1. An 11-year-old child falls and cuts his hand. The wound becomes infected. Bacteria extend into the extracellular matrix around capillaries. In the inflammatory response to this infection, which of the following cells removes the bacteria?

- A B lymphocyte
- B Fibroblast
- C Macrophage
- D Mast cell
- E T lymphocyte

2. A 53-year-old woman has had a high fever and cough productive of yellowish sputum for the past 2 days. Her vital signs include temperature of 37.8°C, pulse 103/min, respirations 25/min, and blood pressure 100/60 mm Hg. On auscultation of the chest, crackles are audible in both lung bases. A chest radiograph shows bilateral patchy pulmonary infiltrates. The microscopic appearance of her lung is shown in the figure. Which of the following inflammatory cell types is most likely to be seen in greatly increased numbers in her sputum specimen?

- A Langhans giant cells
- B Macrophages
- C Mast cells
- D Neutrophils
- E T lymphocytes

3. A 4-year-old child has had a high-volume diarrhea for the past 2 days. On examination she is dehydrated. A stool sample examined by serologic assay is positive for rotavirus. She is treated with intravenous fluids and recovers. Which of the following components is found on intestinal cells and recognizes double-stranded RNA of this virus to signal transcription factors that upregulate interferon production for viral elimination?

- A Caspase-1
- B Complement receptor
- C Lectin
- D T cell receptor
- E Toll-like receptor
4. A 72-year-old man with severe emphysema has had worsening right ventricular failure for the past 5 years. For the past 4 days, he has had fever and increasing dyspnea. A chest radiograph shows an accumulation of fluid in the pleural spaces. Fluid obtained by thoracentesis has a specific gravity of 1.030 and contains degenerating neutrophils. The most likely cause of this fluid accumulation is due to changes in which of the following?
   A. Colloid osmotic pressure
   B. Leukocytic diapedesis
   C. Lymphatic pressure
   D. Renal sodium retention
   E. Vascular permeability

5. A 35-year-old man has had increasing dyspnea for the past 24 hours. A chest radiograph shows large, bilateral pleural effusions. Thoracentesis yields 500 mL of slightly cloudy yellow fluid from the right pleural cavity. Cytologic examination of the fluid shows many neutrophils, but no lymphocytes or RBCs. Which of the following mechanisms contributes most to the pleural fluid accumulation?
   A. Arteriolar vasoconstriction
   B. Endothelial contraction
   C. Inhibition of platelet adherence
   D. Lymphatic obstruction
   E. Neutrophil release of lysosomes

6. A 6-year-old child has a history of recurrent infections with pyogenic bacteria, including *Staphylococcus aureus* and *Streptococcus pneumoniae*. The infections are accompanied by a neutrophilic leukocytosis. Microscopic examination of a biopsy specimen obtained from an area of soft tissue necrosis shows microbial organisms, but very few neutrophils. An analysis of neutrophil function shows a defect in rolling. This child’s increased susceptibility to infection is most likely caused by a defect involving which of the following molecules?
   A. Complement C3b
   B. Integrins
   C. Leukotriene B4
   D. NADPH oxidase
   E. Selectins

7. In an experiment, bacteria are introduced into a perfused tissue preparation. Leukocytes leave the vasculature and migrate to the site of bacterial inoculation. The movement of these leukocytes is most likely to be mediated by which of the following substances?
   A. Bradykinin
   B. Chemokines
   C. Complement C3a
   D. Histamine
   E. Prostaglandins

8. A 12-month-old boy with a 6-month history of repeated infections has had a fever and cough for the past 3 days. A Gram stain of sputum shows many gram-positive cocci in chains. CBC shows neutrophilia. Laboratory studies show that the patient’s neutrophils phagocytose and kill organisms promptly in the presence of normal human serum, but not in his own serum. The neutrophils migrate normally in a chemotaxis assay. Which of the following is the most likely cause of this boy’s increased susceptibility to infection?
   A. Abnormality of selectin expression
   B. Diminished opsonization
   C. Defective neutrophil generation of hydrogen peroxide
   D. Deficiency of integrins
   E. Phagocytic cell microtubular protein defect

9. A 5-year-old child has a history of recurrent bacterial infections, including pneumonia and otitis media. Analysis of leukocytes collected from the peripheral blood shows a deficiency in myeloperoxidase. A reduction in which of the following processes is the most likely cause of this child’s increased susceptibility to infections?
   A. Hydrogen peroxide (H2O2) elaboration
   B. Hydroxy-halide radical (HOCl–) formation
   C. Failure of migration resulting from complement deficiency
   D. Phagocytic cell oxygen consumption
   E. Prostaglandin production

10. In an experiment, neutrophils collected from peripheral blood are analyzed for a “burst” of oxygen consumption. This respiratory burst is an essential step for which of the following events in an acute inflammatory response?
    A. Attachment to endothelial cells
    B. Generation of microbicidal activity
    C. Increased production in bone marrow
    D. Opsonization of bacteria
    E. Phagocytosis of bacteria

11. A 4-year-old girl has had numerous infections with *Staphylococcus aureus* since infancy. Genetic testing shows a defect leading to a lack of β2 integrin production. Which of the following abnormalities of neutrophil function is most likely responsible for these clinical symptoms?
    A. Decreased generation of hydroxy-halide radicals (HOCl–)
    B. Diminished phagocytosis of bacteria opsonized with IgG
    C. Failure of migration to the site of infection
    D. Inadequate adhesion on cytokine-activated endothelium
    E. Reduced respiratory burst after phagocytosis

12. In an experiment, peripheral blood cells are isolated and placed into a culture medium that preserves their metabolic activity. Interferon-γ is added to this culture, along with viable *Escherichia coli* organisms. Which of the following blood cell types in this medium is the most likely to have bactericidal activity against *E. coli*?
    A. Basophil
    B. B lymphocyte
    C. CD4+ lymphocyte
    D. CD8+ lymphocyte
    E. Monocyte
    F. Natural killer cell
    G. Neutrophil
UNIT I  General Pathology

13 In an experiment, T lymphocytes from peripheral blood are placed in a medium that preserves their function. The lymphocytes are activated by contact with antigen and incubated for 4 hours. The supernatant fluid is collected and is found to contain a substance that is a major stimulator of monocytes and macrophages. Which of the following substances released into this fluid medium is most likely to stimulate macrophages?

