Chapter 43: The Immune System

Our students consider this chapter to be a particularly challenging and important one. Expect to work your way slowly through the first three concepts. Take particular care with Concepts 43.2 and 43.3. It is rewarding, however, in Concept 43.4 to put your new knowledge to work and truly understand the devastation caused by the destruction of helper T cells by HIV.

Overview

The immune responses of animals can be divided into innate immunity and adaptive immunity. As an overview, complete this figure indicating the divisions of both innate and adaptive immunity.

See page 930 of your text for the labeled figure.

Concept 43.1 In innate immunity, recognition and response rely on shared traits of pathogens

1. We first encountered phagocytosis in Concept 7.5, but it plays an important role in the immune systems of both invertebrates and vertebrates. Review the process by briefly explaining the six steps to ingestion and destruction of a microbe by a phagocytic cell.

See page 930 of your text for the labeled figure.

1. Pseudopodia surround pathogens.
2. Pathogens are engulfed by endocytosis.
3. Vacuole forms, enclosing pathogens.
4. Vacuole and lysosome fuse.
5. Toxic compounds and lysosomal enzymes destroy pathogens.
6. Debris from pathogens is released by exocytosis.

2. Explain the role of the Toll receptor in producing antimicrobial peptides.

Signal transduction from the Toll receptor to the cell nucleus leads to synthesis of a set of antimicrobial peptides active against fungi.

3. List the three innate defenses vertebrates share with invertebrates and the two defenses unique to vertebrates.

Vertebrates and invertebrates alike share the innate defenses of barrier defenses, phagocytosis, and antimicrobial peptides. Vertebrates alone have natural killer cells, inflammatory response, and interferons.

4. In the following chart, list five examples of barrier defenses and how they work.

<table>
<thead>
<tr>
<th>Barrier Defense</th>
<th>How the Barrier Repels Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous membranes</td>
<td>Mucus, a viscous fluid, enhances defenses by trapping microbes and other particles.</td>
</tr>
<tr>
<td>Saliva, tears</td>
<td>Bathe various exposed epithelia, providing a washing action that also inhibits colonization by fungi and bacteria</td>
</tr>
<tr>
<td>Stomach acid</td>
<td>Kills most of the microbes in food and water before they can enter the intestines</td>
</tr>
</tbody>
</table>

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Secretions from oil and sweat glands | Give human skin a pH ranging from 3 to 5, acidic enough to prevent the growth of many bacteria
---|---
Skin | Blocks entry of many pathogens

5. Explain how *Toll-like receptors* are used in cellular innate defenses, using TLR3 and TLR4 as examples.

Each mammalian Toll-like receptor binds to fragments of molecules characteristic of a set of pathogens. For example, TLR3, on the inner surface of vesicles formed by endocytosis, is the sensor for double-stranded RNA, a form of nucleic acid characteristic of certain viruses. Similarly, TLR4, located on immune cell plasma membranes, recognizes lipopolysaccharide, a type of molecule found on the surface of many bacteria.

6. In the chart below, explain the role of the four phagocytic cells.

<table>
<thead>
<tr>
<th>Phagocytic Cell Type</th>
<th>Role in Innate Defense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>Circulate in the blood, are attracted by signals from infected tissues and then engulf and destroy the infecting pathogens</td>
</tr>
<tr>
<td>Macrophages</td>
<td>Some migrate throughout the body, whereas others reside permanently in organs and tissues where they are likely to encounter pathogens</td>
</tr>
<tr>
<td>Dendritic cells</td>
<td>Populate tissues, such as skin, that contact the environment. They stimulate adaptive immunity against pathogens they encounter and engulf</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Often found beneath mucosal surfaces, have low phagocytic activity but are important in defending against multicellular invaders, such as parasitic worms</td>
</tr>
</tbody>
</table>

7. *Natural killer cells* are not phagocytic. How do they assist in innate defenses and what types of cells do they detect?

