 Innate Defenses

- **Classical pathway** of complement activation
  - Most rapid and effective mode of activation
  - Begins with binding of complement protein C1
    - To two antibodies attached to antigen
  - Bound protein acts as an enzyme
    - Catalyzes chain reaction
The most rapid and effective activation of the complement system occurs through the classical pathway.

Antibodies bind to bacterial cell wall

Attachment of C1
C1 must attach to two antibodies for its activation.

Activation and Cascade
The attached C1 protein acts as an enzyme, catalyzing a series of reactions involving other complement proteins that split C3 into C3a and C3b. C3a diffuses away and activates an inflammatory response.

C3b Attachment (classical pathway)
C3b binds to the bacterial cell wall and enhances phagocytosis.
22-3 Innate Defenses

- **Lectin pathway** of complement activation
  - Mannose-binding lectin (MBL) binds to carbohydrates on pathogen surfaces

- **Alternative pathway** of complement activation
  - Begins when several complement proteins interact
    - Properdin (factor P)
    - Factor B
    - Factor D
The lectin pathway is activated by the protein mannose-binding lectin (MBL). MBL binds to carbohydrates on bacterial surfaces.

**C3 Activation**
Bound MBL forms a complex that splits C3 into C3a and C3b. C3a activates an inflammatory response.

**C3b Attachment (lectin pathway)**
C3b binds to bacterial surface and enhances phagocytosis.
Figure 22–13 Pathways of Complement Activation (Part 3 of 4).

**Alternative Pathway**

The alternative pathway is important in the defense against bacteria, some parasites, and virus-infected cells.

**Complement proteins interact in plasma**

Properdin
Factor B
Factor D

C3a
C3b

Bacterial cell wall

The alternative pathway begins when several complement proteins, notably properdin, interact in the plasma causing C3 to split into C3a and C3b. This interaction can be triggered by exposure to foreign materials, such as the capsule of a bacterium. C3a activates an inflammatory response.

**C3b Attachment (alternative pathway)**

C3b protein binds to the bacterial cell wall.
22-3 Innate Defenses

- All three complement system pathways involve
  - Conversion of inactive C3 protein to activated C3b and C3a proteins

- Effects of complement activation
  - Killing of pathogen by cell lysis
    - Proteins may form membrane attack complex (MAC)
  - Enhanced phagocytosis (opsonization)
  - Inflammation (histamine release)
**Killing of Pathogen (Cell Lysis)**

Once an activated C3b protein has attached to the cell wall, additional complement proteins may form a **membrane attack complex (MAC)** in the membrane that destroys the integrity of the target cell.

**Enhanced Phagocytosis (Opsonization)**

The attached C3b may also act to enhance phagocytosis. This enhancement of phagocytosis, a process called **opsonization**, occurs because macrophage membranes contain receptors that detect and bind to complement proteins and bound antibodies.

**Inflammation (Histamine Release)**

Release of histamine by mast cells and basophils increases the degree of local inflammation, attracts and activates phagocytes, and accelerates blood flow to the region.
22-3 Innate Defenses

- **Inflammation**
  - Localized tissue response to injury
  - Triggered by any stimulus that kills cells or injures tissue
  - Cardinal signs and symptoms of inflammation
    - Redness
    - Swelling
    - Heat
    - Pain
22-3 Innate Defenses

- Effects of inflammation
  - Temporarily repair injury
    - Prevent additional pathogens from entering wound
  - Slow spread of pathogens to surrounding areas
  - Mobilize local, regional, and systemic defenses
    - To overcome pathogens and facilitate permanent repairs (regeneration)
22-3 Innate Defenses

- Products of inflammation
  - **Necrosis**
    - Local tissue destruction in area of injury
  - **Pus**
    - Mixture of debris, fluid, dead and dying cells, and necrotic tissue
  - **Abscess**
    - Accumulation of pus in an enclosed space
Figure 22–14 Inflammation and the Steps in Tissue Repair (Part 1 of 2).

- **Tissue Damage**
- **Chemical change in interstitial fluid**
- **Mast Cell Activation**
  - Release of histamine and heparin from mast cells
Figure 22–14 Inflammation and the Steps in Tissue Repair (Part 2 of 2).

