Chapter 22

The Lymphatic System and Immunity

An Introduction to the Lymphatic System and Immunity

- **Pathogens**
  - Microscopic organisms that cause disease:
    - Viruses
    - Bacteria
    - Fungi
    - Parasites
  - Each attacks in a specific way

22-1 Overview of the Lymphatic System

- **The Lymphatic System**
  - Protects us against disease
  - Lymphatic system cells respond to:
    - Environmental pathogens
    - Toxins
    - Abnormal body cells, such as cancers

22-1 Overview of the Lymphatic System

- **Specific Defenses**
  - Lymphocytes
    - Part of the immune response
    - Identify, attack, and develop immunity
      - To a specific pathogen

22-1 Overview of the Lymphatic System

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

22-1 Overview of the Lymphatic System

- **Nonspecific Defenses**
  - Block or attack any potential infectious organism
  - Cannot distinguish one attack from another

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22-2 Structures of Body Defenses

- Organization of the Lymphatic System
  1. **Lymph**
     - A fluid similar to plasma but does not have plasma proteins
  2. **Lymphatic vessels (lymphatics)**
     - Carry lymph from peripheral tissues to the venous system
  3. **Lymphoid tissues and lymphoid organs**
  4. Lymphocytes, phagocytes, and other immune system cells

22-2 Structures of Body Defenses

- Function of the Lymphatic System
  o To produce, maintain, and distribute lymphocytes

  **Lymphocyte Production**
  o Lymphocytes are produced
    - In lymphoid tissues (e.g., tonsils)
    - Lymphoid organs (e.g., spleen, thymus)
    - In red bone marrow
  o Lymphocyte distribution
    - Detects problems
    - Travels into site of injury or infection

22-2 Structures of Body Defenses

- Lymphocyte Circulation
  o From blood to interstitial fluid through capillaries
  o Returns to venous blood through lymphatic vessels

  **The Circulation of Fluids**
  o From blood plasma to lymph and back to the venous system
  o Transports hormones, nutrients, and waste products

22-2 Structures of Body Defenses

- Lymphatic Vessels
  o Are vessels that carry lymph
  o Lymphatic system begins with smallest vessels
    - Lymphatic capillaries (terminal lymphatics)

22-2 Structures of Body Defenses

- **Lymphatic Capillaries**
  o Differ from blood capillaries in four ways
    1. Start as pockets rather than tubes
    2. Have larger diameters
    3. Have thinner walls
    4. Flat or irregular outline in sectional view
22-2 Structures of Body Defenses

- **Lymphatic Capillaries**
  - Endothelial cells loosely bound together with overlap
  - Overlap acts as one-way valve
    - Allows fluids, solutes, viruses, and bacteria to enter
    - Prevents return to intercellular space

22-2 Structures of Body Defenses

- **Lymph Flow**
  - From lymphatic capillaries to larger lymphatic vessels containing one-way valves
  - Lymphatic vessels travel with veins
- **Lacteals**
  - Are special lymphatic capillaries in small intestine
  - Transport lipids from digestive tract

22-2 Structures of Body Defenses

- **Lymphatic Vessels**
  - Superficial lymphatics
  - Deep lymphatics
  - Are located in:
    - Skin
    - Mucous membranes
    - Serous membranes lining body cavities

22-2 Structures of Body Defenses

- **Superficial and Deep Lymphatics**
  - The deep lymphatics
    - Are larger vessels that accompany deep arteries and veins
  - Superficial and deep lymphatics
    - Join to form large lymphatic trunks
    - Trunks empty into two major collecting vessels
      1. Thoracic duct
      2. Right lymphatic duct

22-2 Structures of Body Defenses

- **Major Lymph-Collecting Vessels**
  - The base of the thoracic duct
    - Expands into cisterna chyli
  - Cisterna chyli receives lymph from:
    - Right and left lumbar trunks
    - Intestinal trunk
22-2 Structures of Body Defenses

- The Inferior Segment of Thoracic Duct
  - Collects lymph from:
    - *Left bronchomediastinal trunk*
    - *Left subclavian trunk*
    - *Left jugular trunk*
  - Empties into left subclavian vein

22-2 Structures of Body Defenses

- The *Right Lymphatic Duct*
  - Collects lymph from:
    - *Right jugular trunk*
    - *Right subclavian trunk*
    - *Right bronchomediastinal trunk*
  - Empties into right subclavian vein

22-2 Structures of Body Defenses

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

- *Lymphocytes*
  - Make up 20–40 percent of circulating leukocytes
  - Most are stored, not circulating

22-2 Structures of Body Defenses

- Types of Lymphocytes
  1. *T cells*
     - Thymus-dependent
  2. *B cells*
     - Bone marrow-derived
  3. *NK cells*
     - Natural killer cells