These cells circulate through the body and detect the abnormal array of surface proteins characteristic of some virus-infected and cancerous cells. Natural killer cells do not engulf stricken cells. Instead, they release chemicals that lead to cell death, inhibiting further spread of the virus or cancer.

8. In the following figure, trace the flow of lymph in four stages. For each stage, explain the role of the lymphatic system in innate defense.

See page 933 of your text for the labeled figure and explanation.

9. Explain the role of the following two antimicrobial compounds.

**Interferon**: Proteins that provide innate defense by interfering with viral infections. Virus-infected body cells secrete interferons, which induce nearby uninfected cells to produce substances that inhibit viral reproduction. In this way, interferons limit the cell-to-cell spread of viruses in the body, helping control viral infections such as colds and influenza.

**Complement**: Consists of roughly 30 proteins in blood plasma. These proteins circulate in an inactive state and are activated by substances on the surface of many microbes. Activation results in a cascade of biochemical reactions that can lead to lysis of invading cells.
10. Use the following figure to explain the three steps of an inflammatory response.

See page 934 of your text for the labeled figure.

1. At the injury site, mast cells release histamines, and macrophages secrete cytokines. These signaling molecules cause nearby capillaries to dilate.
2. Capillaries widen and become more permeable, allowing fluid containing antimicrobial peptides to enter the tissue. Signals released by immune cells attract neutrophils.
3. Neutrophils digest pathogens and cell debris at the site, and the tissue heals.

11. It might seem like pathogens have little hope of mounting an infection, but do not forget that pathogens are constantly evolving ways to circumvent our immune system. As examples, how do the pathogens that cause pneumonia and tuberculosis avoid our immune responses?

The bacterium that causes tuberculosis rather than being destroyed within host cells grows and reproduces, effectively hidden from the body’s innate immune defenses. In the bacterium that causes pneumonia, Streptococcus pneumoniae, an outer capsule covers the surface of the bacterium making molecular recognition difficult.

**Concept 43.2 In adaptive immunity, lymphocyte receptors provide pathogen-specific recognition**

12. From the first four paragraphs of this concept, summarize where T cells and B cells develop, and give an overview of their functions. (Note that they are a type of white blood cell known as a lymphocyte.)

Like all blood cells, lymphocytes originate from stem cells in the bone marrow. Lymphocytes have cell-surface antigen receptors for foreign molecules. All receptor proteins on a single B or T cell are the same, but there are millions of B and T cells in the body that differ in their foreign molecule that their receptors recognize. Upon infection, B and T cells specific for the pathogen are activated.

13. What is immunological memory, and why is it important?

Immunological memory is responsible for the long-term protection that a prior infection or vaccination provides against many diseases, such as chickenpox.

14. Explain how cytokines help coordinate the innate and adaptive immune responses.

Cytokines promote blood flow to the site of injury or infection. The increase in local blood supply causes the redness and increased skin temperature typical of the inflammatory response. In adaptive immune responses, cytokines are exchanged as signals between the T cell and the class II MHC molecule.

15. The following brief questions will serve as a beginning primer for immune system recognition.

a. What is an antigen?

A substance that elicits an immune response by binding to receptors of B cells, antibodies, or of T cells.
b. What is the relationship between an antigen receptor, an antibody, and an immunoglobin?

An antigen receptor is a general term for a surface protein, located on B cells and T cells, that binds to antigens, initiating adaptive immune responses. An antibody is a protein secreted by plasma cells (differentiated B cells) that binds to a particular antigen; also called immunoglobin.

c. How is an epitope related to an antigen? (Look at Figure 43.10 in your text.)

An epitope is the accessible portion of an antigen that binds to an antigen receptor. It is also known as an antigenic determinant.

16. In the figure of a B cell below, label the antigen-binding sites, light and heavy chains, variable and constant regions, transmembrane region, and disulfide bridges.