**Redness, Swelling, Heat, and Pain**
- Dilation of blood vessels, increased blood flow, increased vessel permeability
- Clot formation (temporary repair)

**Phagocyte Attraction**
- Attraction of phagocytes, especially neutrophils
  - Release of cytokines
  - Removal of debris by neutrophils and macrophages; stimulation of fibroblasts
  - Activation of specific defenses

**Tissue Repair**
- Pathogen removal, clot erosion, scar tissue formation
22-3 Innate Defenses

- Fever
  - A body temperature greater than 37.2°C (99°F)
    - Increases metabolic rate
    - Accelerates defenses
    - Inhibits some viruses and bacteria
22-3 Innate Defenses

- **Pyrogens**
  - Fever-inducing agents
  - Produced by bacteria, molds, viruses, and yeasts
  - Cause hypothalamus to raise body temperature
  - Endogenous pyrogens
    - Interleukin-1, interferons, and tumor necrosis factor
22-4 Adaptive Defenses

- Adaptive (specific) defenses
  - Result from coordinated activities of T cells and B cells
22-4 Adaptive Defenses

- Primary types of T cells
  - **Cytotoxic T cells**
    - Attack antigens physically and chemically
  - **Helper T cells**
    - Stimulate responses of T cells and B cells
  - **Regulatory T cells**
    - Moderate immune response
  - **Memory T cells**
    - Respond to antigens previously encountered
22-4 Adaptive Defenses

- Types of regulatory T cells
  - Inflammatory T cells
  - Suppressor/inducer T cells

- B cells
  - Make up 10–15 percent of circulating lymphocytes
  - Differentiate into plasma cells
    - Produce and secrete antibodies

- Natural killer (NK) cells
  - Make up 5–10 percent of circulating lymphocytes
Figure 22–15 Classes of Lymphocytes.

**Classes of Lymphocytes**

**T Cells**
- Approximately 80% of circulating lymphocytes are classified as T cells.
  - **Cytotoxic T Cells**: Cytotoxic T cells attack foreign cells or body cells infected by viruses.
  - **Helper T Cells**: Helper T cells stimulate the activation and function of both T cells and B cells.
  - **Regulatory T Cells**: Regulatory T cells moderate both T cells and B cells.
  - **Memory T Cells**: Memory T cells are a subset of T cells that respond to a previously encountered antigen.

**B Cells**
- B cells make up 10–15% of circulating lymphocytes.
  - **Plasma Cells**: When stimulated, B cells can differentiate into plasma cells, which produce and secrete antibodies.

**NK Cells**
- NK cells make up the remaining 5–10% of circulating lymphocytes.
22-4 Adaptive Defenses

- **Cell-mediated immunity** *(cellular immunity)*
  - Provided by cytotoxic T cells
  - Defends against abnormal cells and pathogens inside cells

- **Antibody-mediated immunity**
  - Provided by B cells
  - Defends against antigens and pathogens in body fluids
Figure 22–16 An Overview of Adaptive Immunity.

**Cell-Mediated Immunity**

- **Phagocytes activated**
- **T cells activated**

**Direct Physical and Chemical Attack**

- Activated T cells find the pathogens and attack them through phagocytosis or the release of chemical toxins.

**Antibody-Mediated Immunity**

- **Activated B cells give rise to cells that produce antibodies.**

**Attack by Circulating Antibodies**

- Destruction of antigens

**Adaptive Immunity**

- Antigen presentation triggers an immune response by specific defenses.

Communication and feedback
22-4 Adaptive Defenses

- Adaptive immunity
  - Antigens
    - Chemical targets that stimulate immune response
  - When a lymphocyte contacts an appropriate antigen
    - It becomes activated
  - An activated lymphocyte divides to produce a clone
  - Clonal selection
    - Process of an antigen “selecting” lymphocytes for cloning
22-4 Adaptive Defenses

- **Forms of immunity**
  - **Innate immunity**
    - Present at birth
  - **Adaptive immunity**
    - Acquired after birth
  - **Active immunity**
    - Develops after exposure to antigen
  - **Passive immunity**
    - Produced by transferring antibodies from another source
Figure 22–17 Forms of Immunity.

Ability to resist infection and disease

Adaptive (Specific) Immunity
Adaptive immunity is not present at birth. You acquire immunity to a specific antigen only when you have been exposed to that antigen or receive antibodies from another source.