A  Histamine  
B  Interferon-γ  
C  Leukotriene B₄  
D  Nitric oxide  
E  Phospholipase C  
F  Tumor necrosis factor (TNF)

14 A woman who is allergic to cats visits a neighbor who has several cats. During the visit, she inhales cat dander, and within minutes, she develops nasal congestion with abundant nasal secretions. Which of the following substances is most likely to produce these findings?

A  Bradykinin  
B  Complement C₅₅a  
C  Histamine  
D  Interleukin-1 (IL-1)  
E  Phospholipase C  
F  Tumor necrosis factor (TNF)

15 In a 6-month randomized trial of a pharmacologic agent, one group of patients receives a cyclooxygenase-2 (COX-2) inhibitor, and a control group does not. Both groups of adult males had mild congestive heart failure and bilateral symmetric arthritis of small joints. Laboratory measurements during the trial show no significant differences between the groups in WBC count, platelet count, hemoglobin, and creatinine. The group receiving the drug reports subjective findings different from those of the control group. Which of the following findings was most likely reported by the group receiving the drug?

A  Increased ankle swelling  
B  Increased susceptibility to bruising  
C  Increased bouts of asthma  
D  Reduced severity of urticaria  
E  Numerous febrile episodes  
F  Reduced arthritis pain

16 A 19-year-old woman develops a sore throat and fever during the past day. Physical examination shows pharyngeal erythema and swelling. Laboratory findings include leukocytosis. She is given naproxen. Which of the following features of the acute inflammatory response is most affected by this drug?

A  Chemotaxis  
B  Emigration  
C  Leukocytosis  
D  Phagocytosis  
E  Vasodilation

17 A 35-year-old woman takes acetylsalicylic acid (aspirin) for arthritis. Although her joint pain is reduced with this therapy, the inflammatory process continues. The aspirin therapy alleviates her pain mainly through reduction in the synthesis of which of the following mediators?

A  Complement C₁q  
B  Histamine  
C  Leukotriene E₄  
D  Nitric oxide  
E  Prostaglandins

18 A 77-year-old woman experiences a sudden loss of consciousness, with loss of movement on the right side of the body. Cerebral angiography shows an occlusion of the left middle cerebral artery. Elaboration of which of the following mediators will be most beneficial in preventing further ischemic injury to her cerebral cortex?

A  Bradykinin  
B  Leukotriene E₄  
C  Nitric oxide  
D  Platelet-activating factor  
E  Thromboxane A₂

19 In an experiment, bacteria are inoculated into aliquots of normal human blood that have been treated with an anticoagulant. It is observed that the bacteria are either phagocytized by neutrophils or undergo lysis. Which of the following blood plasma components is most likely to facilitate these effects?

A  Complement  
B  Fibrin  
C  Kallikrein  
D  Plasmin  
E  Thrombin

20 Patients with extensive endothelial injury from Escherichia coli sepsis have consumption of coagulation factors as well as an extensive inflammatory response. Administration of activated protein C is most likely to decrease this inflammatory response by reducing the amount of which of the following substances?

A  Complement  
B  Fibrin  
C  Kallikrein  
D  Plasmin  
E  Thrombin

21 A 95-year-old woman touches a pot of boiling water. Within 2 hours, she has marked erythema of the skin of the fingers of her hand, and small blisters appear on the finger pads. This has led to which one of the following inflammatory responses?

A  Fibrinous inflammation  
B  Granulomatous inflammation  
C  Purulent inflammation  
D  Serous inflammation  
E  Ulceration

22 A 24-year-old, sexually active woman has experienced lower abdominal pain for the past day. Her temperature is 37.9°C, and on palpation, the left lower abdomen is markedly tender. Laboratory findings include a total WBC count of 29,000/mm³ with 75% segmented neutrophils, 6% bands, 14% lymphocytes, and 5% monocytes. Laparotomy reveals a distended, fluid-filled, reddened left fallopian tube that is about to rupture. A left salpingectomy is performed. Which of the following is most likely to be seen on microscopic examination of the excised fallopian tube?

A  Fibroblastic proliferation  
B  Langhans giant cells  
C  Liquefactive necrosis  
D  Mononuclear infiltrates  
E  Squamous metaplasia
23] A 68-year-old man has had worsening shortness of breath for the past week. On physical examination, his temperature is 38.3°C. On percussion, there is dullness over the left lung fields. Thoracentesis performed on the left pleural cavity yields 800 mL of cloudy yellow fluid that has a WBC count of 2500/mm³ with 98% neutrophils and 2% lymphocytes. A Gram stain of the fluid shows gram-positive cocci in clusters. Which of the following terms best describes the process occurring in his left pleural cavity?

A  Abscess  
B  Chronic inflammation  
C  Edema  
D  Fibrinous inflammation  
E  Purulent exudate  
F  Serous effusion

24] An 87-year-old woman has had a cough productive of yellowish sputum for the past 2 days. On examination her temperature is 37°C. A chest radiograph shows bilateral patchy infiltrates. Her peripheral blood shows leukocytosis. A week later she is afebrile. Which of the following is the most likely outcome of her pulmonary disease?

A  Chronic inflammation  
B  Fibrous scarring  
C  Neoplasia  
D  Resolution  
E  Ulceration

25] A 53-year-old woman has experienced abdominal pain for 2 weeks. She is afebrile. There is mild upper abdominal tenderness on palpation, and bowel sounds are present. An upper gastrointestinal endoscopy is performed. The figure shows microscopic examination of a biopsy specimen of a duodenal lesion. Which of the following pathologic processes is most likely present?

A  Abscess  
B  Caseating granuloma  
C  Chronic inflammation  
D  Purulent exudate  
E  Serous effusion  
F  Ulceration

26] A 92-year-old woman is diagnosed with *Staphylococcus aureus* pneumonia and receives a course of antibiotic therapy. Two weeks later, she no longer has a productive cough, but she still has a temperature of 38.1°C. A chest radiograph shows the findings in the figure. Which of the following terms best describes the outcome of the patient’s pneumonia?

A  Abscess formation  
B  Complete resolution  
C  Fibrous scarring  
D  Chronic inflammation  
E  Tissue regeneration

27] A 29-year-old woman with a congenital ventricular septal defect has had a persistent temperature of 38.6°C and headache for the past 3 weeks. A head CT scan shows an enhancing 3-cm, ring like lesion in the right parietal lobe of her brain. Which of the following actions by inflammatory cells has most likely produced this CT finding?

