Innate Host Defenses

Page 1: Introduction
- Surface barriers (the skin, mucous membranes, and their secretions) are the first line of defense to keep invaders out.
- Innate internal defenses (the cells and extracellular fluid chemicals) are the second line of defense. They respond to pathogens as soon as they are encountered.
- When infection does occur, innate and adaptive defense mechanisms cooperate to clear pathogens from the body.

Page 2: Goals
- To describe the physical and chemical surface barriers to infection.
- To describe the cells, antimicrobial proteins, and processes that form the innate internal defenses.
- To understand the purpose, sequence of events, and cardinal signs of inflammation.
- To recognize that innate defense mechanisms may be insufficient to prevent or clear infections.
- To learn that innate and adaptive defenses interact in many ways and that innate defenses often trigger and define the nature of adaptive defense responses.

Page 3: Surface Barriers: Introduction
- Physical barriers, such as intact skin and mucous membranes, prevent most pathogens from gaining access to body tissues.

Page 4: Surface Barriers: Skin
- Keratin provides toughness.
- Intercellular junctions help keep the skin impermeable.
- Acid and enzymatic secretions keep pathogens from growing on the surface.

Page 5: Surface Barriers: Mucous Membranes
- Acid, lysozyme, and digestive enzymes block pathogen entry.
- Thick mucus traps pathogens.
- Mucus is moved out of the respiratory tract by cilia.

Page 6: Five Lines of Innate Internal Defense
- Innate internal defenses are fast acting, are nonspecific, and provide crude protection against a wide variety of pathogens.
- The five lines of innate internal defense are phagocytes, NK cells, antimicrobial proteins, inflammation, and fever.
- The innate internal defenses can influence the nature of the adaptive defenses that are subsequently mobilized.

Page 7: Phagocytes: Neutrophils Versus Macrophages
- Neutrophils and macrophages are the two types of professional phagocytes that ingest and dispose of particulate matter such as pathogens and cellular debris.
- Neutrophils are the first cells to leave the blood and enter tissue at sites of infection or trauma.
- Neutrophils have limited phagocytic capacity.
- Monocytes differentiate into macrophages, which can be free or fixed.
- Macrophages have a vast phagocytic capacity.
- Both neutrophils and macrophages can use enzymes and highly reactive chemicals to kill pathogens, either internally or externally.

**Page 8: Phagocytes: Recognizing the Enemy**
- Phagocytes recognize invaders using receptors such as Toll-like receptors (TLRs) and the mannose receptor.
- Binding of these receptors enhances phagocytosis and also causes secretion of chemicals that initiate adaptive immune responses.

**Page 9: Phagocytes: Killing Mechanisms**
- Phagocytes engulf pathogens.
- Acidification of phagosomes inhibits pathogens.
- Enzymes in the phagocyte produce reactive oxygen intermediates in a respiratory burst.
- Fusion of lysosomes with phagosomes exposes pathogens to hydrolytic enzymes, defensins, and more reactive oxygen intermediates.

**Page 10: Phagocytes: Evasion Tactics of Pathogens**
- Some bacteria have evolved capsules to avoid phagocytosis. The immune system counters this tactic using opsonins.
- Other pathogens avoid digestion in phagosomes and can live and reproduce there. The immune system counters this tactic using T cells to activate macrophages and amplify their killing ability.

**Page 11: NK Cells: Characteristics**
- NK cells are unusual in that they are lymphocytes, but they are part of innate, not adaptive, defense mechanisms.
- NK cells kill body cells that have been invaded by pathogens or become cancerous.
- NK cells are larger than B and T cells and have granular cytoplasm.
- NK cells lack the antigen receptors expressed by the more abundant B and T cells.

**Page 12: NK Cells: Identification of Target Cells**
- NK cells look for the absence of normally present cell surface markers to identify their targets.