Active Immunity
Develops in response to antigen exposure

Naturally Acquired Active Immunity
Develops after exposure to antigens in environment

Artificially Acquired Active Immunity
Develops after administration of an antigen to prevent disease

Passive Immunity
Produced by transfer of antibodies from another source

Naturally Acquired Passive Immunity
Conferred by transfer of maternal antibodies across placenta or in breast milk

Artificially Acquired Passive Immunity
Conferred by administration of antibodies to combat infection

Innate (Nonspecific) Immunity
Genetically determined—no prior exposure or antibody production involved
22-4 Adaptive Defenses

- Active immunity
  - Naturally acquired active immunity
    • Through environmental exposure to pathogens
  - Artificially acquired active immunity
    • Through **vaccines**

- Passive immunity
  - Naturally acquired passive immunity
    • Antibodies acquired from the mother
  - Artificially acquired passive immunity
    • By an injection of antibodies
22-4 Adaptive Defenses

- Four properties of adaptive immunity
  - **Specificity**
    - Each T or B cell responds only to a specific antigen and ignores all others
  - **Versatility**
    - The body produces many types of lymphocytes
      - Each fights a different type of antigen
      - An activated lymphocyte clones itself to fight a specific antigen
Four properties of immunity

- **Memory**
  - Some inactive lymphocytes (memory cells)
    - Stay in circulation
    - Provide immunity against new exposure

- **Tolerance**
  - Immune system ignores “normal” antigens (self-antigens)
22-5 T Cells and Immunity

- T cells are activated by exposure to an antigen

- **Antigen presentation**
  - T cells recognize only antigens that are “presented” by antigen-presenting cells
  - **MHC proteins**
    - Membrane glycoproteins that bind antigens
    - Genetically coded by **major histocompatibility complex (MHC)** in chromosome 6
22-5 T Cells and Immunity

- Two classes of MHC proteins
  - **Class I MHC proteins**
    - Found in membranes of all nucleated cells
    - Pick up small peptides in cell and carry them to the surface
    - T cells ignore normal peptides
    - Abnormal peptides or viral proteins activate T cells to destroy cell
Antigen presentation by class I MHC proteins is triggered by viral or bacterial infection of a body cell.

The infection results in the appearance of abnormal peptides in the cytoplasm.

The abnormal peptides are incorporated into class I MHC proteins as they are synthesized at the endoplasmic reticulum.

The abnormal peptides are displayed by class I MHC proteins on the plasma membrane.

After export to the Golgi apparatus, the MHC proteins reach the plasma membrane within transport vesicles.

Infected body cell.
Two cells exposed to fluorescent-tagged antibodies. The green cell is an APC and the red cell is a lymphocyte.
22-5 T Cells and Immunity

- **Class II MHC proteins**
  - Found in membranes of lymphocytes and **antigen-presenting cells (APCs)** such as **dendritic cells**
  - Antigenic fragments
    - From **antigen processing** of pathogens
    - Bind to class II proteins
    - Inserted into plasma membrane
  - APC then presents the protein-antigen complex to T cells
Figure 22–18c Antigens and MHC Proteins.

1. Phagocytic APCs engulf the extracellular pathogens.

2. Lysosomal action produces antigenic fragments.

3. The endoplasmic reticulum produces class II MHC proteins.

4. Antigenic fragments are bound to class II MHC proteins.

5. Antigenic fragments are displayed by class II MHC proteins on the plasma membrane.

Antigen-presenting cell (APC).
22-5 T Cells and Immunity

- **Antigen recognition**
  - Inactive T cells have receptors
    - That bind to class I or class II MHC proteins
    - Also have binding sites for specific antigen
  - Binding occurs when antigen matches receptor on T cell
22-5 T Cells and Immunity

- **CD markers**
  - Also called *cluster of differentiation* markers
    - In T cell membranes
    - Molecular mechanism of antigen recognition
    - More than 350 types

- **CD3 receptor complex**
  - Found in all T cells
22-5 T Cells and Immunity

- Important CD markers
  - **CD8** markers
    - Found on cytotoxic T cells and regulatory T cells
    - Respond to antigens on class I MHC proteins
  - **CD4** markers
    - Found on helper T cells
    - Respond to antigens on class II MHC proteins

