Chapter 21 The Lymphatic and Immune Systems
Incomplete Outline Key

I. The Lymphatic System
  A. Functions
    1. Fluid Recovery: fluid continually filters from the blood capillaries into the tissue spaces
      a. Reabsorbs 2 to 4 L over the course of the day to return excess fluid in the tissues back to the blood
    2. Immunity: picks up foreign cells and chemicals and takes them to the lymph nodes where immune cells can detect if anything is harmful
    3. Lipid absorption: absorb dietary lipids
  B. Lymph and Lymphatic Vessels
    1. Lymph: clear, colorless fluid that is similar to blood plasma
      a. May contain macrophages, hormones, viruses, cellular debris, traveling cancer cells
    2. Lymphatic vessels: lymph flow through a system of these vessels
      a. Lymphatic capillaries: the beginnings of lymphatic vessels that are present in nearly every tissue
        i They are closed at one end and consist of a sac of thin endothelial cells that loosely overlap each other like the shingles of a roof
      b. Vessel Layers: tunica interna with valves, tunica media, and outer tunica externa
    3. Route of tissue fluid back to the bloodstream: lymphatic capillaries ->collecting vessels -> six lymphatic trunks -> two collecting ducts ->subclavian veins
  C. Lymphatic Cells
    1. Natural killer (NK) cells: lymphocytes that attack and destroy bacteria, responsible for immune surveillance
    2. T lymphocytes (T cells): mature in the thymus, several subclasses introduced later
    3. B lymphocytes (B cells): mature in the bone marrow, differentiate into plasma cells
    4. Macrophages: develop from monocytes, phagocytize tissue debris
      a. Antigen-presenting cell: displays antigenic fragments of foreign matter in its surface
    5. Dendritic cells: antigen-presenting cells found in the epidermis and mucous membranes
    6. Reticular cells: branched stationary cells that contribute to the stroma of the lymphatic organs and act as antigen-presenting cells
  D. Lymphatic Tissues: aggregations of lymphocytes
    1. Diffuse lymphatic tissue: where lymphocytes are scattered rather than densely clustered
    2. Mucosa-associated lymphatic tissue: found in body passages that are open to the exterior
      a. Respiratory, digestive, urinary, and reproductive tracts
    3. Lymphatic nodules: dense masses of lymphocytes and macrophages that come and go as pathogens invade the tissues
    4. Peyer Patches: lymphatic nodules in clusters found at the distal portion of the small intestine
  E. Lymphatic organs
    1. Primary lymphatic organs: sites where B and T lymphocytes become immunocompetent
      a. Red bone marrow: site of B cell maturation
      b. Thymus: site of T cell maturation
        ii Reticular epithelial cells: forms a blood-thymus barrier to isolate developing lymphocytes

2. Secondary lymphatic organs: sites populated with immunocompetent lymphocytes only after they have been matured
    a. Lymph nodes: cleanses the lymph and is a site to activate T and B cells
        iii Several afferent vessels lead in and only 1-3 efferent vessels lead out to create a bottleneck to slow lymph down to allow for more cleansing time
        iv Lymphadenitis: painful swelling of a lymph node when they are under challenge from a foreign antigen
    b. Tonsils: lymphatic tissues located at the entrance to the pharynx that guard against ingested and inhaled pathogens
        v 3 sets of tonsils
            - Pharyngeal: single tonsil on the wall of the pharynx
            - Palatine: 2 tonsils on the posterior margin of the oral cavity
            - Lingual: many tonsils on each side of the root of the tongue
        vi Tonsillarcrypts: deep pits that often contain food debris, dead leukocytes, bacteria, antigenic chemicals
    c. Spleen: the body's largest lymphatic organ
        vii Red pulp: consists of sinuses gorged with concentrated erythrocytes
        viii White pulp: consists of lymphocytes and macrophages aggregated along small branches of the splenic artery

II. Nonspecific Resistance: guards equally against a broad range of pathogens and the effectiveness does not depend on prior exposure
A. Body's Lines of Defense
    1. First Line of Defense: external barriers, skin, mucous membranes
    2. Second Line of Defense: leukocytes, macrophages, antimicrobial proteins, immune surveillance
    3. Third Line of Defense: the immune systems that leaves the body with a memory (not nonspecific defense)
B. Leukocytes and Macrophages
    1. Neutrophils: main function is to kill bacteria by phagocytosis and digestion
        a. Produces highly toxic chemicals (like hydrogen peroxide) that forms a killing zone destroying surrounding bacteria
            ix It also kills the neutrophil during the attack
    2. Eosinophils: stand guard against parasites and allergens
        a. Promote the action of basophils and mast cells, limit the action of histamine
        b. Phagocytize and degrade antigen-antibody complexes
    3. Basophils: secrete chemicals that aid in the mobility and action of other leukocytes
        a. Histamine: increases blood flow and speeds the delivery of leukocytes to the area
        b. Heparin: anticoagulant that inhibits the formation of blood clots
    4. Monocytes: transform into macrophages
        a. Microglia: in the CNS
        b. Alveolar macrophages: in the lungs
        c. Hepatic macrophages: in the liver
C. Antimicrobial Proteins
    1. Interferons: proteins that are secreted when certain cells become infected with a virus
        a. They are the "dying words" that alert neighboring cells and protect them from becoming infected
    2. Complement system: globulins that make contributions to both nonspecific resistance and specific immunity