A  Elaboration of nitric oxide by macrophages  
B  Formation of immunoglobulin by B lymphocytes  
C  Generation of prostaglandin by endothelium  
D  Production of interferon-γ by T lymphocytes  
E  Release of lysosomal enzymes from neutrophils

28] A 37-year-old man has had midepigastric pain for the past 3 months. An upper gastrointestinal endoscopy shows a 2-cm, sharply demarcated, shallow ulceration of the gastric antrum. Microscopic examination of a biopsy from the ulcer base shows angiogenesis, fibrosis, and mononuclear cell infiltrates with lymphocytes, macrophages, and plasma cells. Which of the following terms best describes this pathologic process?

A  Acute inflammation  
B  Chronic inflammation  
C  Fibrinous inflammation  
D  Granulomatous inflammation  
E  Serous inflammation
29. A 65-year-old man develops worsening congestive heart failure 2 weeks after an acute myocardial infarction. An echo-cardiogram shows a markedly decreased ejection fraction. Now, capillaries, fibroblasts, collagen, and inflammatory cells have largely replaced the infarcted myocardium. Which of the following inflammatory cell types in this lesion plays the most important role in the healing process?

A. Eosinophils
B. Epithelioid cells
C. Macrophages
D. Neutrophils
E. Plasma cells

30. A 9-year-old boy has had a chronic cough and fever for the past month. A chest radiograph shows enlargement of hilar lymph nodes and bilateral pulmonary nodular interstitial infiltrates. A sputum sample contains acid-fast bacilli. A transbronchial biopsy specimen shows granulomatous inflammation with epithelioid macrophages and Langhans giant cells. Which of the following mediators is most likely to contribute to giant cell formation?

A. Complement C3b
B. Interferon-γ
C. Interleukin-1 (IL-1)
D. Leukotriene B4
E. Tumor necrosis factor (TNF)

31. A 32-year-old woman has had a chronic cough with fever for the past month. On physical examination, her temperature is 37.5° C. A chest radiograph shows many small, ill-defined nodular opacities in all lung fields. A transbronchial biopsy specimen shows interstitial infiltrates with lymphocytes, plasma cells, and epithelioid macrophages. Which of the following infectious agents is the most likely cause of this appearance?

A. Candida albicans
B. Cytomegalovirus
C. Enterobacter aerogenes
D. Mycobacterium tuberculosis
E. Plasmodium falciparum
F. Staphylococcus aureus

32. One month after an appendectomy, a 25-year-old woman palpates a small nodule beneath the skin at the site of the healed right lower quadrant sutured incision. The nodule is excised, and microscopic examination shows macrophages, collagen deposition, small lymphocytes, and multinucleated giant cells. Polarizable, refractile material is seen in the nodule. Which of the following complications of the surgery best accounts for these findings?

A. Abscess formation
B. Chronic inflammation
C. Exuberant granulation tissue
D. Granuloma formation
E. Healing by second intention

33. A 43-year-old man has had a cough and fever for the past 2 months. A chest CT scan shows the findings in the figure (A). A transbronchial lung biopsy is performed, yielding a specimen with the microscopic appearance shown in the figure (B). Which of the following chemical mediators is most important in the pathogenesis of this lesion?

A. Bradykinin
B. Complement C5a
C. Interferon-γ
D. Nitric oxide
E. Prostaglandins

34. An 8-year-old girl has had difficulty swallowing for the past day. On examination, her pharynx is swollen and erythematous with an overlying yellow exudate. Laboratory studies show neutrophilia. *Streptococcus pyogenes* (group A streptococcus) is cultured from her pharynx. Which of the following substances is most likely to increase in response to pyrogens released by this organism?

A. Hageman factor
B. Immunoglobulin E
C. Interleukin-12 (IL-12)
D. Nitric oxide
E. Prostaglandins
35. A 41-year-old man has had a severe headache for the past 2 days. On examination, his temperature is 39.2°C. A lumbar puncture is performed, and the cerebrospinal fluid obtained has a WBC count of 910/mm³ with 94% neutrophils and 6% lymphocytes. Which of the following substances is the most likely mediator for the fever observed in this man?

A. Bradykinin  
B. Histamine  
C. Leukotriene B₄  
D. Nitric oxide  
E. Tumor necrosis factor (TNF)

36. A 43-year-old man with a ventricular septal defect has had a cough and fever for the past 2 days. On examination, he has a temperature of 37.6°C and a cardiac murmur. A blood culture grows *Streptococcus*, viridans group. His erythrocyte sedimentation rate (ESR) is increased. Microbial cells are opsonized and cleared. Which of the following chemical mediators is most important in producing these findings?

A. Bradykinin  
B. C-reactive protein  
C. Interferon-γ  
D. Nitric oxide  
E. Prostaglandin  
F. Tumor necrosis factor (TNF)

37. In an experiment, a group of test animals is infected with viral hepatitis. Two months later, complete recovery of the normal liver architecture is observed microscopically. A control test group is infected with bacterial organisms, and after the same period of time, fibrous scars from resolving hepatic abscesses are seen microscopically. Which of the following factors best explains the different outcomes for the two test groups?

A. Extent of damage to the biliary ducts  
B. Extent of the hepatocyte injury  
C. Injury to the connective tissue framework  
D. Location of the lesion within the liver  
E. Nature of the injurious etiologic agent

38. A 51-year-old woman tests positive for hepatitis A antibody. Her serum AST level is 275 U/L, and ALT is 310 U/L. One month later, these enzyme levels have returned to normal. Which phase of the cell cycle best describes the hepatocytes 1 month after her infection?

A. G₀  
B. G₁  
C. S  
D. G₂  
E. M

39. A 54-year-old man undergoes laparoscopic hernia repair. In spite of the small size of the incisions, he has poor wound healing. Further history reveals that his usual diet has poor nutritional value and is deficient in vitamin C. Synthesis of which of the following extracellular matrix components is most affected by this deficiency?

A. Collagen  
B. Elastin  
C. Fibronectin  
D. Integrin  
E. Laminin

40. In an experiment, glass beads are embolized into the coronary arteries of rats, resulting in myocardial injury. After 7 days, sections of the myocardium are studied using light microscopy. The microscopic appearance of one of these sections is shown in the figure. Which of the following mediators is most likely being expressed to produce this appearance?