- CD8 and CD4 markers
  - Bind to CD3 receptor complex
  - Prepare cell for activation
Costimulation
- For T cell to be activated, it must be costimulated
  • By binding to stimulating cell at second site
  • Which confirms the first signal
22-5 T Cells and Immunity

- **CD8 T cells**
  - Activated by exposure to antigens on class I MHC proteins
    - One responds quickly, producing cytotoxic T cells and memory T cells
    - Other responds slowly, producing regulatory T cells
To destroy target cell, a cytotoxic T cell may

- Release perforins to destroy target cell’s plasma membrane,
- Release cytokines and activate genes in target cell to trigger apoptosis, or
- Secrete poisonous lymphotoxin
Figure 22–19 Antigen Recognition and Activation of Cytotoxic T Cells (Part 1 of 2).

**Antigen Recognition**

Antigen recognition occurs when a CD8 T cell encounters an appropriate antigen on the surface of another cell, bound to a class I MHC protein.

- Infected cell
- Viral or bacterial antigen
- Inactive CD8 T cell

**Activation and Cell Division**

Antigen recognition and costimulation result in T cell activation and cell division, producing active T<sub>C</sub> cells and memory T<sub>C</sub> cells.

- Active T<sub>C</sub> cells
- Memory T<sub>C</sub> cells (inactive)

**Costimulation**

Costimulation activates CD8 T cell

- CD8 protein
- Class I MHC
- T cell receptor

Before activation can occur, a T cell must be chemically or physically stimulated by the abnormal target cell.
Figure 22–19 Antigen Recognition and Activation of Cytotoxic T Cells (Part 2 of 2).

**Destruction of Target Cell**

The active T_c cell destroys the antigen-bearing cell. It may use several different mechanisms to kill the target cell.

- Lysed cell
- Perforin release
- Destruction of plasma membrane
- Cytokine release
- Stimulation of apoptosis
- Lymphotoxin release
- Disruption of cell metabolism
22-5 T Cells and Immunity

- **Memory T<sub>C</sub> cells**
  - Produced with cytotoxic T cells
  - Stay in circulation
  - Immediately form cytotoxic T cells if same antigen appears again

- **Regulatory T cells**
  - Secrete suppression factors
  - Inhibit responses of T and B cells
  - Act after initial immune response
  - Limit immune reaction to single stimulus
 Activation of CD4 T cells
  - Active helper T cells (T\textsubscript{H} cells)
    • Secrete cytokines
  - Memory T\textsubscript{H} cells
    • Remain in reserve
Antigen Recognition by CD4 T Cell

- Foreign antigen
- Class II MHC
- Antigen-presenting cell (APC)
- Antigen
- CD4 protein
- T cell receptor
- T\(_H\) cell
- Inactive CD4 (T\(_H\)) cell

Costimulation
CD4 T Cell Activation and Cell Division

Memory $T_H$ cells (inactive)

Active $T_H$ cells

Active helper T cells secrete cytokines that stimulate both cell-mediated and antibody-mediated immunity.
Cytokines

- Chemicals released by cells involved in immune response
- Six major groups of cytokines
  - Interleukins
  - Interferons
  - Tumor necrosis factors
  - Phagocyte-activating chemicals
  - Colony-stimulating factors
  - Miscellaneous cytokines
Functions of interleukins

1. Increasing T cell sensitivity to antigens exposed on macrophage membranes
2. Stimulating B cell activity, plasma cell formation, and antibody production
3. Enhancing innate immunity by stimulating inflammation, mast cells, ACTH secretion, scar tissue formation, elevation of body temperature
4. Suppressing immune function and shortening immune response
22-5 T Cells and Immunity

- **Interleukins**
  - IL-1 and IL2, are important in stimulating and maintaining the immune response
  - When released by activated macrophages and lymphocytes, these cytokines stimulate activities of other immune cells and of the secreting cell
  - Result is a positive feedback loop that helps to recruit additional immune cells
22-5 T Cells and Immunity

- Tumor necrosis factors (TNFs)
  - Slow growth of tumor and kill sensitive tumor cells
  - Stimulate granular leukocyte production, promote eosinophil activity, cause fever, and increase T cell sensitivity to interleukins
  - Activated macrophages secrete one type of TNF and carry the molecules in their membranes
  - Cytotoxic T cells produce a different type of TNF
22-5 T Cells and Immunity