22-2 Structures of Body Defenses

- *T Cells*
  - Make up 80 percent of circulating lymphocytes
  - Main Types of T Cells
    - Cytotoxic T (*T<sub>C</sub>*) cells
    - Memory T cells
    - Helper T (*T<sub>H</sub>*) cells
    - Suppressor T (*T<sub>S</sub>*) cells
22-2 Structures of Body Defenses

- **Cytotoxic T Cells**
  - Attack cells infected by viruses
  - Produce cell-mediated immunity

- **Memory T Cells**
  - Formed in response to foreign substance
  - Remain in body to give “immunity”

- **Helper T Cells**
  - Stimulate function of T cells and B cells

22-2 Structures of Body Defenses

- **Suppressor T Cells**
  - Inhibit function of T cells and B cells

- **Regulatory T Cells**
  - Are helper and suppressor T cells
  - Control sensitivity of immune response

22-2 Structures of Body Defenses

- **Other T Cells**
  - **Inflammatory T cells**
  - **Suppressor/inducer T cells**

- **B Cells**
  - Make up 10–15 percent of circulating lymphocytes
  - Differentiate (change) into **plasma cells**
  - Plasma cells
    - Produce and secrete antibodies (immunoglobulin proteins)

22-2 Structures of Body Defenses

- **Antigens**
  - Targets that identify any pathogen or foreign compound

- **Immunoglobulins** (Antibodies)
  - The binding of a specific antibody to its specific target antigen initiates *antibody-mediated immunity*

22-2 Structures of Body Defenses

- **Antibody-Mediated Immunity**
  - A chain of events that destroys the target compound or organism

- **Natural Killer (NK) Cells**
  - Also called large granular lymphocytes
  - Make up 5–10 percent of circulating lymphocytes
  - Responsible for *immunological surveillance*
  - Attack foreign cells, virus-infected cells, and cancer cells

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22-2 Structures of Body Defenses

- 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

22-2 Structures of Body Defenses

- Lymphocyte Production
  - Also called lymphopoiesis, involves:
    - Bone marrow
    - Thymus
    - Peripheral lymphoid tissues
  - Hemocytoblasts
    - In bone marrow, divide into two types of lymphoid stem cells

22-2 Structures of Body Defenses

- Lymphoid Stem Cells
  - Group 1
    - Remains in bone marrow and develop with help of stromal cells
    - Produces B cells and natural killer cells
  - Group 2
    - Migrates to thymus
    - Produces T cells in environment isolated by blood–thymus barrier

22-2 Structures of Body Defenses

- T Cells and B Cells
  - Migrate throughout the body
    - To defend peripheral tissues
  - Retaining their ability to divide
    - Is essential to immune system function

22-2 Structures of Body Defenses

- Differentiation
  - B cells differentiate
    - With exposure to hormone called cytokine (interleukin-7)
  - T cells differentiate
    - With exposure to several thymic hormones

22-2 Structures of Body Defenses

- Lymphoid Tissues
Connective tissues dominated by lymphocytes

- **Lymphoid Nodules**
  - Areolar tissue with densely packed lymphocytes
  - Germinal center contains dividing lymphocytes

### 22-2 Structures of Body Defenses

- **Distribution of Lymphoid Nodules**
  - Lymph nodes
  - Spleen
  - Respiratory tract (*tonsils*)
  - Along digestive, urinary, and reproductive tracts

- **Mucosa-Associated Lymphoid Tissue (MALT)**
  - Lymphoid tissues associated with the digestive system
  - **Aggregated Lymphoid Nodules**
    - Clustered deep to intestinal epithelial lining
  - **Appendix (Vermiform Appendix)**
    - Contains a mass of fused lymphoid nodules

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

- **Lymphoid Organs**
  - Lymph nodes
  - Thymus
  - Spleen
    - Are separated from surrounding tissues by a fibrous connective tissue capsule

- **Lymph Nodes**
  - Trabeculae
    - Bundles of collagen fibers
    - Extend from capsule into interior of lymph node
  - Hilum
    - A shallow indentation where blood vessels and nerves reach the lymph
22-2 Structures of Body Defenses

- Lymph Nodes
  - **Afferent lymphatics**
    - Carry lymph
      - From peripheral tissues to lymph node
  - **Efferent lymphatics**
    - Leave lymph node at hilum
    - Carry lymph to venous circulation

22-2 Structures of Body Defenses

- Lymph Flow
  - Flows through lymph node in a network of sinuses
    - From *subcapsular* space
      - Contains macrophages and *dendritic cells*
    - Through *outer cortex*
      - Contains B cells within germinal centers
    - Through *deep cortex*
      - Dominated by T cells
    - Through the core (*medulla*)
      - Contains B cells and plasma cells, organized into *medullary cords*
    - Finally, into hilum and efferent lymphatics

22-2 Structures of Body Defenses

- Lymph Node Function
  - A filter
    - Purifies lymph before return to venous circulation
  - Removes:
    - Debris
    - Pathogens
    - 99 percent of antigens

