1 **Innate Immunity: Nonspecific Defenses of the Host**

2

3 **Big Picture: Immunity**

4 **Big Picture: Immunity**

5 **Big Picture: Immunity**

- White blood cell (WBC) counts measure leukocytes in the blood
- High WBC counts may indicate bacterial infections, autoimmune diseases, or side effects of medications
- Low WBC counts may indicate viral infections, pneumonia, autoimmune diseases, or cancers

6 **Big Picture: Immunity**

7 **The Concept of Immunity**

Learning Objectives

16-1 Differentiate innate and adaptive immunity.

16-2 Define *Toll-like receptors*.

8 **The Concept of Immunity**

- Immunity: ability to ward off disease
- Susceptibility: lack of resistance to a disease
- Innate immunity: defenses against any pathogen; rapid, present at birth
- Adaptive immunity: immunity or resistance to a specific pathogen; slower to respond, has memory component

9 **The Concept of Immunity**

- Toll-like receptors (TLRs) on host cells attach to pathogen-associated molecular patterns (PAMPs)
- TLRs bound to PAMPs induce the release of cytokines from the host cell that regulate the intensity and duration of immune responses
-

10 **Host Defenses: The Big Picture**

11

Check Your Understanding

✓ Which defense system, innate or adaptive immunity, prevents entry of microbes into the body?
16-1

✓ What relationship do TLRs have to pathogen-associated molecular patterns?
16-2

12 **First Line of Defense: Skin and Mucous Membranes**

Learning Objectives

16-3 Describe the role of the skin and mucous membranes in innate immunity.

16-4 Differentiate physical from chemical factors, and list five examples of each.
16-5 Describe the role of normal microbiota in innate immunity.

13 **Physical Factors**

- Skin
  - Dermis: inner portion made of connective tissue
  - Epidermis: outer portion made of tightly packed epithelial cells containing keratin, a protective protein
- Shedding and dryness of skin inhibits microbial growth

14 **Figure 16.1 A section through human skin.**

15 **Physical Factors**

- Mucous membranes
  - Epithelial layer that lines the gastrointestinal, respiratory, and genitourinary tracts
  - Mucus: viscous glycoproteins that trap microbes and prevent tracts from drying out
  - Lacrimal apparatus: drains tears; washes eye

16

17 **Physical Factors**

- Ciliary escalator transports microbes trapped in mucus away from the lungs
- Earwax prevents microbes from entering the ear
- Urine cleans the urethra via flow
- Vaginal secretions move microorganisms out of the vaginal tract
- Peristalsis, defecation, vomiting, diarrhea

18

19 **Chemical Factors**

- Sebum forms a protective film and lowers the pH (3–5) of skin
- Lysozyme in perspiration, tears, saliva, and urine destroys bacterial cell walls
- Low pH (1.2–3.0) of gastric juice destroys most bacteria and toxins
- Low pH (3–5) of vaginal secretions inhibit microbes

20 **Normal Microbiota and Innate Immunity**

- Normal microbiota compete with pathogens via microbial antagonism
  - Produce substances harmful to pathogens
  - Alter conditions that affect pathogen survival
- Commensalism: one organism benefits while the other (host) is unharmed
- Probiotics: live microbial cultures administered to exert a beneficial effect

21

Check Your Understanding

✓ Identify one physical factor and one chemical factor that prevent microbes from entering the body through skin and mucous membranes.
16-3

✓ Identify one physical factor and one chemical factor that prevent microbes from entering or

colonizing the body through the eyes, digestive tract, and respiratory tract.
16-4

✓ Distinguish microbial antagonism from commensalism.
16-5

22 **Second Line of Defense**

Learning Objectives

16-6 Classify leukocytes, and describe the roles of granulocytes and monocytes.

16-7 Describe the eight different types of WBCs, and name a function for each type.

16-8 Differentiate the lymphatic and blood circulatory systems.