- Phagocyte-activating chemicals
  - Several cytokines coordinate immune defenses by adjusting activities of phagocytic cells
  - Some attract free macrophages and microphages and prevent premature departure from site of injury

- Colony-stimulating factors (CSFs)
  - Produced by active T cells, cells of the monocyte–macrophage system, endothelial cells, and fibroblasts
  - Stimulate production of blood cells in red bone marrow and lymphocytes in lymphoid tissues and organs
Cytokines are often classified according to origins
- Lymphokines are produced by lymphocytes
- Monokines are secreted by active monocytes, macrophages, and other antigen-presenting cells
- Lymphocytes and macrophages may secrete the same cytokines
- Cells involved in adaptive immunity and tissue repair can also secrete cytokines
Functions of cytokines

- Stimulate T cell divisions
  - Produce memory T cells
  - Accelerate cytotoxic T cell maturation
- Attract and stimulate macrophages
- Attract and stimulate activity of cytotoxic T cells
- Promote activation of B cells
**Activation by class I MHC proteins**

Antigen bound to class I MHC protein

Indicates that the cell is infected or otherwise abnormal

CD8 T Cells

Cytotoxic T Cells
- Attack and destroy infected and abnormal cells displaying antigen

Memory T<sub>C</sub> Cells
- Await reappearance of the antigen

Regulatory T Cells
- Control or moderate immune response by T cells and B cells
Figure 22b A Summary of the Pathways of T Cell Activation.

**b Activation by class II MHC proteins**

Antigen bound to class II MHC protein

Indicates presence of pathogens, toxins, or foreign proteins

CD4 T Cells

Helper T Cells

Stimulate immune response by T cells and B cells

Memory $T_H$ Cells

Await reappearance of the antigen
22-6 B Cells and Immunity

- **B cells**
  - Responsible for antibody-mediated immunity
  - Attack antigens by producing specific antibodies
  - Millions of populations, each with different antibody molecules
B cell sensitization

- Antigens in interstitial fluids bind to corresponding B cell receptors
- B cell prepares for activation
- During sensitization, antigens are
  - Taken into B cell
  - Processed
  - Reappear on surface, bound to class II MHC proteins
Figure 22–23 The Sensitization and Activation of B Cells (Part 1 of 3).

1 Sensitization

Antigens

Class II MHC

Antibodies

Inactive B cell

Antigens bound to antibody molecules

Antigen binding

Sensitized B cell
Helper T cells

- Sensitized B cell is prepared for activation but needs helper T cell to become activated
- Helper T cell binds to MHC complex
  - Secretes cytokines that promote B cell activation
Figure 22–23 The Sensitization and Activation of B Cells (Part 2 of 3).

Activation

Class II MHC T cell receptor

Antigen

B cell

T cell

Cytokine costimulation

Helper T cell

Sensitized B cell
Activated B cell divides into

- **Plasma cells**
  - Synthesize and secrete antibodies into interstitial fluid

- **Memory B cells**
  - Like memory T cells, remain in reserve to respond to next infection
Division and Differentiation

Stimulation by cytokines

ANTIBODY PRODUCTION

Activated B cells

Plasma cells

Memory B cells (inactive)
22-6 B Cells and Immunity

- **Antibodies**
  - Soluble proteins
  - Two pairs of polypeptide chains
    - One pair of **heavy chains**
    - One pair of **light chains**
  - Each chain contains
    - Constant segments
    - Variable segments
A diagrammatic view of the structure of an antibody.
A computer-generated image of a typical antibody.
22-6 B Cells and Immunity

- Constant segments of heavy chains determine classes of antibodies, or **immunoglobulins (Igs)**
  - IgG
  - IgE
  - IgD
  - IgM
  - IgA
B Cells and Immunity

- IgG
  - Largest and most diverse class of antibodies
  - 80 percent of all antibodies
  - Responsible for resistance against many viruses, bacteria, and bacterial toxins
  - Can cross placenta
  - Maternal IgG provides passive immunity to fetus
  - Anti-Rh antibodies produced by Rh-negative mothers
    - Produce hemolytic disease of newborn
IgE

