Damjanov: Pathology for the Health Professions, 5th Edition

Chapter 02: Inflammation

Answer Key for End of Chapter Review Questions

1. Explain why inflammation cannot occur in an ameba or in a dead body.
Inflammation represents the coordinated response of many cell types in a multicellular organism, including nerves, capillary endothelial cells, and blood cells. It is a vital reaction occurring in living organisms. It cannot occur in single cells or in dead (necrotic) tissue.

2. Does inflammation have beneficial or noxious effects on the human body?
Inflammation has a protective and healing role, helping to remove pathogens and repair injured tissue. However, it may occasionally overshoot its mark or become uncontrollable. Harmful effects of inflammation include severe fever and massive bleeding.

3. What are the cardinal signs of inflammation?
The four cardinal signs of acute inflammation recognized since ancient Roman time are calor (heat), rubor (redness), tumor (swelling), and dolor (pain).

4. Explain the sequence of events that leads to active hyperemia in inflamed tissues.
Changes in blood flow represent the body's first response to injury. Injury stimulates nerves to signal smooth muscle cells to contract, causing immediate vasoconstriction. This is followed within seconds by vasodilatation (relaxation of precapillary sphincters), allowing blood to rush into the capillaries. This process of increased blood flow is termed active hyperemia. It is responsible for the redness and warmth (calor) that is observed at the sites of acute inflammation.

5. What happens to the leukocytes inside the blood vessels in inflamed tissue?
During acute inflammation, white blood cells (polymorphonuclear leukocytes) move to the periphery of the bloodstream (marginate) and attach to activated endothelial cells (pavement). This process of cell-cell adhesion facilitates the movement of leukocytes out of the blood and into the sites of tissue injury.

6. Why does the permeability of blood vessels increase during acute inflammation?
Increased permeability of blood vessels delivers fluids, nutrients, and blood cells to sites of tissue injury. The extravascular edema fluid that accumulates serves to protect the site from further trauma and washes antigenic debris (if present) from the site of injury to regional lymph nodes for immunologic stimulation. Increased vascular permeability is mediated primarily by vasoactive chemicals that (1) increase intracapillary hydrostatic pressure and (2) cause retraction of adjacent endothelial cells forming microscopic gaps.

7. Describe the consequences of activation of Hageman factor in acute inflammation.
Hageman factor (clotting factor XII) is a blood protein that becomes activated at the sites of tissue injury. Hageman factor stimulates increased vascular permeability (bradykinin formation), clotting (fibrin deposition), and thrombolysis (plasmin formation).

8. Why are some complement fragments called opsonins, anaphylatoxins, or chemotactic factors?
The complement system of flood proteins is an important source of vasoactive mediators. Complement fragments formed during inflammation serve many functions, including (1) opsonization (coating bacteria to improve recognition by phagocytes), (2) anaphylaxis (direct stimulation of mast cells to release histamine), and (3) chemotaxis (directed cell mobility).

9. How is membrane attack complex (MAC) formed, and how does it damage red blood cells?
The MAC is the end product of the complement cascade. The MAC assembles within the lipid bilayer of a target cell, creating a cytotoxic pore. In patients with autoimmune hemolytic anemia, antibody binding to the RBC surface stimulates the assembly of the MAC, which causes rapid hemolysis.

10. Explain the formation of leukotrienes and prostaglandins in acute inflammation.
Leukotrienes and prostaglandins are small molecular weight mediators of inflammation that are synthesized de novo in activated leukocytes. They are derived by enzymatic modification of arachidonic acid, which is liberated from plasma membrane phospholipids by phospholipases. Leukotrienes are synthesized via the lipoxygenase pathway, whereas prostaglandins are synthesized via the cyclooxygenase pathway. Aspirin is a potent anti-inflammatory agent because it blocks the cyclooxygenase pathway of prostaglandin biosynthesis.

11. How does a transudate differ from an exudate?
Transudates and exudates are examples of extravascular edema fluid. A transudate is a clear sterile filtrate of the blood, whereas an exudate is rich in proteins and lipids. Exudates often contain acute inflammatory cells.

12. How do polymorphonuclear neutrophils emigrate from blood vessels toward bacteria in the tissue?
Polymorphonuclear leukocytes (also referred to as segmented neutrophils) emigrate through the walls of blood vessels (postcapillary venules) at sites of tissue injury through an active process that includes (1) endothelial cell adhesion (margination), (2) insertion of pseudopods between the tight junctions of endothelial cells, (3) passage through the capillary basement membrane, and finally (4) ameboid movement toward bacteria (chemotaxis).

13. What are the most important chemotactic substances, and how do they promote inflammation?
The most important neutrophil chemotactic factors are (1) bacterial products (e.g., formylated amino acids and lipopolysaccharides); (2) complement fragments (C5, C6, and C7); and (3) cytokines, polypeptide signaling molecules released by natural killer cells, and tissue macrophages (e.g., gamma interferon and tumor necrosis factor-alpha).