22-2 Structures of Body Defenses

- Antigen Presentation
  - First step in immune response
  - Extracted antigens are "presented" to lymphocytes
    - Or attached to dendritic cells to stimulate lymphocytes

22-2 Structures of Body Defenses

- Lymphatic Functions
  - Lymphoid tissues and lymph nodes
- Distributed to monitor peripheral infections
- Respond before infections reach vital organs of trunk
  - Lymph nodes of gut, trachea, lungs, and thoracic duct
  - Protect against pathogens in digestive and respiratory systems

### 22-2 Structures of Body Defenses

**Lymph Nodes (Glands)**
- Large lymph nodes at groin and base of neck
- Swell in response to inflammation

**Lymphadenopathy**
- Chronic or excessive enlargement of lymph nodes
  - May indicate infections, endocrine disorders, or cancer

### 22-2 Structures of Body Defenses

**The Thymus**
- Located in mediastinum
- Atrophies after puberty
  - Diminishing effectiveness of immune system

**Divisions of the Thymus**
- Thymus is divided into two **thymic lobes**
- **Septa** divide lobes into smaller **lobules**

### 22-2 Structures of Body Defenses

**A Thymic Lobule**
- Contains a dense outer cortex and a pale central medulla

**Lymphocytes**
- Divide in the **cortex**
- T cells migrate into **medulla**
- Mature T cells leave thymus by medullary blood vessels

### 22-2 Structures of Body Defenses

**Thymic Epithelial Cells in the Cortex**
- Surround lymphocytes in cortex
- Maintain blood–thymus barrier
- Secrete thymic hormones that stimulate:
  - Stem cell divisions
  - T cell differentiation

### 22-2 Structures of Body Defenses

**Thymic Epithelial Cells in the Medulla**
- Form concentric layers known as **thymic (Hassall’s) corpuscles**
The medulla has no blood–thymus barrier
  - T cells can enter or leave bloodstream
- Thymus Hormones
  - Thymosin – an extract from the thymus that promotes development of lymphocytes

22-2 Structures of Body Defenses
- Three 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

22-2 Structures of Body Defenses
- 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

22-2 Structures of Body Defenses
- Histology of the Spleen
  - Inside fibrous capsule
    - Red pulp contains many red blood cells
    - White pulp resembles lymphoid nodules

22-2 Structures of Body Defenses
- 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

22-2 Structures of Body Defenses
- Splenic Circulation
  - Blood passes through:
    - Network of reticular fibers
  - Then enters large sinusoids (lined by macrophages)
    - Which empty into trabecular veins
22-2 Structures of Body Defenses

- Spleen Function
  - Phagocytes and other lymphocytes in spleen
    - Identify and attack damaged and infected cells
    - In circulating blood

22-2 Structures of Body Defenses

- The Lymphatic System and Body Defenses
  - Body defenses provide resistance to fight infection, illness, and disease
  - Two categories of defenses
    1. Innate (nonspecific) immunity
    2. Adaptive (specific) immunity

22-2 Structures of Body Defenses

- Innate (Nonspecific) Immunity
  - Always works the same way
  - Against any type of invading agent
  - Nonspecific resistance

- Adaptive (Specific) Immunity
  - Protects against specific pathogens
  - Depends on activities of lymphocytes
  - Specific resistance (immunity)
    - Develops after exposure to environmental hazards

22-3 Nonspecific Defenses

- Seven Major Categories of Innate (Nonspecific) Immunity
  1. Physical barriers
  2. Phagocytes
  3. Immune surveillance
  4. Interferons
  5. Complement
  6. Inflammatory response
  7. Fever

22-3 Nonspecific Defenses

- Physical Barriers
  - Keep hazardous materials outside the body

- Phagocytes
  - Attack and remove dangerous microorganisms

- Immune Surveillance
  - Constantly monitors normal tissues
With natural killer cells (NK cells)

22-3 Nonspecific Defenses

- Interferons
  - Chemical messengers that trigger production of antiviral proteins in normal cells
  - Antiviral proteins
    - Do not kill viruses
    - Block replication in cell
- Complement
  - System of circulating proteins
  - Assists antibodies in destruction of pathogens

22-3 Nonspecific Defenses

- Inflammatory Response
  - Localized, tissue-level response that tends to limit spread of injury or infection
- Fever
  - A high body temperature
    - Increases body metabolism
    - Accelerates defenses
    - Inhibits some viruses and bacteria

22-3 Nonspecific Defenses

- Physical Barriers
  - Outer layer of skin
  - Hair
  - Epithelial layers of internal passageways
  - Secretions that flush away materials
    - Sweat glands, mucus, and urine
  - Secretions that kill or inhibit microorganisms
    - Enzymes, antibodies, and stomach acid

22-3 Nonspecific Defenses

- Two Classes of Phagocytes
  1. Microphages
    - Neutrophils and eosinophils
    - Leave the bloodstream
    - Enter peripheral tissues to fight infections