- Attaches as an individual molecule to exposed surfaces of basophils and mast cells
- When an antigen is bound by IgE molecules
  - Cell is stimulated to release histamine and other chemicals that accelerate inflammation
- Also important in allergic response
22-6 B Cells and Immunity

- IgD
  - An individual molecule on surfaces of B cells, where it can bind antigens in extracellular fluid
  - Binding can play a role in the sensitization of the B cell involved
22-6 B Cells and Immunity

- **IgM**
  - First class of antibody secreted after an antigen is encountered
  - Concentration declines as production accelerates
  - Plasma cells secrete individual IgM molecules
    - Polymerize and circulate as five-antibody starburst
  - Anti-A and anti-B antibodies responsible for agglutination of incompatible blood types
  - May also attack bacteria that are insensitive to IgG
22-6 B Cells and Immunity

- IgA
  - Found primarily in glandular secretions such as mucus, tears, saliva, and semen
  - Attack pathogens before they gain access to internal tissues
  - Circulate in blood individually or in pairs
  - Epithelial cells absorb them from blood and attach a secretory piece
    - Confers solubility before secreting IgA molecules onto epithelial surface
22-6 B Cells and Immunity

- Variable segments of light and heavy chains
  - Determine specificity of antibody molecule
- Free tips of two variable segments
  - Form **antigen-binding sites** of antibody molecule
  - Bind to **antigenic determinant sites (epitopes)** of antigen molecule
- **Antigen–antibody complex**
  - An antibody bound to an antigen
Antibodies bind to portions of an antigen called antigenic determinant sites, or epitopes.
Antigen–antibody complex

- **Complete antigen**
  - Has at least two antigenic determinant sites
  - Binds to both antigen-binding sites of variable segments of antibody

- Exposure to a complete antigen leads to
  - B cell sensitization
  - Immune response
22-6 B Cells and Immunity

- Actions of antibodies
  - **Neutralization** of antigen binding sites
  - **Precipitation** and **agglutination**—formation of immune complexes
  - Activation of complement system
  - Attraction of phagocytes
  - Opsonization increasing phagocyte efficiency
  - Stimulation of inflammation
  - Prevention of bacterial and viral adhesion
22-6 B Cells and Immunity

- Hapten (partial antigens)
  - Must attach to a carrier molecule to act as a complete antigen
  - Antibodies will attack both hapten and carrier molecule
  - If carrier is normal,
    - Antibody attacks normal cells
    - Example: penicillin allergy
Antibody molecules can bind a hapten (partial antigen) once it has become a complete antigen by combining with a carrier molecule.
Responses to antigen exposure

- First exposure
  - Produces **primary response**

- Next exposure
  - Triggers **secondary response**
  - More extensive and prolonged
  - Memory cells already primed
22-6 B Cells and Immunity

- Primary response
  - Takes time to develop
  - Antigens activate B cells
  - Plasma cells differentiate
  - **Antibody titer**—level of antibodies in plasma
    - Slowly rises
22-6 B Cells and Immunity

- Primary response
  - Peak response
    - Can take two weeks to develop
    - Declines rapidly
  - IgM
    - Produced faster than IgG
    - Less effective than IgG
The primary response takes about 2 weeks to develop peak antibody levels (titers). IgM and IgG antibody levels do not remain elevated.
Secondary response
- Activates memory B cells
  - At lower antigen concentrations than original B cells
  - Secrete antibodies in massive quantities
- IgG
  - Rises very high and very quickly
  - Can remain elevated for extended time
- IgM
  - Production is also quicker
The secondary response has a very rapid increase in IgG antibody concentration and rises to levels much higher than those of the primary response. Antibody levels remain elevated for an extended period after the second exposure to the antigen.
Immunocompetence

- Ability to produce immune response after exposure to antigen

Combined responses to bacterial infection
- Neutrophils and NK cells begin killing bacteria
- Cytokines draw phagocytes to area
- Antigen presentation activates helper T cells and cytotoxic T cells
- B cells activate and differentiate
- Plasma cells increase antibody levels
The Course of the Body’s Response to a Bacterial Infection.