a. Four methods of pathogen destruction
   x Inflammation
   xi Immune clearance: binds Ag-Ab complexes to RBCs, so as these RBCs circulate through the liver and spleen, the macrophages of those organs destroy the Ag-Ab complexes
   xii Phagocytosis
   xiii Cytolysis

D. Immune Surveillance: when NK cells continually patrol the body "on the lookout" for pathogens or diseased host cells
   1. Once an NK cells bind to an enemy cell it released perforinsthat creates a hole in the enemy cells. The hole allows for a rapid inflow of water and salt into the enemy cell to weaken it. The NK cells then releases granzymeswhich destroy cellular enzymes and induce apoptosis.

E. Fever: an adaptive mechanism that does more harm than good in moderation
   1. Beneficial aspects
      a. Promotes interferon activity
      b. Elevates metabolic rate and accelerates tissue repair
      c. Inhibits reproduction of bacteria and viruses
   2. Course of a Fever
      a. Onset: body temperature rises, person has chills
      b. Stadium: body temperature oscillates around a new set point
      c. Defervescence: body temperature returns to normal
   3. Fevers above 105F can make a person delirious and a fever above 111F can result in a coma, death, or brain damage

F. Inflammation: local defensive response to tissue injury
   1. General purposes
      a. Limit the spread of pathogens
      b. Remove debris of damaged tissue
      c. Initiate tissue repair
   2. Four cardinal signs: redness, swelling, heat, pain
   3. Cytokines: small proteins that regulate inflammation and immunity
   4. Three major processes of inflammation
      a. Mobilization of Defenses: getting defensive leukocytes to the site quickly
         xiv Vasoactive chemicals are released to make the blood vessels dilate and become more permeable.
         xv Leukocytes then adhere to the vessel wall (margination) and crawl through the gaps between the cells (diapedesis)
      b. Containment and destruction of Pathogens: preventing the spreading of the pathogen
         xvi Heparin prevents clotting in the area of injury so bacteria or other pathogens are trapped
      c. Tissue Cleanup and Repair: monocytes are in charge of clean up
         xvii Edema contributes by compressing veins and reducing venous drainage
         xviii Pus: a yellowish fluid of dead cells, other tissue debris, and tissue fluid
         xix Platelet-derived growth factor: a secreted agents that stimulates fibroblasts

III. General Aspects of Specific Immunity
   A. Differences between nonspecific resistance and immunity
      1. Specificity: directed towards a specific pathogen
      2. Memory: develops a memory so when rexposed to the same pathogen the body will react quickly

B. Forms of Immunity
   1. Cellular (cell-mediated) immunity: employs lymphocytes that directly attack and destroy foreign cells or diseased host cells
   2. Humoral(antibody-mediated) immunity: do not directly destroy a pathogen but mark them for destruction
   3. Humoral immunity can work only against the extracellular stages of infectious microorganisms. But when these microorganisms invade host cells (intracellular stages), they are still vulnerable to cellular immunity, which destroys them by killing the host cell.
   4. Active/passive and natural/artificial immunity classifications
      a. Natural active immunity: production of one's own antibodies or T cells as a result of natural exposure to an antigen
      b. Artificial active immunity: production of one's own antibodies or T cells as a result of a vaccination
      c. Natural passive immunity: temporary immunity that results from acquiring antibodies produced by another person
      d. Artificial passive immunity: temporary immunity that results from the injection of an immune serum

C. Antigens: any molecule that triggers an immune response
   1. Generally complex molecules like proteins, polysaccharides, glycoproteins, glycolipids
   2. Epitopes: certain region of an antigen molecule that stimulates immune responses
      a. One antigen molecule can have several different epitopes that can stimulate the production of different antibodies

D. Lymphocytes
   1. T Lymphocytes: the birth, maturation, and deployment of a T cell is as follows...
      a. T cells are born in the red bone marrow which then colonize in the thymus to mature to functional T cells
      b. T cells develop surface antigen receptors and are now considered immunocompetent (capable of recognizing antigens)
      c. The T cells are then tested to make sure that they are not faulty by presenting self antigens to them
         xx They can fail the test by not being able to recognize them or reacting to the self antigens
      d. If the T cells fail the test they must be eliminated by a process called negative selection. There are two outcomes.
         xxi Clonal deletion: the T will die
         xxii Anergy: the T cells remain alive but unresponsive
      e. If the Tcells pass the test they undergo positive selection
         xxiiiThey multiply and form clones programmed to respond to a particular antigen
      f. T cells that are immunocompetent but haven't encountered a foreign antigen is said to be a naïve T cell.
      g. The naïve T cells are now ready to do battle.
   2. B Lymphocytes: remains in the bone marrow to differentiate into B cells
      a. They undergo anergy or clonal deletion just like a self-reactive T cell