22-3 Nonspecific Defenses

- Two Classes of Phagocytes
2. **Macrophages**
   - Large phagocytic cells derived from monocytes
   - Distributed throughout body
   - Make up monocyte–macrophage system (reticuloendothelial system)

22-3 Nonspecific 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 Nonspecific Defenses

- **Two Types of Macrophages**
  1. **Fixed macrophages**
     - Also called histiocytes
     - Stay in specific tissues or organs
       - For example, dermis and bone marrow
  2. **Free macrophages**
     - Also called wandering macrophages
     - Travel throughout body

22-3 Nonspecific Defenses

- **Special Histiocytes**
  - Microglia found in central nervous system
  - Kupffer cells found in liver sinusoids
- **Free Macrophages**
  - Special free macrophages
    - Alveolar macrophages (phagocytic dust cells)

22-3 Nonspecific Defenses

- **Movement and Phagocytosis**
  - All macrophages:
    - 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 Nonspecific Defenses

- **Immunological Surveillance**
Is carried out by natural killer (NK) cells

Activated NK Cells
1. Identify and attach to abnormal cell (nonselective)
2. Golgi apparatus in NK cell forms perforin vesicles
3. Vesicles release proteins called **perforins** (exocytosis)
4. Perforins lyse abnormal plasma membrane
   - Also attack cancer cells and cells infected with viruses

### 22-3 Nonspecific Defenses
- **Immunological Surveillance**
  - Cancer cells
    - With **tumor-specific antigens**
      - Are identified as abnormal by NK cells
      - Some cancer cells avoid NK cells (**immunological escape**)
  - Viral infections
    - Cells infected with viruses
      - Present abnormal proteins on plasma membranes
      - Allow NK cells to identify and destroy them

### 22-3 Nonspecific Defenses
- **Interferons**
  - Proteins (cytokines) released by activated lymphocytes and macrophages
    - **Cytokines**
      - Chemical messengers released by tissue cells
        - To coordinate local activities
        - To act as hormones to affect whole body

### 22-3 Nonspecific Defenses
- **Three Types of Interferons**
  1. **Alpha-interferons**
     - Produced by leukocytes
     - Stimulate NK cells
  2. **Beta-interferons**
     - Secreted by fibroblasts
     - Slow inflammation
  3. **Gamma-interferons**
     - Secreted by T cells and NK cells
     - Stimulate macrophage activity
22-3 Nonspecific Defenses

- Complement
  - Plasma contains 30 special complement (C) proteins
    - That form complement system and complement antibody action
  - Complement activation
    - Complements work together in cascades
    - Two pathways activate the complement system
      1. Classical pathway
      2. Alternative pathway

22-3 Nonspecific Defenses

- Complement Activation: The Classical Pathway
  - Fast method C1 binds to:
    - Antibody molecule attached to antigen (bacterium)
  - Bound protein acts as enzyme
    - Catalyzes chain reaction

22-3 Nonspecific Defenses

- Complement Activation: The Alternative Pathway
  - Slow method exposed to antigen
    - Factor P (properdin)
    - Factor B
    - Factor D
    - Interact in plasma

22-3 Nonspecific Defenses

- Complement Activation
  - Both pathways end with:
    - Conversion of inactive complement protein C3
    - To active form C3b

22-3 Nonspecific Defenses

- Effects of Complement Activation
  - Pore formation
    - Destruction of target plasma membranes
    - Five complement proteins join to form membrane attack complex (MAC)
  - Enhancement of phagocytosis by opsonization
    - Complements working with antibodies (opsonins)
  - Histamine release
    - Increases the degree of local inflammation and blood flow

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22-3 Nonspecific Defenses

- **Inflammation**
  - Also called *inflammatory response*
  - A localized response
  - Triggered by any stimulus that kills cells or injures tissue

22-3 Nonspecific Defenses

- **Cardinal Signs and Symptoms**
  - Swelling (*tumor*)
  - Redness (*rubor*)
  - Heat (*calor*)
  - Pain (*dolor*)

22-3 Nonspecific Defenses

- Three Effects of Inflammation
  1. Temporary repair and barrier against pathogens
  2. Retards spread of pathogens into surrounding areas
  3. Mobilization of local and systemic defenses
     - And facilitation of repairs (*regeneration*)

22-3 Nonspecific Defenses

- **Products of Inflammation**
  - Necrosis
    - Local tissue destruction in area of injury
  - Pus
    - Mixture of debris and necrotic tissue
  - Abscess
    - Pus accumulated in an enclosed space

22-3 Nonspecific Defenses

- **Fever**
  - A maintained body temperature above 37.2°C (99°F)
  - Pyrogens
    - Any material that causes the hypothalamus to raise body temperature
      - Circulating pathogens, toxins, or antibody complexes
  - *Endogenous pyrogens or interleukin-1 (IL-1)*
    - Pyrogen released by active macrophages
    - A cytokine