23 **Formed Elements in Blood**

- Cells and cell fragments suspended in plasma
  - Erythrocytes (red blood cells)
  - Leukocytes (white blood cells)
  - Platelets
- Created in red bone marrow stem cells via hematopoiesis

24

25 **Formed Elements in Blood**

- Granulocytes are leukocytes with granules in their cytoplasm that are visible with a light microscope
  - Neutrophils: phagocytic; work in early stages of infection
  - Basophils: release histamine; work in allergic responses
  - Eosinophils: phagocytic; toxic against parasites and helminths

26

27 **Formed Elements in Blood**

- Agranulocytes are leukocytes with granules in their cytoplasm that are not visible with a light microscope
  - Monocytes: mature into macrophages in tissues where they are phagocytic
  - Dendritic cells: found in the skin, mucous membranes, and thymus; phagocytic
  - Lymphocytes: T cells, B cells, and NK cells; play a role in adaptive immunity

28

29 **The Lymphatic System**

Learning Objective

16-8 Differentiate the lymphatic and blood circulatory systems.

30 **The Lymphatic System**

- Lymph, lymphatic vessels, lymphoid tissue, and red bone marrow
- Contains lymphocytes and phagocytic cells
- Lymph carries microbes to lymph nodes where lymphocytes and macrophages destroy the pathogen

31

32

33 **Host Defenses: Overview**

34

Check Your Understanding

✓ Compare the structures and functions of monocytes and neutrophils.
16-6

✓ Define *differential white blood cell count.*
16-7

✓ What is the function of lymph nodes?
16-8

•

35 **Phagocytes**

Learning Objectives

16-9 Define *phagocyte* and *phagocytosis.*

16-10 Describe the process of phagocytosis, and include the stages of adherence and ingestion.

16-11 Identify six mechanisms of avoiding destruction by phagocytosis.

36 **Phagocytes**

- *Phago:* from the Greek, meaning eat
- *Cyte:* from the Greek, meaning cell
- Fixed macrophages are residents in tissues and organs
- Free (wandering) macrophages roam tissues and gather at sites of infection

37

38 **The Mechanism of Phagocytosis**

- Chemotaxis
  - Chemical signals attract phagocytes to microorganisms
- Adherence
  - Attachment of a phagocyte to the surface of the microorganism
- Ingestion
  - Opsonization: microorganism is coated with serum proteins, making ingestion easier
- Digestion
  - Microorganism is digested inside a phagolysosome

39

40 **Phagocytosis: Overview**

41 **Phagocytosis: Mechanism**

42 **Microbial Evasion of Phagocytosis**

43 **Virulence Factors: Hiding from Host Defenses**

44 **Virulence Factors: Inactivating Host Defenses**

45 **Phagocytosis: Microbes That Evade It**

46

Check Your Understanding

- ✓ What do fixed and wandering macrophages do? 16-9
- ✓ What is the role of TLRs in phagocytosis? 16-10
- ✓ How does each of these bacteria avoid destruction by phagocytes? *Streptococcus pneumoniae, Staphylococcus aureus, Listeria monocytogenes, Mycobacterium tuberculosis, Rickettsia* 16-11

47 **Inflammation**

Learning Objectives

16-12 List the stages of inflammation.

16-13 Describe the roles of vasodilation, kinins, prostaglandins, and leukotrienes in inflammation.

16-14 Describe phagocyte migration.

48 **Inflammation**

- Four signs and symptoms: redness, swelling (edema), pain, heat
- Destroys injurious agent or limits its effects on the body
- Repairs and replaces tissue damaged by the injurious agent

49 **Inflammation**

- Inflammation activates acute-phase proteins by the liver that cause vasodilation and increased permeability of blood vessels
  - Histamine
  - Kinins
  - Prostaglandins
  - Leukotrienes
  - Cytokines

50

51 **Inflammation: Overview**

52 **Inflammation: Steps**

53 **Phagocyte Migration and Phagocytosis**

- Margination is the sticking of phagocytes to blood vessels in response to cytokines at the site of inflammation
- Phagocytes squeeze between endothelial cells of blood vessels via diapedesis

54

55 **Tissue Repair**

- Cannot be completed until all harmful substances are removed or neutralized
- Stroma is the supporting connective tissue that is repaired
- Parenchyma is the functioning part of the tissue that is repaired

56

57

Check Your Understanding

✓ What purposes does inflammation serve?
16-12

✓ What causes the redness, swelling, and pain associated with inflammation?
16-13

✓ What is margination?
16-14

58 **Fever**

Learning Objective

16-15 Describe the cause and effects of fever.