E. Antigen-Presenting Cells: help T cells recognize foreign antigens
   1. MHC proteins: proteins on the surface of APC that are shaped like hotdog buns that act as ID tags
   2. When an APC encounters an antigen, it internalizes it by endocytosis, digests it into fragments, and displays a fragment (its epitopes) in the grooves of the MCH protein

IV. Cellular Immunity: defense in which T lymphocytes directly attack and destroy diseased or foreign cells

A. Four Classes of T cells:
   1. Cytotoxic T cells: carry out the attack
   2. Helper T cells: promote the action of Tc cells
      a. This is the only type of T cell that is also involved in humoral immunity
   3. Memory T cells: responsible for memory

B. Recognition
   1. Antigen presenting: T cells respond to two classes of MHCPs on antigen presenting cells
      a. MCH-I proteins occur on every nucleated cell
         xxiv They pick up small peptides and display them. If they are viral or abnormal proteins they elicit T cell response to kill the cell.
      b. MHC-II proteins occur only on APCs and display only foreign antigens
      c. NOTE: Tc cells respond only to MHC-I proteins and Th cells respond only to MHC-II.
   2. T cell Activation: begins when aTc or Th cell binds to an MHCP displaying an epitope that the T cell is programmed to recognize.
      a. To make sure that it has really bound to a foreign antigen, it must bind to another for a double check. The double check process is called costimulation and is used to make sure the immune system doesn't launch an attack in the absence of an enemy.
      b. Successful costimulation triggers a process called clonal selection (when the T cell undergoes repeated mitosis)

C. Attack
   1. Th cells coordinate roles in both humoral and cellular immunity
      a. They attract neutrophils and NK cells, they attract macrophages, and stimulate B and T cell mitosis and maturation
   2. Tc cells directly attack and kill other cells
      a. They deliver a lethal hit of cytotoxic chemicals
         xxv Perforins and granzymes: kill the target cell
         xxvi Interferons: inhibit viral replication
         xxvii Tumor necrosis factor: kills cancer cells

D. Memory: memory cells are long lived and much more numerous than naïve T cells
   1. Upon reexposure, memory cells mount a quick attack

V. Humoral Immunity: a more indirect method of defense

A. Recognition: B cell activation begins when an antigen binds to one of several receptors on the B cell surface.
   1. The B cell then digests the antigen and displays it on its surface and waits for a T helper cell to bind to the this Ag-MHCP complex
   2. Once the Th cell binds, this triggers clonal selection.
      a. Most clones differentiate into plasma cells

B. Attack
   1. Basic structure of an antibody: composed of two large heavy chains and two light chains.
      a. All four chains have a variable region that gives and antibody its uniqueness and a constant region that has the same amino acid sequence in all antibodies
      b. Five classes of antibodies
         xxviii IgA: prevents pathogens from adhering to epithelia
         xxix IgD: activation of B cells by antigens
         xxx IgE stimulates basophils to release histamine; attracts eosinophils to sites of parasitic infections

xxxi IgG: 80% of circulating antibodies; secondary immune response, crosses the placenta

xxxii IgM: constitutes 10% of antibodies; primary immune response; very strong agglutinating

2. Four mechanisms antibodies use to render antigens
   a. Neutralization: neutralize an antigen by masking active regions
   b. Complement fixation: binding to an enemy cell and change shape, exposing their complement –binding sites
   c. Agglutination: sticking enemy cells together so that they are immobilized and prevents them from spreading
   d. Precipitation: antibodies link antigen molecules(not whole cells) together

C. Memory: during clonal selection, some clones become memory B cells
   1. They mount a very quick secondary response

VI. Immune System Disorders

A. Hypersensitivity: an excessive, harmful immune reaction to antigens that most people can tolerate
   1. Type I (acute): allergens bind to IgE on the membranes of basophils and mast cells and stimulate them to secrete histamine and other inflammatory and vasoactive chemicals
      a. Asthma: local inflammatory reaction to inhaled allergens
      b. Anaphylaxis: severe type I reaction

         xxxiii Anaphylactic shock: occurs when an allergen enters the bloodstream of an allergic individual
   2. Type II (antibody-dependent cytotoxic): occurs when IgG or IgM attacks antigens bound to cell surfaces
      a. Ex: myasthenia gravis
   3. Type III (immune complex): occurs when IgG or IgM forms antigen-antibody complexes that precipitate beneath the endothelium
      a. Triggers intense inflammation, causing tissue destruction
   4. Type IV (delayed): a cell-mediated reaction where sign appear 12-72 hours after exposure
      a. Begins when APCs display antigens to helper T cells
      b. Cosmetics, poison ivy, TB skin tests