See page 935 of your text for the labeled figure.

17. What forms the specific antigen-binding site? (Be sure to recognize that each B cell produces only one antigen receptor. For any one cell, all antigen receptors or antibodies produced are identical.)

Parts of a heavy-chain V region and a light-chain V region form an asymmetrical binding site for an antigen.

18. In the figure of a T cell below, label the antigen-binding site, alpha and beta chain, variable and constant regions, transmembrane region, and disulfide bridge.

See page 936 of your text for the labeled figure

19. T cells also display only one receptor on the surface of the cell. Compare and contrast a T cell with a B cell.

Lymphocytes in the thymus mature into T cells, while lymphocytes in the bone marrow mature into B cells. Each B cell antigen receptor is a Y-shaped molecule consisting of four polypeptide chains: two identical heavy chains and two identical light chains, with disulfide bridges linking the chains together. A transmembrane region near one end of each heavy chain anchors the receptor in the cell’s plasma membrane. A short tail region at the end of the heavy chain extends into the cytoplasm. For a T cell, the antigen receptor consists of two different polypeptide chains, linked by a disulfide bridge. Near the base of the T cell antigen receptor is a transmembrane region that anchors the molecule in the cell’s plasma membrane. At the outer tip of the molecule, the variable regions of each chain together form an antigen-binding site. The remainder of the molecule is made up of the constant (C) regions. The T and B cells, however function differently. Whereas the antigen receptors of B cells bind to epitopes of intact antigens circulating in body fluids, those of T cells bind only to fragments of antigens that are displayed on the surface of host cells.

20. B cell receptors recognize and bind to antigens whether they are free antigens (like a secreted toxin) or on the surface of a pathogen. Explain the role of the major histocompatibility complex (MHC) to T cell receptor binding.

T cells bind only to fragments of antigens that are displayed on the surface of host cells. The host protein that displays the antigen fragment on the cell surface is called an MHC (major histocompatibility complex) molecule.
21. Explain how a host cell uses the MHC to display an antigen.

Inside the host cell, enzymes in the cell cleave the antigen into smaller peptides. Each peptide, called an antigen fragment, then binds to an MHC molecule inside the cell. Movement of the MHC molecule and bound antigen fragment to the cell surface results in antigen presentation, the display of the antigen fragment in an exposed groove of the MHC protein.

22. Using Figure 43.12 in your text as a guide, label completely the figure below.

See page 937 of your text for the labeled figure.

23. List four major characteristics of the adaptive immune system.

1. There is an immense diversity of lymphocytes and receptors, enabling the immune system to detect pathogens never before encountered.
2. Self-tolerance
3. Cell proliferation triggered by activation greatly increases the number of B and T cells specific for an antigen.
4. Immunological memory allows for a more rapid response to an antigen previously encountered.

24. One of the early problems in immunology was trying to understand how an organism with a limited number of genes (for humans, about 20,500) could produce a million different B-cell protein receptors and 10 million different T-cell protein receptors! The answer resulted in a Nobel Prize and a startling exception to the notion that all cells have exactly the same DNA. Use the figure below to label and explain the four steps producing genetically unique B cell receptors.

See page 938 of your text for the labeled figure and explanation.

25. Explain how the body develops self-tolerance in the immune system.

As lymphocytes mature in the bone marrow or thymus, their antigen receptors are tested for self-reactivity. Some B and T cells with receptors specific for the body’s own molecules are destroyed by apoptosis, which is a programmed cell death. The remaining self-reactive lymphocytes are typically rendered nonfunctional, leaving only those that react to foreign molecules.

26. Define the following terms.

- effector cells: Short-lived cells that take effect immediately against the antigen and any pathogens producing that antigen
- memory cells: Long-lived cells that can give rise to effector cells if the same antigen is encountered later in the animal’s life
- clonal selection: The proliferation of a lymphocyte into a clone of cells in response to binding to an antigen, so called because an encounter with an antigen selects which lymphocyte will divide to produce a clonal population of thousands of cells specific for a particular epitope
27. Using the blue text in the margin of Figure 43.14, explain the three key events to clonal selection.

