CHAPTER 22

LECTURE OUTLINE

I.  INTRODUCTION
   A.  The ability to ward off the pathogens that produce disease is called resistance.
   B.  Lack of resistance is called susceptibility.
   C.  Resistance to disease can be grouped into two broad areas.
      1.  Nonspecific resistance or innate immunity are present at birth and includes defense
          mechanisms that provide general protection against invasion by a wide range of
          pathogens.
      2.  Immunity involves activation of specific lymphocytes that combat a particular
          pathogen or other foreign substance.
   D.  The body system that carries out immune responses is the lymphatic system.

II. LYMPHATIC SYSTEM STRUCTURE AND FUNCTION
   A.  The lymphatic system consists of a fluid called lymph flowing within lymphatic vessels,
       several structures and organs that contain lymphatic tissue (specialized reticular tissue
       containing large numbers of lymphocytes), and bone marrow, which is the site of lymphocyte
       production (Figure 22.1).
       1.  Interstitial fluid and lymph are basically the same.
       2.  Their major difference is location.
   
   B.  Functions of the Lymphatic System
       1.  The lymphatic system functions to drain interstitial fluid, return leaked plasma
           proteins to the blood, transport dietary fats, and protect against invasion by
           nonspecific defenses and specific immune responses.
   
   C.  Lymphatic Vessels and Lymph Circulation
       1.  Lymphatic vessels begin as blind-ended lymph capillaries in tissue spaces between
           cells (Figure 22.2).
           a.  Interstitial fluid drains into lymphatic capillaries, thus forming lymph.
           b.  Lymph capillaries merge to form larger vessels, called lymphatic vessels,
               which convey lymph into and out of structures called lymph nodes (Figure
               22.1).
       2.  Lymphatic Capillaries
a. Lymphatic capillaries are found throughout the body except in avascular tissue, the CNS, portions of the spleen, and red bone marrow.

b. Lymphatic capillaries have a slightly larger diameter than blood capillaries and have overlapping endothelial cells which work as one-way valves for fluid to enter the lymphatic capillary.

c. Anchoring filaments attach endothelial cells to surround tissue (Figure 22.2).

d. A lymphatic capillary in the villus of the small intestine is the lacteal. It functions to transport digested fats from the small intestine into blood.

3. Lymph Trunk and Ducts

a. The principal lymph trunks, formed from the exiting vessels of lymph nodes, are the lumbar, intestinal, bronchomediastinal, subclavian, and jugular trunks (Figure 22.3).

b. The thoracic duct begins as a dilation called the cisterna chyli (Figure 22.3) and is the main collecting duct of the lymphatic system.
   1) The thoracic duct receives lymph from the left side of the head, neck, and chest, the left upper extremity, and the entire body below the ribs.
   2) It drains lymph into venous blood via the left subclavian vein.

c. Right Lymphatic Duct (Figure 22.3)
   1) The right lymphatic duct drains lymph from the upper right side of the body.
   2) It drains lymph into venous blood via the right subclavian vein.

D. Formation and Flow of Lymph

1. Interstitial fluid drains into lymph capillaries.

2. The passage of lymph is from arteries and blood capillaries (blood) to interstitial spaces (interstitial fluid) to lymph capillaries (lymph) to lymphatic vessels to lymph trunks to the thoracic duct or right lymphatic duct to the subclavian veins (blood) (Figure 22.4).
   a. Lymph flows as a result of the milking action of skeletal muscle contractions and respiratory movements.
   b. It is also aided by lymphatic vessel valves that prevent backflow of lymph.

E. Lymphatic Organs and Tissues
1. The primary lymphatic organs are those in which cells become immunocompetent (capable of mounting an immune response) the red bone marrow (B cells) and the Thymus gland (T cells).
   a. The secondary lymphatic organs are the lymph nodes and spleen.
   b. Included as secondary lymphatic tissues are lymphatic nodules.
   c. Most immune responses occur in secondary lymphatic organs and tissues.

2. Thymus Gland
   a. The thymus gland lies between the sternum and the heart and functions in immunity as the site of T cell maturation (Figure 22.5a).
   b. The thymus gland is large in the infant and after puberty is largely replaced by adipose and areolar connective tissue.