22-4 Specific Defenses

- Adaptive (Specific) Defenses
Specific resistance (immunity)
  - Responds to specific antigens
  - With coordinated action of T cells and B cells

22-4 Specific Defenses
- Specific Defenses
  - T Cells
    - Provide cell-mediated immunity
    - Defend against abnormal cells and pathogens inside cells
  - B Cells
    - Provide antibody-mediated immunity
    - Defend against antigens and pathogens in body fluids

22-4 Specific Defenses
- Forms of Immunity
  1. Innate
    - Present at birth
  2. Adaptive
    - After birth
  3. Active
    - Antibodies develop after exposure to antigen
  4. Passive
    - Antibodies are transferred from another source

22-4 Specific Defenses
- Active Immunity
  - Naturally acquired
    - Through environmental exposure to pathogens
  - Artificially induced
    - Through vaccines containing pathogens

22-4 Specific Defenses
- Passive Immunity
  - Naturally acquired
    - Antibodies acquired from the mother
  - Artificially induced
    - By an injection of antibodies

22-4 Specific Defenses
- Four Properties of Immunity
  1. Specificity
    - Each T or B cell responds only to a specific antigen and ignores all
2. **Versatility**
   - The body produces many types of lymphocytes
     - Each fights a different type of antigen
     - Active lymphocyte **clones** itself to fight specific antigen

### 22-4 Specific Defenses
- **Four Properties of Immunity**
  3. **Memory**
     - Some active lymphocytes (*memory* cells):
       - Stay in circulation
       - Provide immunity against new exposure
  4. **Tolerance**
     - Immune system ignores “normal” antigens (*self-antigens*)

### 22-4 Specific Defenses
- **An Introduction to the Immune Response**
  - Two main divisions
    1. Cell-mediated immunity (T cells)
    2. Antibody-mediated immunity (B cells)

### 22-5 T Cells and Immunity
- **Four Major Types of T Cells**
  1. **Cytotoxic T cells** (also called T\(_C\) cells)
     - Attack cells infected by viruses
     - Responsible for cell-mediated immunity
  2. **Memory T cells**
     - Clone more of themselves in response to “remembered” antigen
  3. **Helper T cells** (also called T\(_H\) cells)
     - Stimulate function of T cells and B cells
  4. **Suppressor T cells** (also called T\(_S\) cells)
     - Inhibit function of T cells and B cells

### 22-5 T Cells and Immunity
- **Antigen Presentation**
  - T cells only recognize antigens that are bound to glycoproteins in plasma membranes
  - **MHC Proteins**
    - The membrane glycoproteins that bind to antigens
    - Genetically coded in chromosome 6
      - The **major histocompatibility complex** (MHC)
      - Differs among individuals
22-5 T Cells and Immunity
- Two Classes of MHC Proteins
  - **Class I**
    - Found in membranes of all nucleated cells
  - **Class II**
    - Found in membranes of antigen-presenting cells (APCs)
    - Found in lymphocytes

22-5 T Cells and Immunity
- **Class I MHC Proteins**
  - 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

22-5 T Cells and Immunity
- **Class II MHC Proteins**
  - Antigenic fragments
    - From antigen processing of pathogens
    - Bind to Class II proteins
    - Inserted in plasma membrane to stimulate T cells
  - Antigen-presenting cells (APCs)
    - Responsible for activating T cells against foreign cells and proteins

22-5 T Cells and Immunity
- Phagocytic APCs
  1. Free and fixed macrophages
    - In connective tissues
  2. Kupffer cells
    - Of the liver
  3. Microglia
    - In the CNS

22-5 T Cells and Immunity
- Non-phagocytic APCs
  - Langerhans cells
    - In the skin
  - Dendritic cells
    - In lymph nodes and spleen

22-5 T Cells and Immunity
- Antigen Recognition
Inactive T cell receptors
- Recognize Class I or Class II MHC proteins
- Recognize a specific antigen
- Binding occurs when MHC protein matches antigen

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 70 types
      - Designated by an identifying number
- CD3 Receptor Complex
  - Found in all T cells

22-5 T Cells and Immunity
- Two Important CD Markers
  1. CD8 Markers
    - Found on cytotoxic T cells and suppressor T cells
    - Respond to antigens on Class I MHC proteins
  2. CD4 Markers
    - Found on helper T cells
    - Respond to antigens on Class II MHC proteins
- CD8 or CD4 Markers
  - Bind to CD3 receptor complex
  - Prepare cell for activation

22-5 T Cells and Immunity
- 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
- Activation of CD8 T Cells
  - Activated by exposure to antigens on MHC proteins
    - One responds quickly
      - Producing cytotoxic T cells and memory T cells
    - The other responds slowly
      - Producing suppressor T cells