14. How do polymorphonuclear neutrophils engulf and kill bacteria?

Polymorphonuclear neutrophils engulf and digest bacteria through several steps. First, the phagocyte attaches to opsonins on the bacterial cell surface. Invagination of the phagocyte cell membrane draws the bacterium into a phagocytic vacuole. Oxygen radicals generated through an oxygen burst kill the bacterium, and lysosome digestive enzymes finish the demolition processes within the heterophagosome.

15. What is pus, and how is it formed?
Pus represents the accumulation of a leukocyte-rich exudate, lytic enzymes released from dying leukocytes, and necrotic tissue debris. Inflammation dominated by pus formation is called purulent or suppurative.

16. Why are polymorphonuclear neutrophils best suited to combat acute bacterial infection?
Polymorphonuclear leukocytes are best suited to combat acute bacterial infections because they are highly mobile cells, armed with preformed stores of hydrolytic enzymes, and able to generate toxic oxygen radicals. In addition, they are capable to ingesting bacteria and secrete long-range mediators of inflammation such as interleukin-1 (IL-1), the endogenous pyrogen.

17. How do eosinophils differ from polymorphonuclear neutrophils?
Eosinophils account for 2% of circulating white cells, whereas polymorphonuclear neutrophils (PMNs) account for 60% to 70% of circulating white cells. During acute inflammation, eosinophils appear 2 to 3 days after PMNs and live longer. In contrast to PMNs, eosinophils have a single nucleus. They are prominent in allergic and parasitic infections.

18. Which inflammatory reactions are mediated by eosinophils and basophils?
Eosinophils and basophils are both prominent in allergic and infections. Basophils are the precursors of tissue mast cells.

19. What are the main functions of macrophages?
Macrophages are tissue histiocytes derived from blood monocytes. They appear at the site of inflammation 3 to 4 days after the onset of infection or tissue injury. The principal functions of macrophages are bacterial engulfment and killing and the secretion of numerous cytokines, which help regulate inflammation and acquired immunity.

20. How do platelets differ from other white blood cells?
Unlike other white blood cells, platelets are non-nucleated fragments of cytoplasm derived from megakaryocytes in the bone marrow. Their cytoplasm contains vacuoles rich in histamine, polypeptide growth factors, and coagulation proteins. Platelets release the contents of these granules upon contact with extracellular matrix, activated endothelial cells, or thrombin. This process is termed *degranulation.*

21. Compare acute with chronic inflammation.

Acute inflammation lasts from hours to days. It is characterized pathologically by the intravascular stimulation of platelets and the accumulation of polymorphonuclear neutrophils. Chronic inflammation may represent the extension of acute inflammation or the persistence of the causative agent. It is characterized pathologically by the accumulation of macrophages and lymphocytes. Chronic inflammation is the first response to viral infections and some foreign substances (e.g., silica dust particles).

22. Compare cellular inflammatory response to a typical viral infection with that occurring in bacterial infection.
Viral infections activate macrophages and lymphocytes (chronic inflammatory cells), whereas bacterial infections strongly activate polymorphonuclear neutrophils (acute inflammatory cells).

23. What are the main causes of inflammation?
The main causes of inflammation are (1) infections (e.g., bacterial, viral, and fungal), (2) chemicals (exogenous or endogenous), and (3) physical agents or effects (e.g., heat, radiation, and trauma).

24. Give an example of both a localized and a systemic inflammation.
A boil or furuncle is an example of localized inflammation. Systemic inflammation is common in immunologically mediated diseases such as systemic lupus erythematosus. Sepsis, characterized by the spread of bacteria through the blood, is also a systemic inflammatory disorder.

25. Give an example of a serous inflammation and describe the pathologic findings.
Serous inflammation is characterized by the exudation of a clear fluid. In pneumonia, it can be observed as a proteinaceous (pink) material within the alveolar spaces with few inflammatory cells. Skin vesicles caused by herpesvirus are another example of a serous inflammation.

26. Give an example of fibrinous inflammation and describe the pathologic findings.
Fibrous inflammation is characterized by an exudate rich in fibrin (the end product of the coagulation cascade). Fibrinous inflammation is seen in many bacterial infections, such as strep throat and bacterial pericarditis.

27. Give an example of a purulent inflammation and describe the pathologic findings.
Purulent inflammation is characterized by pus-forming bacteria (most commonly staphylococcus or streptococcus), which elicit a strong neutrophilic response. Pus is a thick yellow fluid composed of dying PMNs and necrotic debris.

28. Give clinical examples of an abscess, sinus, fistula, and emphysema.
Brain abscess is a clinical example of a localized purulent inflammation. The central portion of this brain abscess is liquid pus. A sinus represents a cavity (usually a previous abscess) that drains through a tract to the surface of the body. A fistula is a similar channel formed between two preexisting cavities or hollow organs (e.g., between two adjacent loops of intestine). Emphysema reflects accumulation of pus within a preformed cavity (e.g., spread of a bacterial pneumonia to the plural cavity).

