1. Immunity = Ability to resist damage from foreign substances (microorganisms, chemicals, etc.).
   a. Categorized as being innate or adaptive.
2. Innate/Nonspecific immune system
   a. Provides the basic means for the destruction of foreign organisms.
   b. Destroys foreign substances, but the response doesn’t depend upon previous exposure.
   c. Consists of mechanical barriers as well as certain cells and chemical mediators.
   d. Main barriers are skin and mucosae.
   e. Cells/chemicals include granulocytes, macrophages, antimicrobial proteins, etc.
   f. A characteristic response of the innate system is inflammation.
3. Adaptive/Specific immune system
   a. Consists of cells that attack particular antigens in particular ways.
   b. Improves and enhances the efficiency of the innate mechanisms and remembers the infection the next time it is encountered.
   c. Specificity (the ability to distinguish pathogens) and memory (the ability to respond more rapidly to a previously encountered pathogen) are characteristics of adaptive immunity.
4. Skin = Repels pathogens in many ways.
   a. Highly keratinized, which provides a physical barrier to pathogens.
   b. Acidity of sweat can kill some pathogens. Sebum is bactericidal.
5. Mucous membranes = Line the digestive, respiratory, urinary, and reproductive tracts - all potential entrance points for pathogens.
   a. Often covered in sticky, pathogen-trapping mucus.
   b. Respiratory mucosa is also ciliated. Cilia sweep bacteria-laden mucus upward to the pharynx where it can be swallowed. Coughing and sneezing also assist in expulsion.
6. Body fluids also provide innate defense
   a. Tears, saliva, and urine wash away microorganisms.
   b. Saliva, intestinal fluid, and tears contain lysozyme, an enzyme that destroys bacteria.
   c. Acidity of certain mucosal secretions (gastric and vaginal) can impair pathogens.
7. Bacterial competition
   a. Growth of disease-causing organisms is inhibited by the growth of non-pathogenic bacteria in the gastrointestinal and urogenital tracts. These bacteria successfully compete w/ the pathogenic ones for nutrients and resources.
8. WBCs and derivatives = The most important cellular component of the innate immune system.
   a. Can exit blood vessels (diapedesis), converge upon areas of infection/damage (positive chemotaxis) and move over, btwn, and through other cells.
9. Neutrophils = Small phagocytes. The first to enter infected tissues. Function as bacteria killers.
10. Eosinophils = Kill multicellular parasites (e.g. worms and flukes).
11. Macrophages = Large phagocytic cells derived from monocytes.
    a. Free (able to move thru tissue spaces) such as the alveolar macrophages in the lungs or fixed (permanent residents of a particular organ) such as the Kupffer cells of the liver.
    b. Perform phagocytosis whereby they ingest something (a bacterium, particulate matter, etc.) and enclose it within a membrane-bound vesicle.
12. Phagocytosis
    a. Begins with the adherence of a microbe to the phagocyte. This is likely when antibodies or complement proteins have bound to the microbe (a process called opsonization).
    b. Phagocyte then extends membrane “arms” that wrap the microbe and engulf it, forming a membrane-bound vesicle containing the pathogen. This vesicle is a phagosome.
    c. The phagosome will fuse with a lysosome, an organelle that contains digestive enzymes.
    d. The enzymes will then destroy the engulfed material.
    e. Whatever indigestible material remains is then exocytosed.
13. Natural killer cells = specialized lymphocyte that destroys virus-infected cells and cancer cells.
14. Antimicrobial proteins = include interferons and complement proteins.
15. Interferons = Proteins produced by cells that have been infected with a virus.
a. Diffuse to nearby cells and stimulate them to synthesize a protein that prevents viral replication. This prevents copies of the original virus from taking over neighboring cells.
b. Stimulate NK cells.
c. Do not save the infected cell but prevent nearby cells from being infected.
d. The same interferons can act against many different types of viruses.

16. Complement system = Refers to a group of about 30 plasma proteins synthesized by the liver.
   a. Normally found in the blood in an inactive state.
   b. May be activated by interacting directly with a pathogen or by members of the adaptive immune system. Activation of complement results in 4 things:
      i. Chemotaxis → activated complement proteins attract WBCs.
      ii. Opsonization → binding of activated complement proteins to bacteria increases the likelihood of their phagocytosis.
      iii. Inflammation → activated complement proteins bind to basophils and mast cells and stimulate histamine release. This results in vasodilation and increased capillary permeability and inflammation.
      iv. Lysis → activated complement proteins can form a “membrane attack complex,” which is a tube that pierces the bacterial cell membrane. This allows salt and water to flow in and results in cell lysis.