**Page 13: NK Cells: Mechanism of Action**
- NK cells kill by inducing apoptosis, which is cell suicide.
- NK cells are early responders.
- NK cells can be activated by T cells and antibody to become more effective killers.
Page 14: Interferons
- Interferons are cytokines (protein mediators) that interfere with viral replication, modulate inflammation, and activate immune cells.
- Viruses must penetrate the cells of the infected host in order to replicate.
- Alpha and beta interferons are proteins released by virus-infected cells.
- Alpha and beta interferons signal uninfected cells that viruses are present.
- Cells stimulated with alpha or beta interferon make proteins that interfere with viral replication.

Page 15: Complement: Introduction
- The complement system is a series of plasma proteins activated sequentially to provide protection against invaders.
- Activation of the complement system leads to inflammation, enhanced phagocytosis, and direct lysis of some bacteria.

Page 16: Complement: Activation
- Because of its potentially lethal effects, the complement cascade provides multiple opportunities for regulation.
- The complement system can be activated by either the adaptive or innate defense mechanisms.
- Activation of complement can be caused by the presence on cells of chemicals that should not be there or by the absence on cells of chemicals that should be there.
- Antibodies activate the classical pathway, certain polysaccharides activate the lectin pathway, and the absence of inhibitory proteins activates the alternative pathway.

Page 17: Complement: Pathways
- The classical, alternative, and lectin pathways of complement activation converge at C3.
- The splitting of complement components C3 and C5 produces products that promote inflammation (C3a and C5a).
- Another product of complement activation is the formation of a membrane attack complex (MAC).
- The MAC is a hole in the target cell membrane and can result in osmotic lysis of some invading bacteria.

Page 18: Inflammation: Cardinal Signs
- Inflammation can be acute or chronic and is one of the most common reasons healthcare professionals are consulted. Inflammatory conditions are designated by the suffix “itis.”
- The cardinal signs of inflammation are pain, heat, redness, and swelling.

Page 19: Inflammation: Vasodilation and Permeability
- The purpose of inflammation is to prevent the spread of injurious agents, dispose of pathogens and dead cells, and set the stage for repair.
- Chemical mediators of inflammation have two key effects: they cause vasodilation and increased vascular permeability.
- Vasodilation increases blood flow, resulting in redness and heat.
• Increased vascular permeability allows cells and proteins to enter the injured area.

**Page 20: Inflammation: Phagocytes**
• Inflammatory mediators induce the expression of cell adhesion molecules on endothelial cells.
• Neutrophils and monocytes marginate, exit the blood vessel by diapedesis, and follow chemotactic signals to the site of injury.

**Page 21: Inflammation: Plasma Proteins**
• Inflammatory mediators cause vascular leakage, which causes edema.
• Antibodies, clotting factors, and complement leak from the blood into the injured area.
• Complement acts as an opsonin and a chemotaxin.
• Clotting factors help immobilize pathogens.

**Page 22: Inflammation: Inflammatory Mediators**
• Inflammatory mediators include histamine, prostaglandins, kinins, and cytokines.

**Page 23: Fever**
• Pyrogens raise the body’s thermostat.
• Fever makes it more difficult for pathogens to grow, while enhancing the ability of the immune system to kill.

**Page 24: Summary**
• The first line of defense consists of the skin and mucous membranes and their secretions.
• The second line of defense, the innate internal defenses, consists of phagocytes, antimicrobial proteins (complement and interferons), natural killer cells, inflammation, and fever.
• Inflammation is a nonspecific local response to injury that brings leukocytes and plasma proteins to the injured area.
• Innate defense mechanisms may be insufficient to prevent or clear infections.
• Innate and adaptive defenses interact in many ways. Innate defenses often trigger and define the nature of adaptive defense responses.

**Study Questions**

1. (Goal 1, Page 3) Name two physical barriers that prevent most pathogens from gaining access to the body.
2. (Goal 1, Page 4) Explain three skin characteristics responsible for forming a tight barrier.
3. (Goal 1, Page 5) Explain two mucous membranes characteristics that help to block pathogen entry.
4. (Goal 1, Pages 3, 4, and 5) Classify each of the following terms into a physical barrier or a chemical barrier to pathogens.