3. Lymph Nodes
   a. Lymph nodes are encapsulated oval structures located along lymphatic vessels (Figures 22.1 and 22.6).
   b. They contain T cells, macrophages, follicular dendritic cells, and B cells.
   c. Lymph enters nodes through afferent lymphatic vessels, and exits through efferent lymphatic vessels.
      1) Foreign substances filtered by the lymph nodes are trapped by nodal reticular fibers.
      2) Macrophages then destroy some foreign substances and cells by phagocytosis
      3) Lymphocytes bring about the destruction of other cells by immune responses.
         i. Lymph nodes are the site of proliferation of plasma cells and T cells.
         ii. Knowledge of the location of the lymph nodes and the direction of lymph flow is important in the diagnosis and prognosis of the spread of cancer by metastasis; many cancer cells are spread by way of the lymphatic system, producing clusters of tumor cells where they lodge. (Clinical Connection)

4. Spleen
a. The spleen is the largest mass of lymphatic tissue in the body and is found in the left hypochondriac region between the fundus of the stomach and the diaphragm.
b. The spleen consists of white and red pulp (Figure 22.7a)
c. The white pulp is lymphatic tissue.
d. Its T lymphocytes directly attack and destroy antigens in blood, primarily via cytolysis.
e. Its B lymphocytes develop into antibody producing plasma cells, and the antibodies inactivate antigens in blood.
f. Macrophages destroy antigens in blood by phagocytosis.
g. The red pulp consists of venous sinuses filled with blood and splenic cords consisting of RBCs, macrophages, lymphocytes, plasma cells, and granulocytes.
h. Macrophages remove worn-out or defective RBCs, WBCs, and platelets by phagocytosis.
i. The spleen stores blood platelets in the red pulp.
j. The red pulp is involved in the production of blood cells during the second trimester of pregnancy.
k. The spleen is often damaged in abdominal trauma. A splenectomy may be required to prevent excessive bleeding (Clinical Connection).

5. Lymphatic Nodules

a. Lymphatic nodules are oval-shaped concentrations of lymphatic tissue.
   1) They are scattered throughout the lamina propria of mucous membranes lining the GI tract, respiratory airways, urinary tract, and reproductive tract.
   2) This is the mucosa-associated lymphatic tissue (MALT).
   3) Peyer’s patches are lymphatic nodules in the ileum of the small intestine.
   4) Tonsils are multiple aggregations of large lymphatic nodules embedded in a mucous membrane at the junction of the oral cavity and the pharynx.
   5) They include the pharyngeal (adenoid), palatine, and lingual tonsils (Figure 23.2b).
6) They are situated strategically to protect against invasion of foreign substances and participate in immune responses by producing lymphocytes and antibodies.

III. DEVELOPMENT OF THE LYMPH TISSUES

A. Lymphatic vessels develop from lymph sacs, which develop from veins. Thus, they are derived from mesoderm.

B. Lymph nodes develop from lymph sacs that become invaded by mesenchymal cells (Figure 22.8).

IV. INNATE IMMUNITY

A. First Line of Defense: Skin and Mucous Membranes

1. Innate immunity (nonselective resistance) refers to a wide variety of body responses against a wide range of pathogens (disease producing organisms) and their toxins, that is present at birth.

2. Mechanical protection includes the intact epidermis layer of the skin, mucous membranes, the lacrimal apparatus, saliva, mucus, cilia, the epiglottis, and the flow of urine. Defecation and vomiting also may be considered mechanical processes that expel microbes.

3. Chemical protection is localized on the skin, in loose connective tissue, stomach, and vagina.
   a. The skin produces sebum, which has a low pH due to the presence of unsaturated fatty acids and lactic acid.
   b. Lysozyme is an enzyme component of sweat that also has antimicrobial properties.
   c. Gastric juice renders the stomach nearly sterile because its low pH (1.5-3.0) kills many bacteria and destroys most of their toxins; vaginal secretions also are slightly acidic.

B. Second Line of Defense: Internal Defenses

1. The second line of defense involves internal antimicrobial proteins, phagocytic and natural killer cells, inflammation, and fever.

