McCance: Pathophysiology, 6th Edition

Chapter 06: Innate Immunity: Inflammation

Key Points – Print

SUMMARY REVIEW

Human Defense Mechanisms

1. There are two types of human defense: innate resistance or immunity conferred by natural barriers and the inflammatory response, and the adaptive (acquired) immune system.

First Line of Defense: Physical, Mechanical, and Biochemical Barriers

1. Physical and mechanical barriers are the first lines of defense encountered by invading pathogens; these include the skin and mucous membranes.
2. Antibacterial peptides in mucous secretions, perspiration, saliva, tears, and other secretions provide a biochemical barrier against invading pathogens in the extracellular space.
3. Cathelicidins and defensins are two classes of antimicrobial peptides produced by epithelial cells.
4. The normal bacterial flora provide protection by inhibiting colonization by pathogens and by releasing chemicals that prevent infection.

Second Line of Defense: The Inflammatory Response

1. The inflammatory response, our body's second line of defense against invading microorganisms, is nonspecific, rapidly initiated, and has no memory cells.
2. The vascular response in acute inflammation includes vasodilation, increased capillary permeability, and white blood cell adherence to inner vessel walls and their migration through vessel walls.
3. Three plasma protein systems provide a biochemical barrier against invading pathogens in the circulation. These include the complement system, the clotting system, and the kinin system.
4. The plasma protein systems work with each other as well as with antimicrobial peptides and the cellular component of the innate immune system to prevent microbial infection.
5. The complement proteins can be activated in three pathways: the classical pathway, the alternative pathway, and the lectin pathway.
6. Activation of the complement pathways results in opsonization, activation of anaphylatoxins, cell lysis, and leukocyte chemotaxis.
7. The clotting (coagulation) cascade prevents spread of microorganisms, contains microorganisms and foreign bodies at site of greatest inflammatory cell activity, and provides a framework for repair and healing.

8. The kinin system proteins promote vasodilation and increased capillary permeability and induce pain.
9. Plasmin and Hageman factor (factor XII) interact to activate the clotting cascade, the complement system, and the kinin proteins.
10. The plasma proteins are finely regulated to prevent injury to host tissue and to guarantee activation when needed. Some of the inhibitors in the plasma protein systems include carboxypeptidase, histaminases, kinases, and C1 esterase inhibitor.
11. Many different types of cells are involved in the inflammatory process including mast cells, neutrophils, monocytes/macrophages, eosinophils, NK cells, platelets, and nonleukocytic cells.
12. The cells of the innate immune system secrete many biochemical mediators that are responsible for the vascular changes associated with inflammation and for modulating the localization and activities of other inflammatory cells. The mediators include histamine, chemotactic factors, leukotrienes, prostaglandins, and platelet-activating factor.
13. The inflammatory response is initiated upon tissue injury or when PAMPs are recognized by PRRs on cells of the innate immune system.
14. The PRRs include TLRs, complement, scavenger, glycan, and mannose receptors.
15. TLRs recognize PAMPs, complement receptors recognize complement fragments, and scavenger receptors promote phagocytosis.
16. Most cells are central cells of inflammation and release histamine chemotactic factors, cytokines, leukotrienes, prostaglandins, growth factors, and other mediators.
17. H1 histamine receptors promote inflammation, and H2 histamine receptors inhibit the inflammatory response.
18. Phagocytosis is the destruction of microorganisms and cellular debris.
19. The stages of phagocytosis include recognition and adherence, engulfment, lysosomal fusion, and destruction.
20. Phagocytic killing can be oxygen-dependent with the production of reactive oxygen intermediates or oxygen-independent with lysosomal enzymes.
21. Neutrophils are the predominant phagocyte of early inflammation. They are attracted to the inflammatory site by chemotactic factors.
22. Monocytes and macrophages arrive at the inflammatory site later than neutrophils and remain longer to clean up debris and promote wound healing.
23. Eosinophils help control mast cell vascular mediators and defend against parasite infection.
24. Basophils are granulocytes that are very similar to mast cells.
25. NK cells recognize and eliminate viruses, cancer cells, and other abnormal cells.
26. Platelets interact with the coagulation cascade to stop bleeding and release a number of mediators that promote and control inflammation.
27. Cytokines are soluble factors that regulate the inflammatory response and include interleukins, interferons, and tumor necrosis factor.

28. ILs are biochemical messengers primarily produced by macrophages and lymphocytes and significantly help regulate the inflammatory response.
29. INFs provide protection from viral infection in uninfected cells.
30. Tumor necrosis factor is primarily produced by macrophages and promotes inflammation with both local and systemic effects.
31. Chemokines are synthesized by a number of different cells and induce leukocytes chemotaxis, and are classified as either CC or CXC, depending on their amino acid arrangement. CC chemokines affect monocytes, lymphocytes, and eosinophils. CXC chemokines generally affect neutrophils.

Local Manifestations of Inflammation

1. Local manifestations of inflammation are the result of the vascular changes associated with the inflammatory process, including vasodilation and increased capillary permeability. The symptoms include redness, heat, swelling, and pain.
2. The functions of the vascular changes are to dilute toxins, carry plasma proteins and leukocytes to the injury site, and carry bacterial toxins and debris away from the site.

Systemic Manifestations of Acute Inflammation

1. The three primary systemic effects of inflammation are fever, leukocytosis, and increase in levels of circulating plasma proteins.
2. Acute phase reactants are proteins produced by the liver during acute inflammation and include fibrinogen, C-reactive protein, haptoglobin, amyloid A, α_1-antitrypsin, and ceruloplasmin.

Chronic Inflammation

1. Chronic inflammation can be a continuation of acute inflammation that lasts 2 weeks or longer. It also can occur as a distinct process without much preceding acute inflammation.
2. Chronic inflammation is characterized by a dense infiltration of lymphocytes and macrophages. The body may wall off and isolate the infection to protect against tissue damage by formation of a granuloma.

Resolution and Repair

1. Resolution (regeneration) is the return of tissue to nearly normal structure and function. Repair is healing by scar tissue formation.
2. Inflammatory lesions proceed to resolution, meaning that original tissue structure and function have been restored if little tissue has been lost or injured tissue is capable of regeneration. This is called *healing by primary intention.*

3. Inflammatory lesions that involve extensive damage or tissues incapable of regeneration heal by the process of repair that results in the formation of a scar. This is called *healing by secondary intention.*
4. Resolution and repair occur in two separate phases: the *reconstructive phase,* in which the wound begins to heal, and the *maturation phase,* in which the healed wound is remodeled.
6. Dysfunctional wound healing can occur as a result of abnormalities in either the inflammatory response or in the reconstructive phase of resolution and repair.

Pediatrics and Mechanisms of Self-Defense

1. Neonates commonly have transiently depressed inflammatory function.
2. Infants often have deficiencies in complement and in a number of collectins, making them more susceptible to bacterial infection.

Aging and Mechanisms of Self-Defense

1. Older adults are at risk for impaired wound healing, often because of underlying illnesses.
2. Diminished immune function may interfere with an older adult's natural ability to ward off infection.