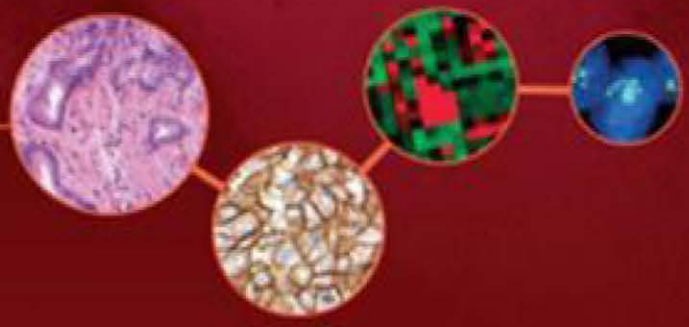
Robbins and Cotran

Review of Pathology

THIRD EDITION



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15. The Lung

PBD7 and PBD8 Chapter 15: The Lung

BP8 Chapter 13: The Lung

BP7 Chapter 13: Lungs and the Upper Respiratory Tract

1 A 63-year-old man has had progressively worsening dyspnea over the past 10 years. He has noticed a 5-kg weight loss in the past 2 years. He has a chronic cough with minimal sputum production and no chest pain. On physical examination, he is afebrile and normotensive. A chest radiograph shows extensive interstitial disease. Pulmonary function tests show low FVC and normal FEV_1/FVC ratio. Increased exposure to which of the following pollutants is most likely to produce these findings?

- □ (A) Silica
- □ (B) Tobacco smoke
- □ (C) Ozone
- □ (D) Wood dust
- □ (E) Carbon monoxide

2 A 50-year-old man has a history of chronic alcoholism. He is found in a stuporous condition after 3 days of binge drinking. On physical examination, his temperature is 39.2°C. A few crackles are heard on auscultation of the right lung base. A chest radiograph shows a 3-cm lesion with an air-fluid level in the right lower lobe. Which of the following organisms are most likely to be detected in bronchoalveolar lavage fluid?

- □ (A) *Staphylococcus aureus* and *Bacteroides fragilis*
- □ (B) *Mycobacterium tuberculosis* and *Aspergillus fumigatus*
- □ (C) *Nocardia asteroides* and *Actinomyces israelii*
- □ (D) Cytomegalovirus and *Pneumocystis carinii*
- □ (E) *Cryptococcus neoformans* and *Candida albicans*

3 A 45-year-old man has smoked two packs of cigarettes per day for 20 years. For the past 4 years, he has had a chronic cough with copious mucoid expectoration. During the past year, he has had several episodes of respiratory tract infections that were diagnosed as “viral flu,” and he developed difficulty breathing, tightness of the chest, and audible wheezing. His breathing difficulty was relieved by inhalation of a β-adrenergic agonist and disappeared after the chest infection had resolved. Which of the following pathologic conditions best describes these clinical findings?

- □ (A) Chronic bronchitis with cor pulmonale
- □ (B) Chronic bronchitis with asthmatic bronchitis
- □ (C) Chronic bronchitis with emphysema
- □ (D) Bronchiectasis
- □ (E) Hypersensitivity pneumonitis

4 A 75-year-old woman has had worsening lower leg edema and dyspnea for the past 5 years. On physical examination, her temperature is 36.9°C, pulse is 74/min, respirations are 19/min, and blood pressure is 110/75 mm Hg. There is dullness to percussion at the lung bases. A low rumbling heart murmur is present. An echocardiogram shows a large (4 cm) atrial septal defect. Which of the following pulmonary conditions is most likely to be present?