- **Neutrophils**
- **Macrophages**
- **Plasma cells**
- **Natural killer cells**
- **Cytotoxic T cells**
- **Antibody level**

**Number of active immune cells**

**Time (weeks)**
**Figure 22–27** An Integrated Summary of the Immune Response.

**Innate (Nonspecific) Immunity**
- Complement system
- NK cells, macrophages

**Adaptive (Specific) Immunity**
- Antigen presentation by APCs

**Cell-Mediated Immunity**
- Antigen and class I MHC Protein
  - Indicates that the cell is infected or otherwise abnormal
  - CD8 T cells
    - Cytotoxic T Cells: Attack and destroy infected and abnormal cells displaying antigen
    - Memory T<sub>C</sub> Cells: Await reappearance of the antigen
    - Regulatory T Cells: Moderate immune response by T cells and B cells
  - Inhibition

**Antibody-Mediated Immunity**
- Antigen and class II MHC Protein
  - Indicates the presence of pathogens, toxins, or foreign proteins
  - CD4 T cells
    - Helper T Cells: Stimulate immune response by T cells and B cells
    - Memory T<sub>H</sub> Cells: Await reappearance of the antigen
    - Activation of B cells
      - Production of memory B cells
      - Production of plasma cells
      - Secretion of antibodies

**Inhibition**
- Direct physical and chemical attack
- Destruction of Antigens
- Attack by circulating proteins
22-7 Immunocompetence

- Bacterial versus viral infections
  - Basic sequence of events in immune response is similar
  - Initial steps differ
    - Cytotoxic T cells provide adaptive defense
    - NK cells provide innate defense
Defenses against bacterial and viral pathogens involve phagocytosis and antigen presentation by APCs. The process includes:

1. **Phagocytosis by macrophages and APCs**
2. **Antigen presentation**
   - Activation of cytotoxic T cells
   - Activation of helper T cells
   - Activation of B cells
   - Antibody production by plasma cells
   - Opsonization and phagocyte attraction
   - Formation of antigen–antibody complexes

**Destruction of bacteria by cell lysis or phagocytosis.**
Defenses against Bacterial and Viral Pathogens.

**VIRUSES**

- Infection of tissue cells
  - Release of interferons
  - Increased resistance to viral infection and spread
  - Appearance of antigen in plasma membrane
  - Stimulation of NK cells
  - Activation of cytotoxic T cells
  - Activation of helper T cells
- Infection of or uptake by APCs
  - Antigen presentation
  - Activation of B cells
  - Antibody production by plasma cells
- Destruction of virus-infected cells
  - Destruction of viruses or prevention of virus entry into cells

Defenses against viruses involve direct contact with virus-infected cells and antigen presentation by APCs.
22-7 Immunocompetence

- Development of immunocompetence
  - Fetus can produce immune response
    - At about three to four months
  - Fetal thymus cells migrate to tissues and become APCs
  - Liver and bone marrow produce B cells
    - Carry IgM antibodies
22-7 Immunocompetence

- Before birth
  - Maternal IgG antibodies
    - Pass through placenta
    - Provide passive immunity to fetus

- After birth
  - Mother’s milk provides IgA antibodies
    - While passive immunity is lost
22-7 Immunocompetence

- Normal resistance
  - Infant produces IgG antibodies through exposure to antigens
  - Antibody, B cell, and T cell levels slowly rise to adult levels
22-7 Immunocompetence

- Stress and immune response
  - Glucocorticoids
    - Secreted to limit immune response
    - Long-term secretion (chronic stress)—inhibits immune response and lowers resistance to disease
  - Functions of glucocorticoids
    - Depression of inflammation
    - Reduction in abundance and activity of phagocytes in peripheral tissues
    - Inhibition of interleukin secretion
22-7 Immunocompetence

- Immune disorders
  - Allergies (hypersensitivities)
  - Autoimmune disorders
  - Immunodeficiency diseases
22-7 Immunocompetence

- **Hypersensitivities** (allergies)
  - Excessive immune responses to antigens
  - **Allergens**
    - Antigens that trigger allergic reactions

- **Categories of hypersensitivities**
  - Immediate hypersensitivity (type I)
  - Cytotoxic reactions (type II)
  - Immune complex disorders (type III)
  - Delayed hypersensitivity (type IV)
22-7 Immunocompetence