A. Epidermal growth factor  
B. Interleukin-2 (IL-2)  
C. Leukotriene B₄  
D. Thromboxane A₂  
E. Tumor necrosis factor (TNF)  
F. Vascular endothelial growth factor

41. A 20-year-old woman undergoes cesarean section to deliver a term infant, and the lower abdominal incision is sutured. The sutures are removed 1 week later. Which of the following statements best describes the wound site at the time of suture removal?

A. Collagen degradation exceeds synthesis  
B. Granulation tissue is still present  
C. No more wound strength will be gained  
D. Type IV collagen predominates  
E. Wound strength is 80% of normal tissue
A 24-year-old man with acute appendicitis undergoes surgical removal of the inflamed appendix. The incision site is sutured. A trichrome-stained section representative of the site with blue appearing collagen is shown in the figure. How long after the surgery would this appearance most likely be seen?

A 1 day  
B 2 to 3 days  
C 4 to 5 days  
D 2 weeks  
E 1 month

A 40-year-old man underwent laparotomy for a perforated sigmoid colon diverticulum. A wound infection complicated the postoperative course, and surgical wound dehiscence occurred. Primary closure was no longer possible, and the wound “granulated in.” Six weeks later, the wound is only 10% of its original size. Which of the following processes best accounts for the observed decrease in wound size over the past 6 weeks?

A Elaboration of adhesive glycoproteins  
B Increase in synthesis of collagen  
C Inhibition of metalloproteinases  
D Myofibroblast contraction  
E Resolution of subcutaneous edema

In an experiment involving observations on wound healing, researchers noted that intracytoplasmic cytoskeletal elements, including actin, interact with the extracellular matrix to promote cell attachment and migration in wound healing. Which of the following substances is most likely responsible for such interaction between the cytoskeleton and the extracellular matrix?

A Epidermal growth factor  
B Fibronectin  
C Integrin  
D Platelet-derived growth factor  
E Type IV collagen  
F Vascular endothelial growth factor

A 23-year-old woman receiving corticosteroid therapy for an autoimmune disease has an abscess on her upper outer right arm. She undergoes minor surgery to incise and drain the abscess, but the wound heals poorly over the next month. Which of the following aspects of wound healing is most likely to be deficient in this patient?

A Collagen deposition  
B Elaboration of VEGF  
C Neutrophil infiltration  
D Reepithelialization  
E Serine proteinase production

An 18-year-old man lacerated his left ear and required sutures. The sutures were removed 1 week later. Wound healing continued, but the site became disfigured over the next 2 months by the process shown in the figure. Which of the following terms best describes the process that occurred in this man?

A Dehiscence  
B Keloid formation  
C Organization  
D Resolution  
E Secondary union

A 58-year-old man had chest pain persisting for 4 hours. A radiographic imaging procedure showed an infarction involving a 4-cm area of the posterior left ventricular free wall. Laboratory findings showed serum creatine kinase of 600 U/L. Which of the following pathologic findings would most likely be seen in the left ventricular lesion 1 month later?

A Chronic inflammation  
B Coagulative necrosis  
C Complete resolution  
D Fibrous scar  
E Nodular regeneration
ANSWERS

1 C Macrophages in tissues derived from circulating blood monocytes are phagocytic cells that respond to a variety of stimuli, and they represent the janitorial crew of the body. The other cells listed are not phagocytes. B cells can differentiate into plasma cells secreting antibodies to neutralize infectious agents. Fibroblasts form collagen as part of a healing response. Mast cells can release a variety of inflammatory mediators. T cells are a key part of chronic inflammatory processes in cell-mediated immune responses.

2 D These signs and symptoms suggest acute bacterial pneumonia. Such infections induce an acute inflammation dominated by neutrophils that fill alveoli, as shown in the figure, and are coughed up, which gives the sputum its yellowish, purulent appearance. Langhans giant cells are seen with granulomatous inflammatory responses. Macrophages become more numerous after initiation of acute events, cleaning up tissue and bacterial debris through phagocytosis. Mast cells are better known as participants in allergic and anaphylactic responses. Lymphocytes are a feature of chronic inflammation.

3 E Nonhuman microbial substances such as double-stranded RNA of viruses, bacterial DNA, and bacterial endotoxin, can be recognized by Toll-like receptors (TLRs) on human cells as part of an innate defense mechanism against infection. Caspase-1 is activated by an inflammasome complex of proteins responding to bacterial organisms, and produces biologically active interleukin-1 (IL-1). Complement receptors on inflammatory cells recognize complement components that aid in triggering immune responses through co-stimulatory signals. Lectins found on cell surfaces can bind a variety of substances, such as fungal polysaccharides, that trigger cellular defenses. T cell receptors respond to peptide antigens to trigger a cell-mediated immune response.

4 E The formation of an exudate containing a significant amount of protein and cells depends on the “leakiness” of blood vessels, principally venules. When exudation has occurred, the protein content of the extravascular space increases, and extravascular colloid osmotic pressure increases, causing extracellular fluid accumulation. Leukocytosis alone is insufficient for exudation because the leukocytes must be driven to emigrate from the vessels by chemotactic factors. The lymphatics scavenge exuded proteinaceous fluid and reduce the amount of extravascular and extracellular fluid. Sodium and water retention helps drive transudation of fluid.

5 B Exudation of fluid from venules and capillaries is a key component of the acute inflammatory process. Several mechanisms of increased vascular permeability have been proposed, including formation of interendothelial gaps by contraction of endothelium. This contraction can be caused by mediators such as histamine and leukotrienes. The vessels then become more “leaky,” and the fluid leaves the intravascular space to accumulate extravascularly, forming effusions in body cavities or edema within tissues. Arteriolar vasoconstriction is a transient response to injury that helps diminish blood loss. Platelets adhere to damaged endothelium and promote hemostasis. Lymphatic obstruction results in the accumulation of protein-rich lymph and lymphocytes, producing a chylous effusion within a body cavity. After neutrophils reach the site of tissue injury outside of the vascular space, they release lysosomal enzymes that promote liquefaction.

6 E Leukocyte rolling is the first step in transmigration of neutrophils from the vasculature to the tissues. Rolling depends on interaction between selectins (P-selectin and E-selectin on endothelial cells, and L-selectin on neutrophils) and their sialylated ligands (e.g., sialylated Lewis X). Integrins are involved in the next step of transmigration, during which there is firm adhesion between neutrophils and endothelial cells. Complement C3b acts as an opsonin to facilitate phagocytosis. Leukotriene B4 is a chemoattractant. NADPH oxidase is involved in phagocytic cell microbicidal activity.