2. Antimicrobial Proteins
   a. Lymphocyte and macrophage cells infected with viruses produce proteins called interferons (IFNs). Once produced and released from virus-infected
cells, IFN diffuses to uninfected neighboring cells and binds to surface receptors, inducing uninfected cells to synthesize antiviral proteins that interfere with or inhibit viral replication.

b. A group of about 20 proteins present in blood plasma and on cell membranes comprises the complement system; when activated, these proteins “complement” or enhance certain immune, allergic, and inflammatory reactions.

c. Iron-binding proteins remove iron from the body fluids thereby inhibiting microbial growth.

d. Anti-microbial substances are peptides that produce anti-microbial activity and attract dendritic and mast cells.

3. Natural Killer Cells and Phagocytes

   a. Natural killer (NK) cells are lymphocytes that lack the membrane molecules that identify T and B cells.

      1) They have the ability to “kill” a wide variety of infectious microbes.
      2) NK cells sometimes release perforins that insert into the plasma membrane of a microbe and make the membrane leaky so that cytolysis occurs
      3) Phagocytes are cells specialized to perform phagocytosis and include neutrophils and macrophages.
      4) The three phases of phagocytosis include chemotaxis, adherence, and ingestion (Figure 22.9).
      5) After phagocytosis has been accomplished, a phagolysosome (Figure 22.9) is formed and the lysosome in the phagolysosome, along with lethal oxidants produced by the phagocyte, quickly kills many types of microbes.
      6) Some of the reasons why a microbe may evade phagocytosis include: capsule formation, toxin production, interference with lysozyme secretion, and the microbe’s ability to counter oxidants produced by the phagocytes (Clinical Connection).

4. Inflammation

   a. Inflammation occurs when cells are damaged by microbes, physical agents, or chemical agents. The injury may be viewed as a form of stress.
b. Inflammation is usually characterized by four symptoms: redness, pain, heat, and swelling. Loss of function may be a fifth symptom, depending on the site and extent of the injury.

c. The three basic stages of inflammation are: 1) vasodilation and increased permeability of blood vessels; 2) phagocyte migration; and, 3) tissue repair (Figure 22.10).

d. Substances that contribute to inflammation are histamines, kinins, prostaglandins, leukotrienes, and complement.

e. After phagocytes engulf damaged tissue and microbes, they eventually die, forming a pocket of dead phagocytes and damaged tissue and fluid called pus. Pus must drain out of the body or it accumulates in a confined space, causing an abscess. When tissue sloughs off then an ulcer is formed (Clinical Connection)

5. Fever

a. Fever is usually caused by infection from bacteria (and their toxins) and viruses. The high body temperature inhibits some microbial growth and speeds up body reactions that aid repair.

b. Table 22.1 summarizes the components of innate defenses.

V. ADAPTIVE IMMUNITY

A. Immunity is the ability of the body to defend itself against specific invading agents.

1. Antigens are substances recognized as foreign by the immune responses.

2. The distinguishing properties of immunity are specificity and memory.

3. The branch of science that deals with the responses of the body when challenged by antigens is called immunology.

B. Maturation of T Cells and B Cells

1. Both T cells and B cells derive from stem cells in bone marrow (Figure 22.11).

a. B cells complete their development, becoming immunocompetent, in bone marrow (Figure 22.11).

b. T cells develop from pre-T cells that migrate to the thymus where they become immunocompetent under the influence of thymic hormones

c. Before T cells leave the thymus or B cells leave bone marrow, they acquire several distinctive surface proteins; some function as antigen receptors, molecules capable of recognizing specific antigens.
C. Types of Adaptive immunity
   1. Cell-mediated immunity refers to destruction of antigens by T cells. It is particularly effective against intracellular pathogens, such as fungi, parasites, and viruses; some cancer cells; and foreign tissue transplants. CMI always involves cells attacking cells.
   2. Antibody-mediated (humoral) immunity refers to destruction of antigens by antibodies. It works mainly against antigens dissolved in body fluids and extracellular pathogens, primarily bacteria, that multiply in body fluids but rarely enter body cells.
   3. Often a pathogen provokes both types of immune response.

D. Clonal selection: The Principle
   1. Clonal selection is the process by which an immune cells proliferates and differentiates in response to a specific antigen.
   2. Two major types of cells result from clonal selection; 1) effector cells; and 2) memory cells.
   3. Effector cells are the cells that actually do the work to destroy the antigen and include: cytotoxic T cells, helper T cells and plasma cells (a clone of B cells)
   4. Memory cells, with long life spans, provide a faster second invasion response by proliferating and differentiating into effector cells.