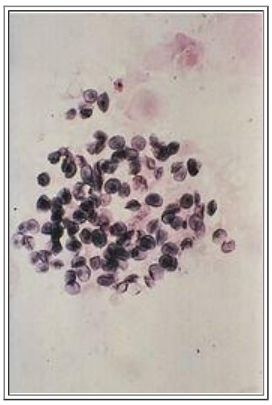
- □ (A) Pulmonary hypertension

□ (B) Interstitial fibrosis

□ (C) Vasculitis

□ (D) Granulomatous inflammation

□ (E) Pulmonary infarction



5 A 40-year-old woman has had malaise and an 11-kg weight loss over the past 3 years. She has had fever and a nonproductive cough with increasing dyspnea for the past 3 days. On physical examination, her temperature is 37.8°C, pulse is 82/min, respirations are 22/min, and blood pressure is 100/60 mm Hg. There is dullness to percussion over the lungs and diffuse crackles on auscultation. A chest radiograph shows extensive bilateral infiltrates. Bronchoalveolar lavage is done, and the fluid is stained with Gomori methenamine silver. The high-power microscopic appearance is shown in the figure. Which of the following underlying conditions is most likely present?

□ (A) Diabetes mellitus

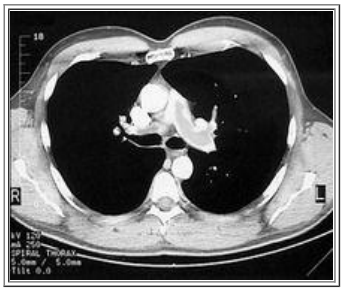
□ (B) Systemic lupus erythematosus

□ (C) AIDS

□ (D) Sarcoidosis

□ (E) Severe combined immunodeficiency

□ (F) Centrilobular emphysema



6 A 60-year-old man had a myocardial infarction 1 year ago and now has congestive heart failure. Over the past 24 hours, he has developed right-sided chest pain. On auscultation, there are lower lobe rales. He is afebrile, his pulse is 70/min, his respirations are 17/min and shallow, and his blood pressure is 130/85 mm Hg. A section of right lower lobe representative of his disease is shown in the figure. Which of the following clinical disorders is most likely to precede the appearance of this lesion?

□ (A) Chronic obstructive pulmonary disease

□ (B) HIV infection

□ (C) Nonbacterial thrombotic endocarditis

□ (D) Phlebothrombosis

□ (E) Polyarteritis nodosa

□ (F) Silicosis

7 A 52-year-old woman has had an increasingly severe cough productive of yellowish sputum for several days. On physical examination, her temperature is 38.9°C, and diffuse crackles are heard in the left lower lung. A chest radiograph shows left lower lung consolidation. Laboratory studies show a WBC count of 11,990/mm^3 with 72% segmented neutrophils, 8% bands, 16% lymphocytes, and 4% monocytes. The representative gross appearance of the lung is shown in the figure. Which of the following pathogens is most likely to be cultured from the patient's sputum?

□ (A) *Mycoplasma pneumoniae*

□ (B) *Streptococcus pneumoniae*

□ (C) *Cryptococcus neoformans*

□ (D) *Mycobacterium kansasii*

□ (E) *Candida albicans*

□ (F) *Pneumocystis jiroveci*

□ (G) *Nocardia brasiliensis*

8 A 44-year-old woman has a 4-month history of mild but persistent right-sided chest pain. On physical examination, there are no remarkable findings. A chest radiograph shows a pleural mass on the right side. No pleural effusions are seen. Chest CT scan shows a localized, circumscribed 3 × 7 cm mass that appears to be attached to the visceral pleura; the lungs and chest wall appear normal. At thoracotomy, the mass is excised. On microscopic examination, the mass is composed of spindle cells resembling fibroblasts with abundant collagenous stroma. The spindle cells mark for CD34, but are cytokeratin-negative. There has been no recurrence of the lesion. The patient does not smoke. She is a research biologist specializing in marine mammals (manatees). Which of the following is the most likely diagnosis?

□ (A) Bronchioloalveolar carcinoma

□ (B) Hamartoma

□ (C) Hodgkin lymphoma, nodular sclerosis type

□ (D) Malignant mesothelioma

□ (E) Metastatic breast carcinoma

□ (F) Solitary fibrous tumor

9 A 34-year-old man suddenly develops severe dyspnea with wheezing and is taken to the emergency department. On physical examination, his vital signs are temperature, 37°C; pulse, 95/min; respirations, 15/min; and blood pressure, 130/80 mm Hg. A chest radiograph shows increased lucency in all lung fields. A sputum cytologic specimen shows Curschmann spirals, Charcot-Leyden crystals, and acute inflammatory cells in a background of abundant mucus. Many of the inflammatory cells are eosinophils. What is the most likely diagnosis?