7 B Chemokines include many molecules that are chemoattractant for neutrophils, eosinophils, lymphocytes, monocytes, and basophils. Bradykinin causes pain and increased vascular permeability. Complement C3a causes increased vascular permeability by releasing histamine from mast cells. Histamine causes vascular leakage. Prostaglandins have multiple actions, but they do not cause chemotaxis.

8 B This immunoglobulin deficiency prevents opsonization and phagocytosis of microbes. Deficiency of integrins and selectins, or a defect in microtubules, would prevent adhesion and locomotion of neutrophils. H2O2 production is part of the oxygen-dependent killing mechanism. This mechanism is intact in this patient because the neutrophils are able to kill bacteria when immunoglobulins in normal serum allow phagocytosis.

9 B Myeloperoxidase is present in the azurophilic granules of neutrophils. It converts H2O2 into HOCl–, a powerful oxidant and antimicrobial agent. Degranulation occurs as phagolysosomes are formed with engulfed bacteria in phagocytic vacuoles within the neutrophil cytoplasm. Oxygen consumption with an oxidative or respiratory burst after phagocytosis is aided by glucose oxidation and activation of neutrophil NADPH oxidase, resulting in generation of...
superoxide that is converted by spontaneous dismutation to \( \text{H}_2\text{O}_2 \). In contrast, prostaglandin production depends on a functioning cyclooxygenase pathway of arachidonic acid metabolism.

10 B The respiratory, or oxidative, burst of neutrophils generates reactive oxygen species (e.g., superoxide anion) that are important in destruction of engulfed bacteria. This burst can be quantitated by flow cytometric analysis. Neutrophil attachment to endothelium is aided by adhesion molecules on both the endothelium and the neutrophil surface. These molecules include selectins and integrins. Myeloperoxidase is an enzyme that is not dependent on generation of superoxide. Bacteria are opsonized by complement C3b and IgG, allowing the bacteria to be more readily phagocytosed.

11 D During acute inflammation, in the first stage of extravasation, the neutrophils “roll over” the endothelium. At this stage, the adhesion between the neutrophils and endothelial cells is weak. Rolling is mediated by binding of selectins to sialylated oligosaccharides. The next step, firm adhesion, is mediated by binding of integrins on the leukocytes to their receptors, intercellular adhesion molecule-1 or vascular cell adhesion molecule-1 (VCAM-1), on endothelial cells. Integrins have two chains, \( \alpha \) and \( \beta \). A genetic lack of \( \beta \) chains prevents firm adhesion of leukocytes to endothelial cells. This process depends on adhesion molecules expressed on the neutrophils and endothelial cells. Formation of HOCl requires myeloperoxidase released from neutrophil granules. Phagocytosis of opsonized organisms depends on engulfment, which requires contractile proteins in the neutrophil cytoplasm. Neutrophil migration to a site of infection depends on the presence of chemotactic factors such as complement C5a that bind to the neutrophil and activate phospholipase C to begin a series of events that culminate in the influx of calcium, which triggers contractile proteins. The respiratory burst to kill phagocytized organisms depends on NADPH oxidase, and a deficiency of this enzyme leads to chronic granulomatous disease.

12 E Monocytes transforming to macrophages contain cytokine-inducible nitric oxide synthase (iNOS), which generates nitric oxide. Nitric oxide, by itself and on interaction with other reactive oxygen species, has antimicrobial activity. CD4 or CD8 lymphocytes can be the source for interferon-\( \gamma \) (IFN-\( \gamma \)), which stimulates macrophage production of NO. Endothelial cells contain a form of NOS (eNOS) that acts to promote vasodilation. B lymphocytes produce immunoglobulins that can opsonize bacteria. Basophils release histamine and arachidonic acid metabolites, which participate in the acute inflammatory process. Natural killer cells have Fc receptors and can lyse IgG-coated target cells; they also generate IFN-\( \gamma \). Neutrophils can phagocytize microbes, but they use NAPDH oxidase and enzymes other than NOS to kill the microbes.

13 B Interferon-\( \gamma \) secreted from lymphocytes stimulates monocytes and macrophages, which secrete their own cytokines that further activate lymphocytes. Interferon-\( \gamma \) also is important in transforming macrophages into epithelioid cells in a granulomatous inflammatory response. Histamine released from mast cells is a potent vasodilator, increasing vascular permeability. Leukotriene \( \text{B}_4 \) generated in the lipoxygenase pathway of arachidonic acid metabolism, is a potent neutrophil chemotactic factor. Nitric oxide generated by macrophages aids in destruction of microorganisms; nitric oxide released from endothelium mediates vasodilation and inhibits platelet activation. Binding of agonists such as epinephrine, collagen, or thrombin to platelet surface receptors activates phospholipase C, which catalyzes the release of arachidonic acid from two of the major membrane phospholipids, phosphatidylinositol and phosphatidylcholine. Tumor necrosis factor (TNF), produced by activated macrophages, mediates many systemic effects, including fever, metabolic wasting, and hypotension.

14 C Histamine is found in abundance in mast cells, which are normally present in connective tissues next to blood vessels beneath mucosal surfaces in airways. Binding of an antigen (allergen) to IgE antibodies that have previously attached to the mast cells by the Fc receptor triggers mast cell degranulation, with release of histamine. This response causes increased vascular permeability and mucous secretions. Bradykinin, generated from the kinin system on surface contact of Hageman factor with collagen and basement membrane from vascular injury, promotes vascular permeability, smooth muscle contraction, and pain. Complement C5a is a potent chemotactic factor for neutrophils. Interleukin-1 (IL-1) and tumor necrosis factor (TNF), both produced by activated macrophages, mediate many systemic effects, including fever, metabolic wasting, and hypotension. Phospholipase C, which catalyzes the release of arachidonic acid, is generated from platelet activation.