<table>
<thead>
<tr>
<th>Keratin</th>
<th>Cilia</th>
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<tbody>
<tr>
<td>Mucus</td>
<td>Acid secretions</td>
</tr>
<tr>
<td>Intercellular junctions</td>
<td>Digestive secretions</td>
</tr>
</tbody>
</table>
5. (Goal 2, Page 6) Describe three characteristics of innate internal defenses.

6. (Goal 2, Page 6) Label each line of innate defense depicted in this diagram.

7. (Goal 2, Page 7) How are macrophages and neutrophils similar, and how do they differ?

8. (Goal 2, Page 8) Explain how phagocytes recognize invading pathogens and what happens when they do.

9. (Goal 2, Page 9) List what happens to a pathogen or cellular debris once it has been recognized by a phagocyte.

10. (Goal 2, Page 10) List examples of how microorganisms have evolved to elude detection by phagocytes and how the immune system responds.

11. (Goal 2, Page 11) Describe characteristics of natural killer cells and the role they play in the innate defense response.

12. (Goal 2, Page 12) How do natural killer cells identify their targets?

13. (Goal 2, Page 13) Explain a natural killer cell’s response to an abnormal cell and how it eliminates the target.

14. (Goal 2, Page 14) List three functions of interferons. What type of molecule is an interferon?

15. (Goal 2, Page 14) Why must a virus enter a host cell? What does the infected host cell release in order to interfere with viral replication in uninfected cells?

16. (Goal 2, Page 15) Describe the complement system and list its three functions. What type of molecule is sequentially activated?

17. (Goal 2, Page 16) Name the two ways the complement system can be activated and why the pathway must be tightly regulated.

18. (Goal 2, Page 16) What triggers activation of the classical pathway, the lectin pathway, and the alternate pathway?
19. (Goal 2, Page 17) All three pathways converge at C3. What happens when C3 is split into C3a? What other complement molecule, when split (activated), will cause a similar effect?

20. (Goal 2, Page 17) Complete the following diagram by filling in the five boxes.

21. (Goal 2, Page 17) Define MAC and explain its functions.

22. (Goal 3, Page 18) Define inflammation and list two types. What does the suffix “itis” mean?

23. (Goal 3, Page 18) List the four cardinal signs of inflammation.

24. (Goal 3, Page 19) Explain the function of inflammation.

25. (Goal 3, Pages 19 and 21) Complete the following table by listing what causes each symptom of inflammation.

<table>
<thead>
<tr>
<th>Heat</th>
<th>Redness</th>
<th>Swelling (Edema)</th>
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<tr>
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</tbody>
</table>
26. (Goal 3, Pages 19 and 22) What mediates an inflammatory response?
27. (Goal 3, Pages 19, 20, and 21) Complete the following table by relating what each chemically-mediated event accomplishes.

<table>
<thead>
<tr>
<th>Increased Vascular Permeability</th>
<th>Increased Blood Flow</th>
<th>Inducing Cell Adhesion Molecules</th>
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</thead>
<tbody>
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28. (Goal 3, Page 23) Fever is caused by pyrogens. What do the pyrogens do to the body’s thermostat?
29. (Goal 3, Page 23) Describe two effects fever has on a pathogen and the immune system in general.
30. (Goal 4, Page 24) True or False. The innate defense system may be insufficient to prevent or clear infections.
31. (Goal 5, Page 24) True or False. The innate and adaptive defenses do not interact in any way.

**Summary**

**Fill-in-the-blanks.** Fill in each blank with the correct term.

The first line of defense consists of ________________, ________________, ________________, and their secretions. The second line of defense is ________________ internal defenses. There are five categories involved in innate internal defenses.

1. 
2. 
3. 

7
4.

5. _________________ is a nonspecific local response to injury that brings ___________ and ______________________ to the site of injury.

Innate and adaptive defenses interact in many ways. Innate defenses often ___________ and define the nature of adaptive defense responses.