59 **Fever**

- Abnormally high body temperature
- Hypothalamus is normally set at 37°C
- Cytokines cause the hypothalamus to release prostaglandins that reset the hypothalamus to a higher temperature
- Body constricts the blood vessels, and shivering occurs (which raises temperature)
- As body temperature falls (crisis), vasodilation and sweating occurs

60

Check Your Understanding

✓ Why does a chill indicate that a fever is about to occur?
16-15

61 **Antimicrobial Substances**

Learning Objectives

16-16 List the major components of the complement system.
16-17 Describe three pathways of activating complement.
16-18 Describe three consequences of complement activation.

62 **Antimicrobial Substances**

Learning Objectives

16-19 Define *interferons*.
16-20 Compare and contrast the actions of IFN-α and IFN-β with IFN-γ.
16-21 Describe the role of iron-binding proteins in innate immunity.
16-22 Describe the role of antimicrobial peptides in innate immunity.

63 **The Complement System**

- Serum proteins produced by the liver that assist the immune system in destroying microbes
  - Act in a cascade in a process called complement activation
- Proteins are designated with uppercase C and numbered in order of discovery
  - Activated fragments are indicated with lowercase *a* and *b*

64 **Complement: Overview**

65 **Complement: Activation**

66 **The Classical Pathway**

- Antibodies bind to antigens, activating C1
- C1 splits and activates C2 and C4
- C2a and C4b combine and activate C3
  - C3a functions in inflammation
  - C3b functions in cytolysis and opsonization

67

68 **The Alternative Pathway**

- C3 present in the blood combines with factors B, D, and P on microbe surface
- C3 splits into C3a and C3b, functioning the same as in the classical pathway
-

69

70 **The Lectin Pathway**

- Macrophages ingest pathogens, releasing cytokines that stimulate lectin production in the liver
- Mannose-binding lectin (MBL) binds to mannose, activating C2 and C4
- C2a and C4b activate C3, which functions the same as in the classical and alternative pathways

71

72 **Outcomes of Complement Activation**

- Cytolysis
  - Activated complement proteins create a membrane attack complex (MAC)
- Opsonization
  - Promotes attachment of a phagocyte to a microbe
- Inflammation
  - Activated complement proteins bind to mast cells, releasing histamine

73

74

75

76 **Complement: Results**

77 **Outcomes of Complement Activation**

- Regulation of complement
  - Regulatory proteins readily break down complement proteins, minimizing host cell destruction
- Complement and disease
  - Lack of complement proteins causes susceptibility to infections
- Evading the complement system
  - Capsules prevent complement activation
-

78

Check Your Understanding

✓ What is complement?
16-16

✓ List the steps of complement activation via the classical, alternative, and lectin pathways.
16-17

✓ Summarize outcomes of complement activation.
16-18

79 **Interferons**

- Cytokines produced by cells; have antiviral activity
- IFN-α and IFN-β: produced by cells in response to viral infections; cause neighboring cells to produce antiviral proteins (AVPs) that inhibit viral replication
- IFN-γ: causes neutrophils and macrophages to kill bacteria

80

81 **Iron-Binding Proteins**

- Transferrin: found in blood and tissue fluids
- Lactoferrin: found in milk, saliva, and mucus
- Ferritin: found in the liver, spleen, and red bone marrow
- Hemoglobin: located in red blood cells
- Bacteria produce siderophores to compete with iron-binding proteins

82 **Antimicrobial Peptides**

- Short peptides produced in response to protein and sugar molecules on microbes
  - Inhibit cell wall synthesis
  - Form pores in the plasma membrane
- Broad spectrum of activity

83

Check Your Understanding

✓ What is interferon?
16-19

✓ Why do IFN-α and IFN-β share the same receptor on target cells, yet IFN-γ has a different receptor?

16-20

✓ What is the role of siderophores in infection?
16-21

✓ Why are scientists interested in AMPs?
16-22