17. Inflammatory response = Occurs whenever tissues are damaged.
   a. Helps to prevent pathogen spread, disposes of pathogens/debris, and allows for repair.
   b. Signs include heat, redness, swelling, pain, and loss of function.
   c. Begins when damaged cells release inflammatory chemicals (histamine, prostaglandins, leukotrienes, kinins, etc.). Most are derived from arachidonic acid (a cell membrane component) and produced via enzymes such as COX and LOX.
   d. Inflammatory chemicals: increase WBCs, increase capillary permeability, cause local vasodilation, attract WBCs, instigate a fever, cause bronchospasm and stimulate pain-sensitive neurons.
   e. Increase in vasodilation and capillary permeability yields an increase in blood flow and capillary fluid loss. This results in swelling, heat, redness, and increased access to the injury site by WBCs, complement proteins, antibodies, and clotting proteins.

18. Fever = Systemic response to infection associated with an abnormally high body temperature.
   a. WBCs and macrophages release chemicals (pyrogens) in response to pathogen exposure.
   b. Pyrogens act on the body’s hypothalamic thermostat to raise body temperature.
   c. Mild increase in temp. accelerates WBC function; impairs bacterial metabolism; and causes the liver and spleen to sequester Zn and Fe, 2 minerals needed by bacteria.
   d. Major increase in temperature can result in protein denaturation and possible loss of life.

19. Adaptive immune system = Responds in strong ways tailored to particular antigens.
   a. Differs from the innate system in that it’s specific, systemic, and it improves.

20. Antigens = Substances that can provoke the adaptive immune system and cause a response.
   a. Large, complex molecules not normally found in the body. (Non-self/foreign antigens.)
   b. Self-antigens are molecules produced by the body that stimulate the adaptive immune system. They can result in autoimmune disease.

21. Lymphocytes = Principal cells of adaptive immunity. 2 main types: B’s and and T’s.
   a. Both are formed initially in the red bone marrow.
   b. B lymphocytes gain immunocompetence (i.e., mature) in the bone marrow.
   c. T lymphocytes gain immunocompetence in the thymus.
   d. Each lymphocyte has many copies ($10^4$-$10^6$) of a receptor on its cell surface. The presence of one specific type of receptor allows each clone to bind/recognize and interact with 1 specific type of antigen.
   e. There are more than a million different varieties of clones, giving the lymphocytes a large variety of antigens to which they can respond.
   f. Once a B or T cell has become immunocompetent, the naïve cells will travel to the lymph nodes, spleen, or other lymphoid organs to await antigens.
22. Antigen-presenting cells = Dendritic cells and macrophages.
   a. Engulf antigens and present antigen fragments to Helper T cells.
   b. Identifying the invading antigens and then displaying it to the specific appropriate lymphocyte and saying – “Hey these invaded us. Find them, build an army, & kill 'em!”

23. Components of the adaptive response
   a. Antibody-mediated immunity and cell-mediated immunity.
   b. Antibody-mediated response (a.k.a. the humoral response) is the body’s response to extracellular antigens, i.e., those antigens found within plasma, ISF, or lymph.
   c. Cell-mediated immunity refers to how the body deals with microorganisms that have invaded cells (e.g., viruses, certain bacteria and fungi).
   d. These 2 branches will overlap and work together.

   a. Suppose a pathogen has invaded the body and is somewhere in the extracellular space
   b. 1st step in the response is for an APC (i.e., a macrophage or dendritic cell) to engulf it.
   c. Once engulfed, the pathogen will be destroyed. The resulting pieces (antigens) will be displayed on the surface of the APC by a molecule known as a class II MHC protein.
   d. The antigen will be recognized by and stimulate a Helper T cell that contains the specific receptor matching the particular antigen.
   e. Helper T cell now proliferates to form many more Helper T cells, which also respond to the same original antigen. Both active and memory Helper T cells will be produced. Activated Helper T cells can release cytokines which will stimulate the body’s innate defenses and also help activate B cells and Killer T cells.
   f. Now suppose that the same pathogen runs into a B cell that carries the specific receptor.
   g. The B cell will engulf it, kill it, and display antigens on its own MHC II proteins.
   h. Once the antigen has been displayed to the previously mentioned Helper T cells, those Helper T cells will stimulate the B cell to begin dividing.
   i. Most of the resulting cells will be plasma cells. Plasma cells secrete 2000 antibodies/s.
   j. Each antibody will specifically bind to the original antigen and mark it for destruction.
   k. A small percentage of the newly formed B cells will be memory cells.
   l. These memory cells have the ability to mount an almost immediate response if the same antigen appears again in the future.