E. Antigens and Antigen Receptors
   1. Antigens are chemical substances that are recognized as foreign by antigen receptors when introduced into the body. Antigens are both immunogenic and reactive. An antigen that gets past the nonspecific defenses can get into lymphatic tissue by entering an injured blood vessel and being carried to the spleen, penetrating the skin and entering lymph vessels leading to lymph nodes, or penetrating mucous membranes and lodging in mucosa-associated lymphoid tissue.
   2. Chemical Nature of Antigens
      a. Antigens are large, complex molecules. They are most often proteins, but sometimes are nucleoproteins, lipoproteins, glycoproteins, and certain large polysaccharides.
      b. Specific portions of antigen molecules, called antigenic determinants, or epitopes, trigger immune responses (Figure 22.12).
   3. Diversity of Antigen Receptors
      a. Antigen receptors exhibit great diversity due to genetic recombination.
   4. Major Histocompatibility Complex Antigens
a. Major histocompatibility complex (MHC) antigens (also called human leucocyte associated, or HLA, antigens) are unique to each person’s body cells. These self-antigens aid in the detection of foreign invaders. All cells except red blood cells display MHC class I antigens. Some cells also display MHC class II antigens.

F. Pathways of Antigen Processing
1. For an immune response to occur, B and T cells must recognize that a foreign antigen is present.
2. B cells can recognize and bind to antigens in extracellular fluid.
3. T cells, however, can only recognize fragments of antigenic proteins that first have been processed and presented in association with MHC self-antigens.
4. Peptide fragments from foreign antigens help stimulate MHC molecules.
5. Processing of Exogenous Antigens
a. Cells called antigen-presenting cells (APCs) process exogenous antigens (antigens formed outside the body) and present them together with MHC class II molecules to T cells (Figure 22.13)
   b. APCs include macrophages, B cells, and dendritic cells.
   c. Steps in processing and presenting an exogenous antigen by an APC include ingestion of the antigen, digestion of antigen into peptide fragments, fusion of vesicles, binding of peptide fragments to MHC-II molecules, and insertion of antigen-MHC-II complex into the plasma membrane.
6. Most cells of the body can process and present endogenous antigens, antigens that were synthesized in a body cell (e.g., viral proteins from virus-infected cells). The process is depicted in Figure 22.14)

G. Cytokines
1. Cytokines are small protein hormones needed for many normal cell functions.
2. Table 22.2 describes some of the cytokines that participate in immune responses.
3. Some cytokines have been used to treat certain types of cancer. (Clinical Connection)

VI. CELL-MEDIATED IMMUNITY
A. In a cell-mediated immune response, an antigen is recognized (bound), a small number of specific T cells proliferate and differentiate into a clone of effector cells (a population of identical cells that can recognize the same antigen and carry out some aspect of the immune attack), and the antigen (intruder) is eliminated.
B. Activation of T Cells
   1. T cell receptors recognize antigen fragments associated with MHC molecules on the surface of a body cell (Figure 22.15)
   2. Proliferation of T cells requires co-stimulation, by cytokines such as interleukin-1 (IL-1) and interleukin-2 (IL-2), or by pairs of plasma membrane molecules, one on the surface of the T cell and a second on the surface of an APC.

C. Activation and clonal selection of helper T Cells
   1. Helper T (TH) cells, or CD4 T cells, display CD4 protein, recognize antigen fragments associated with MHC-II molecules, and secrete several cytokines, most important, interleukin-2, which acts as a co-stimulator for other helper T cells, cytotoxic T cells, and B cells.
   2. Once a helper T cell is activated it creates clones of other helper T and memory T cells (Figure 22.15).

D. Activation and clonal selection of helper T Cells
   1. Cytotoxic T (TC) cells, or CD8 T cells, develop from T cells that display CD8 protein and recognize antigen fragments associated with MHC-I molecules.
   2. Once activated cytotoxic T cells undergo clonal selection to form more active cytotoxic T cells and memory cytotoxic T cells (Figure 22.16)

E. Elimination of invaders
   1. Cytotoxic T cells fight foreign invaders by killing the target cell (the cell that bears the same antigen that stimulated activation or proliferation of their progenitor cells) without damaging the cytotoxic T cell itself (Figure 22.17).
   2. One killing mechanism uses perforin to cause cytolysis of the target cell.
   3. The second mechanism uses lymphotoxin to activate damaging enzymes within the target cell.