15 F The COX-2 enzyme is inducible with acute inflammatory reactions, particularly in neutrophils, in synovium, and in the central nervous system. The cyclooxygenase pathway of arachidonic acid metabolism generates prostaglandins, which mediate pain, fever, and vasodilation. Ankle swelling is most likely to result from peripheral edema secondary to congestive heart failure. Increased susceptibility to bruising results from prolonged glucocorticoid administration, which also causes leukopenia. Asthma results from bronchoconstriction mediated by leukotrienes that are generated by the lipoxygenase pathway of arachidonic acid metabolism. Inhibition of histamine released from mast cells helps reduce urticaria. Fever can be mediated by prostaglandin release, not inhibition.

16 E Naproxen, a nonsteroidal anti-inflammatory drug, targets the cyclooxygenase pathway of arachidonic acid metabolism and leads to reduced prostaglandin generation.
Prostaglandins promote vasodilation at sites of inflammation. Chemotaxis is a function of various chemokines, and complement C3b may promote phagocytosis, but neither is affected by aspirin. Leukocyte emigration is aided by various adhesion molecules. Leukocyte release from bone marrow can be driven by the cytokines interleukin-1 (IL-1) and tumor necrosis factor (TNF).

**17 E** Prostaglandins are produced through the cyclooxygenase pathway of arachidonic acid metabolism. Aspirin and other nonsteroidal anti-inflammatory drugs block the synthesis of prostaglandins, which can produce pain. Complement C5a is generated in the initial stage of complement activation, which can eventually result in cell lysis. Histamine is mainly a vasodilator. Leukotrienes are generated by the lipoxygenase pathway, which is not blocked by aspirin. Nitric oxide released from endothelium is a vasodilator.

**18 C** Endothelial cells can release nitric oxide to promote vasodilation in areas of ischemic injury. Bradykinin mainly increases vascular permeability and produces pain. Leukotriene E4, platelet-activating factor, and thromboxane A2 have vasoconstrictive properties.

**19 A** Activation of complement may occur via microbial cell wall components such as polysaccharides (alternative pathway) or mannose (lectin pathway), or antibody attached to surface antigens (classical pathway). A variety of complement components are generated, including complement C5a, a neutrophil chemoattractant; complement C3b, an opsonin; and complement C5-9, the membrane attack complex. The remaining options are more closely associated with coagulation. Fibrin is generated by the coagulation system, but not with anticoagulation. Kallikrein may aid in generation of bradykinin and plasmin, but participates just in complement C5a generation. Plasmin is generated from plasminogen and helps lyse clots. Thrombin is generated by the coagulation cascade.

**20 E** Ongoing activation of coagulation generates an inflammatory response that further amplifies coagulation, creating a vicious cycle. Protein C antagonizes coagulation factor V, which catalyzes activation of prothrombin to thrombin, thereby breaking the cycle of thrombin generation. Complement components can become activated by plasmin (C3) and kallikrein (C3), forming anaphylatoxins (C3a and C5a) that promote inflammation. Fibrin, the end product of coagulation pathways, forms a meshwork entrapping platelets and creating a plug. Kallikrein is generated by activation of Hageman factor (XII) and leads to formation of bradykinin. Plasmin is generated from plasminogen activated by thrombosis to promote clot lysis.

**21 D** Serous inflammation is the mildest form of acute inflammation. A blister is a good example of serous inflammation. It is associated primarily with exudation of fluid into the subcorneal or subepidermal space. Because the injury is mild, the fluid is relatively protein-poor. A protein-rich exudate results in fibrin accumulation. Granulomatous inflammation is characterized by collections of transformed macrophages called epithelioid cells. Acute inflammatory cells, mainly neutrophils, exuded into a body cavity or space form a purulent (suppurative) exude, typically associated with liquefactive necrosis. Loss of the epithelium leads to ulceration.

**22 C** This patient is experiencing an acute inflammatory response, with edema, erythema, and pain of short duration. Neutrophils form an exudate and release various proteases, which can produce liquefactive necrosis, starting at the mucosa and extending through the wall of the tube. This mechanism results in perforation. Fibroblasts are more likely participants in chronic inflammatory responses and in healing responses, generally appearing more than 1 week after the initial event. Langhans giant cells are a feature of granulomatous inflammation. Mononuclear infiltrates are more typical of chronic inflammation of the fallopian tube, in which rupture is less likely. Epithelial metaplasia is most likely to occur in the setting of chronic irritation with inflammation.

**23 E** Bacterial infections often evoke an acute inflammatory response dominated by neutrophils. The extravasated neutrophils attempt to phagocytose and kill the bacteria. In the process, some neutrophils die, and the release of their lysosomal enzymes can cause liquefactive necrosis of the tissue. This liquefied tissue debris and both live and dead neutrophils comprise pus, or purulent exudate. Such an exudate is typical of bacterial infections that involve body cavities. Another term for purulent exudate in the pleural space is empyema. An abscess is a localized collection of neutrophils within tissues. Chronic inflammation occurs when there is a preponderance of mononuclear cells, such as lymphocytes, macrophages, and plasma cells, in a process that has gone on for more than a few days—more likely weeks or months—or that accompanies repeated bouts of acute inflammation. Edema refers to increased cellular and interstitial fluid collection within tissues, leading to tissue swelling. In fibrinous inflammation, exudation of blood proteins (including fibrinogen, which polymerizes to fibrin) gives a grossly shaggy appearance to surfaces overlying the inflammation. A serous effusion is a watery-appearing transudate that resembles a ultrafiltrate of blood plasma, with a low cell and protein content.

**24 D** If inflammation is limited and brief, and the involved tissue can regenerate, then resolution is the likely outcome, without significant loss of function. In older persons this may take longer, but can still occur. Multiple bouts of acute inflammation, or ongoing inflammation, can become chronic, and there tends to be loss of some tissue function.
significant tissue destruction occurs, there is likely to be formation of a fibrous scar in the region of the tissue loss. Acute inflammation is not a preneoplastic event. Ulceration refers to loss of an epithelial surface with acute inflammation; if the epithelium regenerates, then there is resolution.

PBD9 92–93 BP9 42 PBD8 66–67 BP8 42–43

25 F Inflammation involving an epithelial surface may cause such extensive necrosis that the surface becomes eroded, forming an ulcer. If the inflammation continues, the ulcer can continue to penetrate downward into submucosa and muscularis. Alternatively, the ulcer may heal, or it may remain chronically inflamed. An abscess is a localized collection of neutrophils in tissues. A caseating granuloma is granulomatous inflammation with central necrosis; the necrosis has elements of both liquefaction and coagulative necrosis. Chronic inflammation occurs when there is a preponderance of mononuclear cells, such as lymphocytes, macrophages, and plasma cells, in a process that has gone on for more than a few days—more likely weeks or months—or that accompanies repeated bouts of acute inflammation. Pus, or a purulent exudate, appears semiliquid and yellowish because of the large numbers of granulocytes present. A serous effusion is a watery-appearing transudate that resembles an ultrafiltrate of blood plasma, with a low cell and protein content.