See page 939 of your text for the labeled figure.

1. Antigens bind to the antigen receptors of only one of the three B cells shown.
2. The selected B cell proliferates, forming a clone of identical cells bearing receptors for the antigen.
3. Some daughter cells develop into long-lived memory cells that can respond rapidly upon subsequent exposure to the same antigen, and other daughter cells develop into short-lived plasma cells that secrete antibodies specific for the antigen.

28. Graphs similar to the one below have been seen on several AP Biology exams. It depicts the primary and secondary immune response. The first arrow shows exposure to antigen A. The second arrow shows exposure to antigen A again, and also antigen B. Label this graph and then use it to explain the difference between a primary and secondary immune response.

See page 940 of your text for the labeled figure.

Primary response peaks about 10–17 days after the initial exposure; selected B cells and T cells give rise to their effector forms. Secondary immune response occurs next. Upon subsequent exposure to the same antigen, the secondary immune response is faster, of greater magnitude, and more prolonged.

Concept 43.3 Adaptive immunity defends against infection of body cells and fluids

29. Explain fully the function of the two divisions of acquired immunity.

humoral immune response: Occurs in the blood and lymph, which were long ago called body humors (fluids). In humoral response, antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph.

cell-mediated immune response: In this response, specialized T cells destroy infected host cells.

30. Helper T cells play a critical role in activation of both T cells and B cells. In full detail, label and explain the three steps involved using Figure 43.16. This is an important step!

See page 941 of your text for the labeled figure.

1. After an antigen-presenting cell engulfs and degrades a pathogen, it displays antigen fragments with class II MHC molecules on the cell surface. Then, a helper T cell binds, and cytokines are secreted by the APC.
2. Helper T cells proliferate and are activated. All have receptors for the MHC-antigen fragment.
3. The helper T cells secrete other cytokines, and now B cells and cytotoxic T cells are activated.

The B cells secrete antibodies (humoral immunity) and the cytotoxic T cells attack the infected cells (cell-mediated immunity)
31. Explain the role of **dendritic cells** and **macrophages** in starting a primary and secondary immune response.

Phagocytosis enables macrophages and dendritic cells to present antigens to, and stimulate, helper T cells, which in turn stimulate the very B cells whose antibodies contribute to phagocytosis. This positive feedback between innate and adaptive immunity contributes to a coordinated, effective response to infection.

32. **Cytotoxic T cells** are the effector cells in cell-mediated immunity.

33. What must occur for a **cytotoxic T cell** to become activated?

To become active, cytotoxic T cells require signaling molecules from helper T cells as well as interaction with a cell that presents an antigen.

34. Completely label the diagram below. Then carefully explain the three primary steps that occur as a cytotoxic T cell destroys a target cell.

See page 941 of your text for the labeled figure.

1. An activated cytotoxic T cell binds to a class I MHC–antigen fragment complex on an infected cell via its antigen receptor and an accessory protein (called CD8).
2. The T cell releases perforin molecules, which form pores in the infected cell membrane, and granzymes, enzymes that break down proteins. Granzymes enter the infected cell by endocytosis.
3. The granzymes initiate apoptosis within the infected cell, leading to fragmentation of the nucleus and cytoplasm and eventual cell death. The released cytotoxic T cell can attack other infected cells.

35. How is B-cell antigen presentation unique?

The B cell presents only the antigen to which it specifically binds. When an antigen first binds to receptors on the surface of a B cell, the cell takes in a few foreign molecules by receptor-mediated endocytosis. The class II MHC protein of the B cell then presents an antigen fragment to a helper T cell.

36. Completely label the diagram below. Then carefully explain the three primary steps that occur in **B cell activation**.

See page 942 of your text for the labeled figure.