F. Immunological Surveillance
   1. Immunological surveillance is carried out by cytotoxic T cells.
   2. They recognize tumor antigens and destroy the tumor cell.
   3. The immune system can recognize proteins in transplanted organs as foreign and mount a graft rejection. (Clinical Connection)

VII. ANTIBODY-MEDIATED IMMUNITY
   A. The body contains not only millions of different T cells but also millions of different B cells, each capable of responding to a specific antigen.
B. Activation and clonal selection of B Cells

1. During activation of a B cell, an antigen binds to antigen receptors on the cell surface (Figure 22.18).
2. B cell antigen receptors are chemically similar to the antibodies that will eventually be secreted by their progeny.
3. Some antigen is taken into the B cell, broken down into peptide fragments and combined with the MHC-II self-antigen, and moved to the B cell surface.
4. Helper T cells recognize the antigen-MHC-II combination and deliver the costimulation needed for B cell proliferation and differentiation.
5. Some activated B cells become antibody-secretion plasma cells. Others become memory B cells.

C. Antibodies

1. An antibody is a protein that can combine specifically with the antigenic determinant on the antigen that triggered its production.

D. Antibody Structure

1. Antibodies consist of heavy and light chains and variable and constant portions (Figure 22.19).
2. Based on chemistry and structure, antibodies are grouped into five principal classes each with specific biological roles (IgG, IgA, IgM, IgD, and IgE). Table 22.3 summarizes the structures and functions of these five classes of antibodies.

E. Antibody actions

1. The functions of antibodies include neutralizing antigen, immobilization of bacteria, agglutination and precipitation of antigen, activation of complement and enhancing phagocytosis.
2. Monoclonal antibodies are pure antibodies produced by fusing a B cell with a tumor cell that is capable of proliferating endlessly. The resulting cell is called a hybridoma. Monoclonal antibodies are important in measuring levels of a drug in a patient’s blood and in the diagnosis of pregnancy, allergies, and diseases such as hepatitis, rabies, and some sexually transmitted diseases. They have also been used in early detection of cancer and assessment of extent of metastasis. They may be useful in preparing vaccines to counteract transplant rejection, to treat autoimmune diseases, and perhaps to treat AIDS. (Clinical Connection)

F. Role of Complement system in immunity
1. group of about 20 proteins present in blood plasma and on cell membranes comprises the complement system; when activated, these proteins “complement” or enhance certain immune, allergic, and inflammatory reactions (Figure 22.20).

G. Immunological Memory
1. Immunological memory is due to the presence of long-lived antibodies and very long-lived lymphocytes that arise during proliferation and differentiation of antigen-stimulated B and T cells.
2. Immunization against certain microbes is possible because memory B cells and memory T cells remain after the primary response to an antigen (Figure 22.21).

H. The secondary response (immunological memory) provides protection should the same microbe enter the body again. There is rapid proliferation of memory cells, resulting in a far greater antibody titer (amount of antibody in serum) than during a primary response.

I. Table 22.4 summarizes the various types of naturally and artificially acquired immunity.

VIII. SELF-RECOGNIZITON AND SELF-TOLERANCE
A. T cells undergo both positive and negative selection to ensure that they can recognize self-MHC antigens (self-recognition) and that they do not react to other self-proteins (tolerance). Negative selection involves both deletion and anergy (Figure 22.22).
B. B cells develop tolerance through deletion and anergy (Figure 22.22a).
C. Much research has centered on cancer immunology, the study of ways to use the immune system for detecting, monitoring, and treating cancer (Clinical Connection).

IX. STRESS AND IMMUNITY
A. The field of psychoneuroimmunology (PNI) deals with common pathways that link the nervous, endocrine, and immune systems.
B. PNI has shown that thoughts, feelings, moods, and beliefs influence the level of health and the course of a disease.

X. AGING AND THE IMMUNE SYSTEM
A. With advancing age, the immune system functions less effectively. Individuals become more susceptible to infections and malignancies, response to vaccines is decreased, and more autoantibodies are produced.
B. Cellular and humoral responses also diminish.
XI. FOCUS ON HOMEOSTASIS: THE LYMPHATIC AND IMMUNE SYSTEMS  Discusses the role of the lymphatic and immune system in maintaining homeostasis

XII. DISORDERS: HOMEOSTATIC IMBALANCES

A. AIDS: Acquired Immunodeficiency Syndrome

1. AIDS is a condition in which a person experiences a telltale assortment of infections as a result of the progressive destruction of immune cells by the human immunodeficiency virus (HIV).