25. Antibodies (A.k.a. immunoglobulins, gamma globulins, or Ig’s)
   a. Consists of 4 polypeptide chains that form a Y-shaped structure (the antibody monomer).
   b. Each has 2 variable parts (the 2 arms of the Y) and a constant part (the stem of the Y).
   c. Variable regions contain the antigen-binding sites. All antibodies released from the same plasma cell have the same antigen-binding sites and are specific for the same antigen.
   d. Constant region binds to other immune chemicals or cells and determines the mechanism by which the bound antigen will be destroyed. The constant regions also determine the antibody class. There are 5 antibody classes: IgM, IgA, IgD, IgG, and IgE. Antibodies of each class have different constant regions and different roles and locations in the body.
   e. Antibodies have several mechanisms of action
   f. Precipitation = occurs when antibodies bind soluble antigens into clumps. This increases the likelihood of phagocytosis.
   g. Lysis = occurs when antibodies activate complement. This results in the formation of a membrane attack complex, and bursting of the bacterial cell.
   h. Agglutination = occurs when antibodies bind cell-bound antigens into clumps. This increases the likelihood of phagocytosis.
   i. Neutralization = occurs when antibodies bind to and mask the dangerous portions of antigens, toxins, and viruses.
   j. Antibodies also activate natural killer cells.

26. Adaptive immune scenario (Cell-mediated response)
   a. Now suppose that the original pathogen has begun invading the body cells.
b. Antibodies are only effective against extracellular antigens. They’re useless against pathogens that have slipped inside body cells.
c. Fragments of intracellular proteins are displayed on the surface of every nucleated body cell by molecules known as class I MHC proteins. This gives a “window” into a cell, that T lymphocytes can “look in” to see if everything is ok.
d. The combination of original antigen and the MHC I protein displaying it will bind to and stimulate a Killer T cell that contains the specific receptor matching the original antigen.
e. With stimulation from our aforementioned Helper T cells, the activated Killer T cell will begin to divide. This results in both mature killer T cells and memory killer T cells.
f. Memory killer T cells persist in case of another infection by the same pathogen.
g. Mature killer T cells will set about to kill those body cells displaying the same specific antigen as the original one that began the activation process, e.g., cells infected by the same type of virus. Killer T cells release chemicals that are capable of causing cell death.

27. Primary vs. Secondary immune responses
   a. The initial encounter with a particular antigen is termed the primary immune response.
   b. It typically has a lag period of 3-6d between the time of exposure to the antigen and the appearance of antibodies specific for that antigen in the plasma.
   c. During this lag period clonal selection and antibody production both take place.
   d. Plasma antibody levels peak at about 10d and then decline.
   e. In the secondary response, the presence of memory cells primed for the original antigen will result in:
      i. A shorter lag time.
      ii. Plasma cells that live and function for a much longer time.
      iii. Achievement of higher antibody levels in a shorter time.
      iv. Higher efficiency of binding between antibodies and antigens.
   f. A similar form of immunological memory will occur with T cells.

28. Classification of Immunity
   a. Active immunity is the result of memory cell production by the body in response to a foreign antigen.
   b. Passive immunity occurs when antibodies from another person (or animal) are transferred to a non-immune individual.
   c. Active immunity can be naturally adaptive in response to infection.
   d. It can also be artificially adaptive due to vaccination – the injection of dead or weakened pathogens into the body. This results in memory cell production, but spares the body of symptoms.
   e. Active immunity lasts for as long as the memory cells remain alive in the body.
   f. Truly long lasting immunity may require continual exposure to the pathogen.
   g. Passive immunity, since it does not involve memory cell production, has a much shorter duration than does active immunity – lasting only as long as the antibodies remain in the circulation.
   h. Passive immunity is natural when antibodies cross the placenta and travel from maternal bloodstream to fetal bloodstream, or when antibodies are excreted in breast milk.
   i. Passive immunity is artificial when antibodies are given by injection.

29. Regulatory T Lymphocytes
   a. Rein in the responses of B and T cells and make sure they do not go overboard.