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• Cytotoxic T (T<sub>C</sub>) Cells
  - Seek out and immediately destroy target cells
    1. Release perforin
      - To destroy antigenic plasma membrane
    2. Secrete poisonous **lymphotoxin**
      - To destroy target cell
    3. Activate genes in target cell
      - That cause cell to die

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

22-5 T Cells and Immunity

• Suppressor T Cells
  - Secrete *suppression factors*
  - Inhibit responses of T and B cells
  - Act *after* initial immune response
  - Limit immune reaction to single stimulus

22-5 T Cells and Immunity

• Activation of CD4 T cells
  - Active helper T cells (T<sub>H</sub> cells)
    - Secrete cytokines
  - **Memory helper (T<sub>H</sub>) cells**
    - Remain in reserve

22-5 T Cells and Immunity

• Four Functions of Cytokines
  1. Stimulate T cell divisions
    - Produce memory T<sub>H</sub> cells
    - Accelerate cytotoxic T cell maturation
  2. Attract and stimulate macrophages
  3. Attract and stimulate activity of cytotoxic T cells
  4. Promote activation of B cells

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

### 22-6 B Cells and Immunity

- **B Cell Sensitization**
  - Corresponding antigens in interstitial fluids bind to B cell receptors
  - B cell prepares for activation
  - Preparation process is **sensitization**
  - During sensitization, antigens are:
    - Taken into the B cell
    - Processed
    - Reappear on surface, bound to Class II MHC protein

### 22-6 B Cells and Immunity

- **Helper T Cells**
  - Sensitized B cell is prepared for activation but needs helper T cell activated by same antigen
- **B Cell Activation**
  - Helper T cell binds to MHC complex
  - Secretes cytokines that promote B cell activation and division

### 22-6 B Cells and Immunity

- **B Cell Division**
  - Activated B cell divides into:
    - Plasma cells
    - **Memory B cells**

### 22-6 B Cells and Immunity

- **Plasma Cells**
  - Synthesize and secrete antibodies into interstitial fluid
- **Memory B Cells**
  - Like memory T cells, remain in reserve to respond to next infection

### 22-6 B Cells and Immunity

- **Antibody Structure**
  - Two parallel pairs of polypeptide chains
    - One pair of **heavy chains**
    - One pair of **light chains**
  - Each chain contains:
    - **Constant segments**
    - **Variable segments**
### 22-6 B Cells and Immunity

- **Five Heavy-Chain Constant Segments**
  - Determine five types of antibodies
    1. IgG
    2. IgE
    3. IgD
    4. IgM
    5. IgA

### 22-6 B Cells and Immunity

- **Variable Segments of Light and Heavy Chains**
  - Determine specificity of antibody molecule

- **Binding Sites**
  - Free tips of two variable segments
    - Form *antigen binding sites* of antibody molecule
    - Which bind to *antigenic determinant sites* of antigen molecule

- **Antigen–Antibody Complex**
  - An antibody bound to an antigen

### 22-6 B Cells and Immunity

- **The Antigen–Antibody Complex**
  - **A Complete Antigen**
    - Has at least two *antigenic determinant sites*
    - Binds to both antigen-binding sites of variable segments of antibody
  - **B Cell Sensitization**
    - Exposure to a complete antigen leads to:
      - B cell sensitization
      - Immune response

### 22-6 B Cells and Immunity

- **Hapten (Partial Antigens)**
  - Must attach to a carrier molecule to act as a complete antigen
  - **Dangers of Haptens**
    - Antibodies produced will attack both hapten and carrier molecule
    - If carrier is “normal”:
      - Antibody attacks normal cells
      - For example, *penicillin* allergy

### 22-6 B Cells and Immunity

- **Five Classes of Antibodies**
  - Also called *immunoglobulins (Igs)*
    - IgG, IgD, IgE, IgM, IgA
- Are found in body fluids
- Are determined by constant segments
- Have no effect on antibody specificity

22-6 B Cells and Immunity
- Five Classes of Antibodies
  - IgG is the largest and most diverse class of antibodies
  - 80 percent of all antibodies
  - IgG antibodies are responsible for resistance against many viruses, bacteria, and bacterial toxins
  - Can cross the placenta, and maternal IgG provides passive immunity to fetus during embryological development
  - Anti-Rh antibodies produced by Rh-negative mothers are also IgG antibodies and produce *hemolytic disease of the newborn*

22-6 B Cells and Immunity
- Five Classes of Antibodies
  - IgE attaches as an individual molecule to the exposed surfaces of basophils and mast cells
  - When an antigen is bound by IgE molecules:
    - The cell is stimulated to release histamine and other chemicals that accelerate inflammation in the immediate area
  - IgE is also important in the allergic response

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

22-6 B Cells and Immunity
- Five Classes of Antibodies
  - IgM is the first class of antibody secreted after an antigen is encountered
  - IgM concentration declines as IgG production accelerates
  - Plasma cells secrete individual IgM molecules, but it polymerizes and circulates as a five-antibody starburst
  - The anti-A and anti-B antibodies responsible for the agglutination of incompatible blood types are IgM antibodies
  - IgM antibodies may also attack bacteria that are insensitive to IgG

22-6 B Cells and Immunity
- Five Classes of Antibodies
IgA is found primarily in glandular secretions such as mucus, tears, saliva, and semen. Attack pathogens before they gain access to internal tissues. IgA antibodies circulate in blood as individual molecules or in pairs. Epithelial cells absorb them from blood and attach a secretory piece, which confers solubility, before secreting IgA molecules onto the epithelial surface.