2. Although HIV has been isolated from several body fluids, the only documented transmissions are by way of blood, semen, vaginal secretions, and breast milk from an infected nursing mother. It does not appear that people become infected as a result of routine, nonsexual contacts.

   a. The AIDS virus is generally thought to be quite fragile outside of the body and easily eliminated with standard disinfecting techniques.

   b. At present, the only means of preventing AIDS is to block transmission of the virus, including abstinence from sex with infected individuals, use of condoms during intercourse, use of sterile hypodermic needles, and avoidance of pregnancy in HIV-infected women. Until there is an effective drug therapy or an effective vaccine, preventing the spread of AIDS must rely on education and safer sexual practices.

   c. HIV is a form of retrovirus with a protein coat wrapped by an envelope of glycoproteins (Figure 22.23).

   d. HIV enters T cells where it sheds its protein coat.

   e. New HIV DNA is produced in the T cell along with new protein coats and then released.

   f. The T cells are ultimately destroyed.

   g. Common signs and symptoms of infection are fever, fatigue, rash, headache, joint pain, sore throat, and swollen lymph nodes. The infected individual ultimately develops antibodies to HIV.

   h. Progression to AIDS occurs because of reduced numbers of T cells and resulting immunodeficiency. AIDS lowers the body’s immunity by decreasing the number of helper T cells; the result is progressive collapse of the immune system, making the person susceptible to opportunistic
infections (invasion of normally harmless microorganisms that now proliferate wildly because of the defective immune system).

i. Treatment of HIV infection with reverse transcriptase inhibitors and protease inhibitors has shown to delay the progression of HIV infection to AIDS.

B. A person who is overly reactive to a substance that is tolerated by most others is said to be hypersensitive (allergic reactions). Whenever an allergic reaction occurs, there is tissue injury. The antigens that induce an allergic reaction are called allergens.

1. There are four basic types of hypersensitivity reactions.
2. Type I (anaphylaxis) reactions are the most common and occur with a few minutes after a person sensitized to an allergen is reexposed to it. Anaphylaxis results from the interaction of allergens with IgE antibodies on the surface of mast cells and basophils. In anaphylactic shock, which may occur in a susceptible individual who has just received a triggering drug or been stung by a wasp, wheezing and shortness of breath as airways constrict are usually accompanied by shock due to vasodilation and fluid loss from blood. This is a life-threatening emergency.
3. Type II (cytotoxic) reactions are caused by antibodies (IgG or IgM) directed against a person’s blood cells or tissue cells. The reaction of antibodies and antigens usually leads to activation of complement. Type II reaction, which may occur in incompatible blood transfusion reactions, damage cells by causing lysis.
4. Type III (immune complex) reactions involve antigens (not part of a host tissue cell), antibodies (IgA or IgM), and complement. Some type II conditions include glomerulonephritis, systemic lupus erythematosus, and rheumatoid arthritis.
5. Type IV (cell-mediated) reactions or delayed hypersensitivity reactions usually appear 12-72 hours after exposure to an allergen and occur when allergens are taken up by antigen-presenting cells that migrate to lymph nodes and present the allergen to T cells. Intracellular bacteria, such as the one that causes tuberculosis, trigger this type of cell-mediated immune response.

C. In an autoimmune disease the immune system fails to display self-tolerance and attacks the person’s own tissue.

D. Infectious mononucleosis is a contagious disease primarily affecting lymphatic tissue throughout the body but also affecting the blood. It is caused by the Epstein-Barr virus which multiplies in B cells. There is no cure, and treatment consists of watching for and treating complications. Usually the disease runs its course in a few weeks.
E. Lymphomas are cancers of the lymphatic organs especially the lymph nodes. The two main types are: Hodgkin disease and non-Hodgkin lymphoma.

F. Systemic lupus erythematosus is a chronic autoimmune, inflammatory disease that affects multiple body systems.

XIII. MEDICAL TERMINOLOGY - Alert students to the medical terms associated with the lymphatic system.