PBD9 91–92 BP9 44 PBD8 68–69 BP8 44–45

26 A The rounded density in the right lower lobe of the lung has liquefied contents that form a central air-fluid level. There are surrounding infiltrates. The formation of a fluid-filled cavity after infection with Staphylococcus aureus suggests that liquefactive necrosis has occurred. The cavity is filled with tissue debris and viable and dead neutrophils (pus).Localized, pus-filled cavities are called abscesses. Some bacterial organisms, such as S. aureus, are more likely to be pyogenic, or pus-forming. With complete resolution, the structure of the lung remains almost unaltered. Scarring or fibrosis may follow acute inflammation as the damaged tissue is replaced by fibrous connective tissue. Most bacterial pneumonias resolve, and progression to continued chronic inflammation is uncommon. Lung tissue, in contrast to liver, is incapable of regeneration, except for epithelium and endothelium.

PBD9 91 BP9 43–44 PBD8 68–69 BP8 42, 44–45

27 E This patient has an infective endocarditis with septic embolization, producing a cerebral abscess. The tissue destruction that accompanies abscess formation as part of acute inflammatory processes occurs from lysosomal enzymatic destruction, aided by release of reactive oxygen species. Nitric oxide generated by macrophages aids in destruction of infectious agents. Immunoglobulin formed by B cells neutralizes and opsonizes infectious agents. Prostaglandins produced by endothelium promote vasodilation. Interferon-γ released from lymphocytes plays a major role in chronic and granulomatous inflammatory responses.

PBD9 91 BP9 43–44 PBD8 68–69 BP8 42–43

28 B One outcome of acute inflammation with ulceration is chronic inflammation. This is particularly true when the inflammatory process continues for weeks to months. Chronic inflammation is characterized by tissue destruction, mononuclear cell infiltration, and repair. In acute inflammation, the healing process of fibrosis and angiogenesis has not begun. In fibrinous inflammation, typically involving a mesothelial surface, there is an outpouring of protein-rich fluid that results in precipitation of fibrin. Granulomatous inflammation is a form of chronic inflammation in which epithelioid macrophages form aggregates. Serous inflammation is an inflammatory process involving a mesothelial surface (e.g., lining of the pericardial cavity), with an outpouring of fluid having little protein or cellular content.


29 C Macrophages, present in such lesions, play a prominent role in the healing process. Activated macrophages can secrete various cytokines that promote angiogenesis and fibrosis, including platelet-derived growth factor, fibroblast growth factor, interleukin-1 (IL-1), and tumor necrosis factor (TNF). Eosinophils are most prominent in allergic inflammations and in parasitic infections. Epithelioid cells, which are aggregations of activated macrophages, are typically seen with granulomatous inflammation, and the healing of acute inflammatory processes does not involve granulomatous inflammation. Neutrophils are most numerous within the initial 48 hours after infarction, but are not numerous after the first week. Plasma cells can secrete immunoglobulins and are not instrumental to healing of an area of tissue injury.

PBD9 92–94 BP9 54 PBD8 54, 71 BP8 54–55

30 B Interferon-γ is secreted by activated T cells and is an important mediator of granulomatous inflammation. It causes activation of macrophages and their transformation into epithelioid cells and then giant cells. Complement C3b acts as an opsonin in acute inflammatory reactions. Interleukin-1 (IL-1) can be secreted by macrophages to produce various effects, including fever, leukocyte adherence, fibroblast proliferation, and cytokine secretion. Leukotriene B₄ induces chemotaxis in acute inflammatory processes. Tumor necrosis factor (TNF) can be secreted by activated macrophages and induces activation of lymphocytes and proliferation of fibroblasts, which are other elements of a granuloma.

PBD9 97–98 BP9 56 PBD8 52 BP8 55–56

31 D These findings suggest a granulomatous inflammation, and tuberculosis is a common cause. Candida is often a commensal organism in the oropharyngeal region and rarely causes pneumonia in healthy (non-immunosuppressed) individuals. Viral infections tend to produce a mononuclear interstitial inflammatory cell response. Bacteria such as Enterobacter and Staphylococcus are more likely to produce acute inflammation. Plasmodium produces malaria, a parasitic infection without a significant degree of lung involvement.

PBD9 97–98 BP9 56–57 PBD8 73–74 BP8 56–57
The polarizable material is the suture, and a multinucleated giant cell reaction, typically with foreign body giant cells, is characteristic of a granulomatous reaction to foreign material. Granulation tissue may form a nodular appearance, and begins to appear 3 to 5 days following injury, but is unlikely to persist for a month. Chronic inflammation alone is unlikely to produce a localized nodule with giant cells. Edema refers to accumulation of fluid in the interstitial space. It does not produce a cellular nodule. If a large, gaping wound is not closed by sutures, it can granulate it and myofibroblastic contraction eventually helps close the wound by second intention.

This acute inflammatory process leads to production of acute-phase reactants, such as C-reactive protein (CRP), fibrinogen, and serum amyloid A (SAA) protein. These proteins, particularly fibrinogen, and immunoglobulins increase RBC rouleaux formation to increase the erythrocyte sedimentation rate (ESR), which is a nonspecific indicator of inflammation. CRP production is upregulated by interleukin-6 (IL-6), whereas fibrinogen and SAA are upregulated mainly by tumor necrosis factor (TNF) and interleukin-1 (IL-1). Interferon-γ is a potent stimulator of macrophages. Nitric oxide can induce vasodilation or can assist in microbial killing within macrophages. Prostaglandins are vasodilators.

The findings here are those of strep throat with acute inflammation. Bacterial organisms often lead to fever accompanying infection through release of exogenous pyrogens that induce inflammatory cells to release endogenous pyrogens such as tumor necrosis factor (TNF) and interleukin-1 (IL-1). The pyrogens stimulate prostaglandin synthesis in the hypothalamus to “reset the thermostat,” so that fever occurs as a sign of the acute inflammatory response. Prostaglandins are mainly involved in the causation of vasodilation and pain in acute inflammatory responses.