□ (A) Bronchiectasis

□ (B) Aspiration

□ (C) Bronchial asthma

□ (D) Centrilobular emphysema

□ (E) Chronic bronchitis

□ (F) Obstructive sleep apnea

10 A 50-year-old man comes to the physician with gradually increasing dyspnea and a 4-kg weight loss over the past 2 years. He admits to smoking two packs of cigarettes per day for 20 years, but states that he has not smoked for the past year. Physical examination shows an increase in the anteroposterior diameter of the chest ("barrel chest"). Auscultation of the chest shows decreased lung sounds. A chest radiograph shows bilateral hyperlucent lungs; the lucency is especially marked in the upper lobes. Pulmonary function tests show that the FEV_1 is markedly decreased, but the FVC is normal, and FEV_1/FVC ratio is decreased. Which of the following is most likely to contribute to the pathogenesis of his disease?

□ (A) Impaired hepatic release of α_1-antitrypsin

□ (B) Release of elastase from neutrophils

□ (C) Abnormal epithelial cell chloride ion transport

□ (D) Decreased ciliary motility with irregular dynein arms

□ (E) Macrophage recruitment and release of interferon-γ

11 A 10-year-old girl who participated in a routine health screening program developed a 10-mm area of induration on the left forearm 3 days after intracutaneous injection of 0.1 mL of purified protein derivative (PPD). She appears healthy. A screening chest radiograph is performed. Which of the following is most likely to be seen on the radiograph?

□ (A) Marked hilar adenopathy

□ (B) Upper lobe calcifications

□ (C) Extensive opacification

□ (D) Cavitary change

□ (E) Bilateral pleural effusions

□ (F) Reticulonodular densities

□ (G) No abnormal findings

12 A 33-year-old man has had increasing dyspnea for the past 8 years. On examination, there are decreased breath sounds over all lung fields. A chest radiograph shows flattened diaphragms and increased lucency in all lung fields. Pulmonary function tests show decreased FEV_1 and increased FVC. A sibling is similarly affected. What is the most likely mechanism for his pulmonary disease?

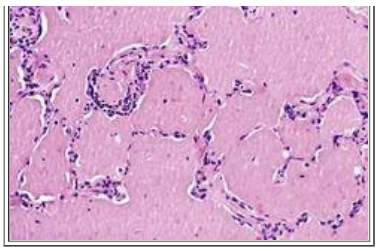
□ (A) Atopy with IgE binding to mast cells

□ (B) *CFTR* gene mutation

□ (C) Increased neutrophil proteases

□ (D) Prior infection with tuberculosis

□ (E) Reduced antielastase activity



13 A 33-year-old woman has had increasing dyspnea with cough for the past 10 days. Over the past 2 days, her cough has become productive of chunks of gelatinous sputum. On physical examination, she is afebrile. There is extensive dullness to percussion over all lung fields. A chest radiograph shows diffuse opacification bilaterally. A transbronchial biopsy is performed; the figure shows the appearance of the light microscopic examination. On electron microscopy, there are many lamellar bodies. Antibody directed against which of the following substances is most likely to cause her illness?

- □ (A) α_1-Antitrypsin
- □ (B) *CFTR*
- □ (C) DNA topoisomerase I
- □ (D) Glomerular basement membrane
- □ (E) Granulocyte-macrophage colony-stimulating factor
- □ (F) Neutrophilic myeloperoxidase

14 A 50-year-old man has developed truncal obesity, back pain, and skin that bruises easily over the past 5 months. On physical examination, he is afebrile, and his blood pressure is 160/95 mm Hg. A chest radiograph shows an ill-defined, 4-cm mass involving the left hilum of the lung. Cytologic examination of bronchial washings from bronchoscopy shows round cells that have the appearance of lymphocytes but are larger. The patient is told that, although his disease is apparently localized to one side of the chest cavity, surgical treatment is unlikely to be curative. He also is advised to stop smoking. Which of the following neoplasms is most likely to be present in this patient?