- **Immediate hypersensitivity** (type I)
  - Rapid, severe response to an antigen
  - Most commonly recognized type of allergy
  - Includes allergic rhinitis (environmental allergies)
  - Sensitization leads to production of large quantities of IgE
  - Second exposure leads to
    - Massive inflammation of affected tissues
22-7 Immunocompetence

- Immediate hypersensitivity
  - Severity of reaction depends on
    - Individual sensitivity
    - Locations involved
  - Allergens in bloodstream may cause anaphylaxis
22-7 Immunocompetence

- **Anaphylaxis**
  - Can be fatal
  - Affects cells throughout body
  - Changes capillary permeability
    - Produces swelling and hives on skin
  - Smooth muscles of respiratory system contract
    - Making breathing extremely difficult
  - Peripheral vasodilation
    - Can cause circulatory collapse (anaphylactic shock)
First Exposure

- Allergen fragment

- Allergens

- Macrophage

- \( T_H \) cell activation

- B cell sensitization and activation

- Plasma cell

- IgE antibodies
Subsequent Exposure

Allergen

Sensitization of mast cells and basophils

Massive stimulation of mast cells and basophils

Release of histamines, leukotrienes, and other chemicals that cause pain and inflammation

Capillary dilation, increased capillary permeability, airway constriction, mucus secretion, pain and itching
22-7 Immunocompetence

- **Antihistamines**
  - Drugs that block action of histamine
  - Can relieve mild symptoms of immediate hypersensitivity
  - Example: Benadryl
Autoimmune disorders

- A malfunction of system that recognizes and ignores “normal” antigens
- Activated B cells make autoantibodies against body cells
- Examples
  - Thyroiditis
  - Rheumatoid arthritis
  - Type 1 diabetes
Immunocompetence

- Immunodeficiency diseases result from
  - Problems with embryological development of lymphoid organs and tissues
    - Can result in **severe combined immunodeficiency disease (SCID)**
  - Viral infections such as HIV
    - Can result in **AIDS**
  - **Immunosuppressive drugs** or radiation treatments
    - Can lead to complete immunological failure
22-8 Effects of Aging on Immune Response

- Immune system diminishes with age
  - Increasing vulnerability to infections and cancer

- Effects of aging
  - Thymic hormone production is greatly reduced
  - T cells become less responsive to antigens
  - Fewer T cells reduces responsiveness of B cells
  - Immune surveillance against tumor cells declines
22-9 Immune System Integration

- Nervous and endocrine systems
  - Influence immune response
Integumentary System
- The Integumentary System provides physical barriers to pathogen entry; dendritic cells in epidermis and macrophages in dermis resist infection and present antigens to trigger the immune response; mast cells trigger inflammation, mobilize cells of lymphatic system
- The lymphatic system provides IgA antibodies for secretion onto integumentary surfaces

Skeletal System
- The Skeletal System supports the production of lymphocytes and other cells involved in the immune response in red bone marrow
- The lymphatic system assists in repair of bone after injuries; osteoclasts differentiate from monocyte–macrophage cell line

Muscular System
- The Muscular System protects superficial lymph nodes and the lymphatic vessels in abdominopelvic mesenteries; muscle contractions help propel lymph along lymphatic vessels
- The lymphatic system assists in repair after injuries

Lymphatic System
- The lymphatic system provides adaptive (specific) defenses against infection for all body systems. It:
  - produces, maintains, and distributes lymphocytes
  - returns fluid and solutes from peripheral tissues to the blood
  - distributes hormones, nutrients, and waste products from their tissues of origin to the general circulation

Nervous System
- The Nervous System has antigen-presenting microglia that stimulate adaptive defenses; glial cells secrete cytokines; innervates antigen-presenting cells
- The lymphatic system produces cytokines that affect production of CRH and TRH by hypothalamus

Endocrine System
- The Endocrine System produces glucocorticoids that have anti-inflammatory effects; thymosins that stimulate development and maturation of lymphocytes; many hormones that affect immune function
- The lymphatic system secretes thymosins from thymus; cytokines affect cells throughout the body

Cardiovascular System
- The Cardiovascular System distributes WBCs; carries antibodies that attack pathogens; clotting response helps restrict spread of pathogens; granulocytes and lymphocytes produced in red bone marrow
- The lymphatic system fights infections of cardiovascular organs; returns tissue fluid to circulation