22-6 B Cells and Immunity
- Seven Functions of Antigen–Antibody Complexes
  1. **Neutralization** of antigen binding sites
  2. **Precipitation** and **agglutination** – formation of **immune complex**
  3. Activation of complement
  4. Attraction of phagocytes
  5. Opsonization increasing phagocyte efficiency
  6. Stimulation of inflammation
  7. Prevention of bacterial and viral adhesion

22-6 B Cells and Immunity
- Primary and Secondary Responses to Antigen Exposure
  - Occur in both cell-mediated and antibody-mediated immunity
  - First exposure
    - Produces initial **primary response**
  - Next exposure
    - Triggers **secondary response**
    - More extensive and prolonged
    - Memory cells already primed

22-6 B Cells and Immunity
- The **Primary Response**
  - Takes time to develop
  - Antigens activate B cells
  - Plasma cells differentiate
  - **Antibody titer** (level) slowly rises

22-6 B Cells and Immunity
- The Primary Response
  - Peak response
    - Can take two weeks to develop
    - Declines rapidly
  - **IgM**
    - Is produced faster than **IgG**
    - Is less effective
22-6 B Cells and Immunity
• The Secondary Response
  o Activates memory B cells
    ▪ At lower antigen concentrations than original B cells
    ▪ Secrete antibodies in massive quantities

22-6 B Cells and Immunity
• Effects of Memory B Cell Activation
  o IgG
    ▪ Rises very high and very quickly
    ▪ Can remain elevated for extended time
  o IgM
    ▪ Production is also quicker
    ▪ Slightly extended

22-6 B Cells and Immunity
• Combined Responses to Bacterial Infection
  o Neutrophils and NK cells begin killing bacteria
  o Cytokines draw phagocytes to area
  o Antigen presentation activates:
    ▪ Helper T cells
    ▪ Cytotoxic T cells
  o B cells activate and differentiate
  o Plasma cells increase antibody levels

22-6 B Cells and Immunity
• Combined Responses to Viral Infection
  o Similar to bacterial infection
  o But cytotoxic T cells and NK cells are activated by contact with virus-infected cells

22-7 Immune System Development
• Immune System Development
  o Fetus can produce immune response (has immunocompetence)
    ▪ After exposure to antigen
    ▪ At about three to four months

22-7 Immune System Development
• Development of Immunocompetence
  o Fetal thymus cells migrate to tissues that form T cells
Liver and bone marrow produce B cells
Four-month fetus produces IgM antibodies

22-7 Immune System Development
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 Immune System Development
Normal Resistance
- Infant produces IgG antibodies through exposure to antigens
- Antibody, B cell, and T cell levels slowly rise to adult levels
  - About age 12

22-7 Immune System Development
Cytokines of the Immune System
- Chemical messengers involved in cellular immunity
  - Hormones and paracrine-like glycoproteins
    - Examples of cytokines:
      - Interferons
      - Interleukins
      - Tumor necrosis factors (TNFs)

22-7 Immune System Development
Interleukins
- Functions include:
  1. Increasing T cell sensitivity to antigens exposed on macrophage membranes
  2. Stimulating B cell activity, plasma cell formation, and antibody production

22-7 Immune System Development
Interleukins
- Functions include:
  3. Enhancing nonspecific defenses
    - Stimulation of inflammation
    - Formation of scar tissue by fibroblasts
o Elevation of body temperature via the preoptic nucleus of the hypothalamus
o Stimulation of mast cell formation
o Promotion of adrenocorticotropic hormone (ACTH) secretion by the anterior lobe of the pituitary gland
4. Moderating the immune response
   o Some interleukins help suppress immune function and shorten the immune response

22-7 Immune System Development
• Interleukins
  o IL-1 and IL2, are important in stimulating and maintaining the immune response
  o When released by activated macrophages and lymphocytes, these cytokines stimulate the activities of other immune cells and of the secreting cell
  o Result is a positive feedback loop that helps to recruit additional immune cells

22-7 Immune System Development
• Three Types of Interferons
  1. Alpha-interferons
     ▪ Produced by leukocytes
     ▪ Stimulate NK cells
  2. Beta-interferons
     ▪ Secreted by fibroblasts
     ▪ Slow inflammation
  3. Gamma-interferons
     ▪ Secreted by T cells and NK cells
     ▪ Stimulate macrophage activity