1. After an antigen-presenting cell engulfs and degrades a pathogen, it displays an antigen fragment complexed with a class II MHC molecule. A helper T cell that recognizes the complex is activated with the aid of cytokines secreted from the antigen-presenting cell.
2. When a B cell with receptors for the same epitope internalizes the antigen, it displays an antigen fragment on the cell surface in a complex with a class II MHC molecule. An activated helper T cell bearing receptors specific for the displayed fragment binds to the B cell. This interaction, with the aid of cytokines from the T cell, activates the B cell.
3. The activated B cell proliferates and differentiates into memory B cells and antibody-secreting plasma cells. The secreted antibodies are specific for the same antigen that initiated the response.

37. What is the difference between plasma cells and memory cells produced from the activation of B cells?

Plasma cells and memory cells are different because plasma cells are antibody-secreting.

38. Explain these three ways antibodies can dispose of antigens.

**viral neutralization:** Antibodies bound to antigens on the surface of a virus neutralize it by blocking its ability to bind to a host cell.

**opsonization:** Binding of antibodies to antigens on the surface of bacteria promotes phagocytosis by macrophages and neutrophils.

**activation of complement:** Binding of antibodies to antigens on the surface of a foreign cell activates the complement system.

39. How do antibodies and natural killer cells work together to fight viral infections while the virus is inside the body?

Viral proteins produced inside the infected cell can be displayed on the cell surface where antibodies can bind to the viral protein. The bound antibody at the cell surface can recruit a natural killer cell. The natural killer cell then releases proteins that cause the infected cell to undergo apoptosis.

40. Using examples, explain the difference between active and passive immunity.

Active immunity refers to long-term defenses that arise when a pathogen infects the body, activating B cells and T cells and the resulting memory cells specific to the pathogen. Passive immunity refers to short-term immunity conferred by the transfer of antibodies, as occurs in the transfer of maternal antibodies to a fetus or nursing infant.

41. Describe how immunizations can serve as an example of active immunity.

Active immunity can develop through the introduction of antigens into the body by immunization. Because the immunization induces a primary immune response and immunological memory, an encounter with the pathogen from which the vaccine was derived triggers a rapid and strong secondary immune response.

42. Explain how monoclonal antibodies are used in home pregnancy kits.

Monoclonal antibodies are used to detect human chorionic gonadotropin (HCG). Because HCG is produced as soon as an embryo implants in the uterus, the presence of this hormone in a woman’s urine is a reliable indicator for a very early stage of pregnancy.
43. Why is the antibody response to a microbial infection *polyclonal*?

A polyclonal response is one where many different clones of plasma cells form, each clone specific for a different epitope. Typically, pathogens have multiple epitopes.

44. Why is immune rejection an example of a healthy immune system?

An immune rejection is expected from a healthy immune system in response to foreign tissue.

45. Briefly describe the following features of immune rejection.

a. Explain how antibodies against blood types are present.

Certain bacteria normally present in the body have epitopes very similar to the A and B carbohydrates. By responding to the bacterial epitope similar to the B carbohydrate, for example, a person with type A blood makes antibodies that will react with the type B carbohydrate. If the person with type A blood receives a transfusion of type B blood, that person’s anti-B antibodies cause an immediate and devastating transfusion reaction.

b. What is the role of MHC in tissue and organ transplants?

In the case of tissue and organ transplants, MHC molecules stimulate the immune response that leads to rejection.

c. Why are bone marrow transplants medically unique?

Prior to receiving transplanted bone marrow, the recipient is typically treated with radiation to eliminate his or her own bone marrow cells, thus destroying the source of abnormal cells. This treatment effectively obliterates the recipient’s immune system, leaving little chance of graft rejection. However, lymphocytes in the donated marrow may react against the recipient.

*Concept 43.4 Disruptions in immune system function can elicit or exacerbate disease*

46. What are allergies?

Allergies are exaggerated (hypersensitive) responses to certain antigens called allergens.