29. What is the difference between an ulcerative and pseudomembranous inflammation?

Ulcerative inflammation represents the loss of an epithelial lining. Pseudomembranous inflammation represents ulceration combined with a fibrinopurulent exudate. *Clostridium difficile* causes pseudomembranous colitis.

30. Describe tissue changes in chronic inflammation, such as pelvic inflammatory disease.
Chronic infections are characterized by exudates rich in lymphocytes, macrophages, and plasma cells. Loss of parenchymal cells is associated with proliferation of fibroblasts and formation of collagen-rich scar tissue. For example, fallopian tubes affected by chronic pelvic inflammatory disease (PID) are twisted and obliterated. PID is the most common cause of infertility in women.

31. Describe possible chemical symptoms of chronic inflammation involving the lungs, heart, and pancreas.
Clinical symptoms of chronic inflammation are organ specific and may include dyspnea (e.g., chronic lung disease), congestive heart failure (e.g., constrictive pericarditis), and indigestion (e.g., pancreatitis).

32. What are the main features of a granulomatous inflammation?
Granulomatous inflammation is commonly caused by antigens that persist at the site of inflammation or by antigens the specifically provoke a cell-mediated hypersensitivity reaction. Granulomatous reactions are mediated by macrophages and T lymphocytes. They destroy tissue and tend to persist for a long time.

33. Compare caseating and noncaseating granulomas with gumma.
The granulomas of tuberculosis are associated with central caseous necrosis, whereas the immunologically mediated granulomas of sarcoidosis are not associated with caseation. The granuloma typical of syphilis (called a gumma) shows central coagulative necrosis, surrounded by a rim of epithelioid giant cells, lymphocytes, and plasma cells.

34. Correlate the typical clinical features of acute appendicitis with the pathologic changes found at surgery.
Clinical features of acute appendix include regional pain, fever, and leukocytosis (elevated white cell count). The pathologic basis of these systemic manifestations is seen at surgery. The affected appendix is painful, swollen, red, and warm. Fever is mediated by the release of pyrogens, and leukocytosis reflects the rapid release of leukocytes from the bone marrow.

35. What are endogenous pyrogens, and how do they act on the hypothalamus?
Endogenous pyrogens, primarily interleukin-1 (IL-1) and tumor necrosis factor (TNF), act on thermoregulatory centers in the brain to raise body temperature. They act by stimulation the synthesis of prostaglandins, which act as short-range chemokines in the brain.

36. Explain the differences between continuously dividing, quiescent, and nondividing cells and give examples of each.
Continuously dividing cells (stem cells) undergo mitosis throughout the entire life span. Quiescent mitotic cells, such as parenchymal cells of the liver or kidney, divide only if necessary to regenerate lost tissue. Nondividing postmitotic cells, such as neurons or cardiac myocytes, do not have the capacity for further mitosis.

37. Which cells participate in wound healing?
Wound healing is mediated by a variety of blood-derived and local tissue cells, including leukocytes, macrophages, connective tissue fibroblasts, and epithelial cells. Myofibroblasts help reduce the size of the wound and hold the margins of the wound together. Angioblasts proliferate to sprout new capillaries (angiogenesis). Fibroblasts produce extracellular matrix that "glues" the wound together.

38. What is granulation tissue, and how does it evolve during wound healing?
Deep wounds heal by formation of granulation tissue, which is rich in capillaries, angioblasts, fibroblasts, macrophages, and extracellular matrix. In the later stages of healing, granulation tissue becomes less vascularized, with only scattered macrophages. Eventually, collagen-rich scar tissue is remodeled along lines of stress.

39. Compare wound healing by primary and secondary intention.
Wound healing occurs by primary intention when the margins of the wound are closely opposed (e.g., surgical incision). In this case, scarring is minimal. Wound healing occurs by secondary intention if there is a gaping wound that contains foreign materials or bacteria. Under these conditions, wound margins are not opposed and scarring is prominent.

40. Explain why various adverse factors delay wound healing.
Wound healing is delayed by several different local and systemic factors. Local factors that delay wound healing include the size and site of the wound, superimposed infection, and movement. Systemic factors that delay wound healing include hormonal status (hypercortisolism), nutritional and metabolic factors (vitamin C deficiency), circulatory status, and age. Patients with chronic diabetes typically have poor wound healing because of chronic ischemia secondary to small vessel disease.

41. Compare wound dehiscence with keloid formation.
Wound dehiscence refers to the bursting open (separation) of an incompletely healed wound. Keloids represent excessive scar formation caused by the persistence of collagen type III and an inability of fibroblasts to generate sufficient collagen type I. In this way, keloids are similar to immature, hypertrophic scars.