22-7 Immune System Development
• Tumor Necrosis Factors (TNFs)
  o TNFs slow the growth of a tumor and kill sensitive tumor cells
  o Activated macrophages secrete one type of TNF and carry the molecules in their plasma membranes
  o Cytotoxic T cells produce a different type of TNF
  o In addition to their effects on tumor cells:
    ▪ TNFs stimulate granular leukocyte production, promote eosinophil activity, cause fever, and increase T cell sensitivity to interleukins

22-7 Immune System Development
• Phagocyte-Activating Chemicals
Several cytokines coordinate immune defenses by adjusting the activities of phagocytic cells. Include factors that attract free macrophages and microphages and prevent their premature departure from the site of an injury.

- **Colony-Stimulating Factors**
  - Factors are produced by active T cells, cells of the monocyte–macrophage system, endothelial cells, and fibroblasts.
  - CSFs stimulate the production of blood cells in red bone marrow and lymphocytes in lymphoid tissues and organs.

### 22-7 Immune System Development

- **Cytokines Are Often Classified According to Their Origins**
  - *Lymphokines* are produced by lymphocytes.
  - *Monokines* are secreted by active macrophages and other antigen-presenting cells.
    - These terms are misleading, because lymphocytes and macrophages may secrete the same cytokines.
  - Cells involved in adaptive immunity and tissue repair can also secrete cytokines.

### 22-7 Immune System Development

- **Immune Disorders**
  - *Autoimmune disorders*
  - *Immunodeficiency disease*
  - *Allergies*

### 22-7 Immune System Development

- **Autoimmune Disorders**
  - A malfunction of system that recognizes and ignores “normal” antigens.
  - Activated B cells make autoantibodies against body cells.
    - Examples:
      - *Thyroiditis*
      - *Rheumatoid arthritis*
      - *Insulin-dependent diabetes mellitus (IDDM)*

### 22-7 Immune System Development

- **Immunodeficiency Diseases**
  - Result from:
    - Problems with embryological development of lymphoid tissues.
      - Can result in severe combined immunodeficiency disease (SCID).
    - Viral infections such as HIV.
      - Can result in AIDS.

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- **Immunosuppressive drugs** or radiation treatments
  - Can lead to complete immunological failure

**22-7 Immune System Development**
- **Allergies**
  - Inappropriate or excessive immune responses to antigens
- **Allergens**
  - Antigens that trigger allergic reactions

**22-7 Immune System Development**
- Four Categories of Allergic Reactions
  1. *Immediate hypersensitivity* (Type I)
  2. *Cytotoxic reactions* (Type II)
  3. *Immune complex disorders* (Type III)
  4. *Delayed hypersensitivity* (Type IV)

**22-7 Immune System Development**
- **Type I Allergy**
  - Also called *immediate hypersensitivity*
  - A rapid and severe response to the presence of an antigen
  - Most commonly recognized type of allergy
  - Includes *allergic rhinitis* (environmental allergies)

**22-7 Immune System Development**
- **Type I Allergy**
  - Sensitization leads to:
    - Production of large quantities of IgE antibodies distributed throughout the body
  - Second exposure leads to:
    - Massive inflammation of affected tissues

**22-7 Immune System Development**
- **Type I Allergy**
  - Severity of reaction depends on:
    - Individual sensitivity
    - Locations involved
  - Allergens (antigens that trigger reaction) in bloodstream may cause anaphylaxis

**22-7 Immune System Development**
- **Anaphylaxis**
Can be fatal
- Affects cells throughout body
- Changes capillary permeability
  - Produces swelling (hives) on skin
- Smooth muscles of respiratory system contract
  - Make breathing difficult
- Peripheral vasodilation
  - Can cause circulatory collapse (anaphylactic shock)

22-7 Immune System Development
- **Antihistamines**
  - Drugs that block histamine released by mast cells
  - Can relieve mild symptoms of immediate hypersensitivity
  - *Benadryl*

22-7 Immune System Development
- Stress and the Immune Response
  - Glucocorticoids
    - Secreted to limit immune response
    - Long-term secretion (chronic stress)
      - Inhibits immune response
      - Lowers resistance to disease

22-7 Immune System Development
- Functions of Glucocorticoids
  - *Depression of the inflammatory response*
  - *Reduction in abundance and activity of phagocytes*
  - *Inhibition of interleukin secretion*

22-8 Effects of Aging on the Immune System
- Immune System Diminishes with Age
  - Increasing vulnerability to infections and cancer
- Four Effects of Aging
  1. Thymic hormone production is greatly reduced
  2. T cells become less responsive to antigens
  3. Fewer T cells reduces responsiveness of B cells
  4. Immune surveillance against tumor cells declines

22-9 Immune System Integration
- Nervous and Endocrine Systems
  - Interact with thymic hormones
  - Adjust sensitivity of immune response