47. Label Figure 43.22 and then use it to explain a typical allergic response.

See page 947 of your text for the labeled figure.

1. IgE antibodies produced in response to initial exposure to an allergen bind to receptors on mast cells.
2. On subsequent exposure to the same allergen, IgE molecules attached to a mast cell recognize and bind the allergens.
3. Cross-linking of adjacent IgE molecules triggers release of histamine and other chemicals, leading to allergy symptoms.
48. Explain what happens if a person experiences **anaphylactic shock**.

Anaphylactic shock is a whole-body, life-threatening reaction that can occur within seconds of exposure to an allergen. Anaphylactic shock develops when widespread release of mast cell contents triggers abrupt dilation of peripheral blood vessels, causing a precipitous drop in blood pressure, as well as constriction of bronchioles.

49. **Autoimmune diseases** occur when the immune system turns against particular molecules of the body. Describe the cause and symptoms of the following autoimmune diseases.

- **lupus**: In lupus, the immune system generates antibodies against histones and DNA released by the normal breakdown of body cells. These self-reactive antibodies cause skin rashes, fever, arthritis, and kidney dysfunction.

- **rheumatoid arthritis**: Rheumatoid arthritis leads to damage and painful inflammation of the cartilage and bone of joints.

- **type 1 diabetes mellitus**: In type 1 diabetes mellitus, the insulin-producing beta cells of the pancreas are the targets of autoimmune cytotoxic T cells.

- **multiple sclerosis**: Multiple sclerosis is the most common chronic neurological disorder in developed countries. In this disease, T cells infiltrate the central nervous system. The result is destruction of the myelin sheath that surrounds parts of many neurons, leading to muscle paralysis through a disruption in neuron function.

50. Explain how **immunodeficiency diseases** are different from **autoimmune diseases**.

Immunodeficiency diseases are those in the response of the immune system is defective or absent, such as SCIDS or AIDS. Autoimmune diseases are different because they can occur when the immune system is active against particular molecules of the body; a loss of self-tolerance can lead to autoimmune diseases such as rheumatoid arthritis or lupus.

51. Just as our immune system has evolved to thwart pathogens, pathogens have evolved to thwart our immune system. Describe the following pathogen strategies.

- **antigenic variation**: One mechanism for escaping the body’s defenses is for a pathogen to alter how it appears to the immune system. Such changes in epitope expression, which are called antigenic variation, are regular events for some viruses and parasites.

- **latency**: After infecting a host, some viruses enter a largely inactive state called latency. Because such dormant viruses cease making most viral proteins and typically produce no free virus particles, they do not trigger an adaptive immune response. Latency typically persists until conditions arise that are favorable for viral transmission, or unfavorable for host survival.

- **attack on the immune system: HIV**: The human immunodeficiency virus (HIV), the pathogen that causes AIDS, both escapes and attacks the adaptive immune response. Once introduced into the body, HIV infects helper T cells with high efficiency. To infect these cells, the virus binds specifically to the CD4. In the cell, the HIV RNA genome is reverse-transcribed, and the product DNA is integrated into the host cell’s genome.
52. Explain how the high mutation rate in surface antigen genes in HIV has hampered development of a vaccine for AIDS. (You might take note that HIV—human immunodeficiency virus—is the virus that causes the disease AIDS—acquired immunodeficiency syndrome. These acronyms are often used incorrectly.)

HIV persists because of antigenic variation. The virus mutates at a very high rate during replication. Altered proteins on the surface of some mutated viruses reduce interaction with antibodies and cytotoxic T cells. Such viruses survive, proliferate, and mutate further. The virus thus evolves within the body.

Test Your Understanding Answers

Now you should be ready to test your knowledge. Place your answers here:

1. b  2. c  3. c  4. d  5. b  6. b  7. c  8. See page A-41 (Appendix) for the answer