Hepatocytes are stable cells with an extensive ability to regenerate. The ability to restore normal architecture of an organ such as the liver depends on the viability of the supporting connective tissue framework. If the connective tissue cells are not injured, hepatocyte regeneration can restore normal liver architecture. This regeneration occurs in many cases of viral hepatitis. A liver abscess associated with liquefactive necrosis of hepatocytes and the supporting connective tissue heals by scarring. The other options listed may explain the amount of liver injury, but not the nature of the response.

Fever is produced by various inflammatory mediators, but the major cytokines that produce fever are interleukin-1 (IL-1) and tumor necrosis factor (TNF), which are produced by macrophages and other cell types. IL-1 and TNF can have autocrine, paracrine, and endocrine effects. They mediate the acute phase responses, such as fever, nausea, and neutrophil release from bone marrow. Bradykinin, generated from the kinin system on surface contact of Hageman factor with collagen and basement membrane from vascular injury, promotes vascular permeability, smooth muscle contraction, and pain. Histamine released from mast cells is a potent vasodilator, increasing vascular permeability. Leukotriene B4 generated in the lipoxygenase pathway of arachidonic acid metabolism, is a potent neutrophil chemotactic factor. Nitric oxide generated by macrophages aids in destruction of microorganisms; nitric oxide released from endothelium mediates vasodilation and inhibits platelet activation.

Vitamin C deficiency leads to scurvy, with reduced lysyl oxidase enzyme activity that helps cross-link fibrillar collagens to provide tensile strength. Though elastin is a fibrillar protein, it tends to regenerate poorly in scar tissue, even with the best of nutrition, explaining why a scar does not stretch like the skin around it. The other listed choices are glycoproteins that have an adhesive quality and are not vitamin C dependent.
40 F The figure shows a subacute infarction with granulation tissue formation containing numerous capillaries stimulated by vascular endothelial growth factor, representing a healing response. Epidermal growth factor aids in reepithelialization of a surface wound. Interleukin-2 (IL-2) mediates lymphocyte activation. Leukotriene B4 mediates reepithelialization of a surface wound. Interleukin-2 (IL-2) mediates migration of macrophages, smooth muscle cells, and platelets; PDGF mediates migration and proliferation of fibroblasts and smooth muscle cells and migration of monocytes. Type IV collagen is found in basement membranes on which cells are anchored. Vascular endothelial growth factor promotes angiogenesis (capillary proliferation) through endothelial cell proliferation and migration in a healing response.

PBD9 106–107 BP9 66 PBD8 102–103 BP8 70–71

41 A At 1 week, wound healing is incomplete, and granulation tissue is still present. More collagen is synthesized in the following weeks. Wound strength peaks at about 80% by 3 months. Type IV collagen is found in basement membranes.

PBD9 106–108 BP9 70–71 PBD8 103, 106 BP8 74–77

42 E The figure shows dense collagen with some remaining dilated blood vessels, typical of the final phase of wound healing, which is extensive by the end of the first month. On day 1, the wound is filled only with fibrin and inflammatory cells. Macrophages and granulation tissue are seen 2 to 3 days postoperatively. Neovascularization is most prominent by days 4 and 5. By week 2, collagen is prominent, and fewer vessels and inflammatory cells are seen.

PBD9 107 BP9 71 PBD8 104–105 BP8 75–76

43 D Wound contraction is a characteristic feature of healing by second intention that occurs in larger wounds. Collagen synthesis helps fill the defect, but does not contract it. Adhesive glycoproteins such as fibronectin help to maintain a cellular scaffolding for growth and repair, but they do not contract. The inhibition of metalloproteinases leads to decreased degradation of collagen and impaired connective tissue remodeling in wound repair. Edema diminishes over time, but this does not result in much contraction.

PBD9 107–108 BP9 70–72 PBD8 104–105 BP8 74–75

44 C Integrins interact with the extracellular matrix proteins (e.g., fibronectin). Engagement of integrins by extracellular matrix proteins leads to the formation of focal adhesions where integrins link to intracellular cytoskeletal elements such as actin. These interactions lead to intracellular signals that modulate cell growth, differentiation, and migration during wound healing. Epidermal growth factor stimulates epithelial cell and fibroblast proliferation. Platelet-derived growth factor (PDGF) can be produced by endothelium, macrophages, smooth muscle cells, and platelets; PDGF mediates migration and proliferation of fibroblasts and smooth muscle cells and migration of monocytes. Type IV collagen is found in basement membranes on which cells are anchored. Vascular endothelial growth factor promotes angiogenesis (capillary proliferation) through endothelial cell proliferation and migration in a healing response.

PBD9 104–105 BP9 63–64 PBD8 96–97 BP8 67–68

45 A Glucocorticoids inhibit wound healing by impairing collagen synthesis. This is a desirable side effect if the amount of scarring is to be reduced, but it results in the delayed healing of surgical wounds. Angiogenesis driven by vascular endothelial growth factor (VEGF) is not significantly affected by corticosteroids. Neutrophil infiltration is not prevented by glucocorticoids. Reepithelialization, in part driven by epidermal growth factor, is not affected by corticosteroid therapy. Serine proteinases are important in wound remodeling.

PBD9 106 BP9 69 PBD8 106 BP8 77

46 B The healing process sometimes results in an exuberant production of collagen, giving rise to a keloid, which is a prominent raised, nodular scar, as shown in the figure. This tendency may run in families. Dehiscence occurs when a wound pulls apart. Organization occurs as granulation tissue is replaced by fibrous tissue. If normal tissue architecture is restored, resolution of inflammation has occurred. Secondary union describes the process by which large wounds fill in and contract.

PBD9 109–110 BP9 69 PBD8 106 BP8 77

47 D The elevated creatine kinase level indicates that myocardial necrosis has occurred. A fibrous scar gradually replaces the area of myocardial necrosis. Chronic inflammation is typically driven by ongoing stimuli such as persistent infection, autoimmunity, or irritation from endogenous or exogenous chemical agents, and it is not a feature of ischemic myocardial infarction. Coagulative necrosis is typical of myocardial infarction, but after 1 month, a scar would be present. The destruction of myocardial fibers precludes complete resolution. Nodular regeneration is typical of hepatocyte injury because hepatocytes are stable cells.

PBD9 103 BP9 66 PBD8 107–108 BP8 70–74