- □ (A) Adenocarcinoma
- □ (B) Bronchial carcinoid
- □ (C) Bronchioloalveolar carcinoma
- □ (D) Large-cell carcinoma
- □ (E) Metastatic renal cell carcinoma
- □ (F) Non-Hodgkin lymphoma
- □ (G) Small-cell carcinoma
- □ (H) Squamous cell carcinoma

15 After a hemicolectomy to remove a colon carcinoma, a 53-year-old man develops respiratory distress. He is intubated and receives mechanical ventilation with 100% oxygen. Three days later, his arterial oxygen saturation decreases. A chest radiograph shows increasing opacification in all lung fields. A transbronchial lung biopsy specimen shows hyaline membranes lining distended alveolar ducts and sacs. Which of the following most likely represents the fundamental mechanism underlying these morphologic changes?

- □ (A) Reduced production of surfactant by type II alveolar cells
- □ (B) Disseminated intravascular coagulation
- □ (C) Aspiration of oropharyngeal contents with bacteria
- □ (D) Leukocyte-mediated injury to alveolar capillary endothelium

□ (E) Release of fibrogenic cytokines by macrophages

16 A previously healthy, 29-year-old man who has had no major illnesses experiences acute onset of hemoptysis. On physical examination, he has a temperature of 37°C, pulse of 83/min, respirations of 23/min, and blood pressure of 150/95 mm Hg. A chest radiograph shows bilateral fluffy infiltrates. A transbronchial lung biopsy shows focal necrosis of alveolar walls associated with prominent intra-alveolar hemorrhage. Two days later, he has oliguria. The serum creatinine level is 2.9 mg/dL, and urea nitrogen is 31 mg/dL. Which of the following serologic tests is most likely to be positive in this patient?

□ (A) Antineutrophil cytoplasmic antibody

□ (B) Anti-DNA topoisomerase I antibody

□ (C) Anti–glomerular basement membrane antibody

□ (D) Antimitochondrial antibody

□ (E) Antinuclear antibody

17 A 49-year-old man has had increasing dyspnea for the past 4 years. He has an occasional cough with minimal sputum production. On physical examination, his lungs are hyperresonant with expiratory wheezes. Pulmonary function tests show increased total lung capacity (TLC) with slightly increased FVC and decreased FEV_1 and FEV_1/FVC ratio. Arterial blood gas measurement shows pH of 7.35; Po_2, 65 mm Hg; and Pco_2, 45 mm Hg. Which of the following disease processes should most often be suspected as a cause of these findings?

□ (A) Primary adenocarcinoma

□ (B) Centrilobular emphysema

□ (C) Diffuse alveolar damage

□ (D) Chronic pulmonary embolism

□ (E) Sarcoidosis

□ (F) Pneumoconiosis

18 A 70-year-old woman is referred to an ophthalmologist because of difficulty with her right eye. She also has pain in the right upper chest. The findings on physical examination include enophthalmos, meiosis, anhidrosis, and ptosis. A chest radiograph shows right upper lobe opacification and bony destruction of the right first rib. Which of the following conditions is most likely to be present?

□ (A) Bronchopneumonia

□ (B) Bronchiectasis

□ (C) Bronchogenic carcinoma

□ (D) Sarcoidosis

□ (E) Tuberculosis

19 A previously healthy, 20-year-old woman has had a low-grade fever for the past 2 weeks. On physical examination, her temperature is 37.7°C; there are no other remarkable findings. The gross appearance of the lung shown in the figure is representative of her disease. Which of the following studies is most likely to report a positive result?

- □ (A) Anticentromeric antibody
- □ (B) Antinuclear antibody
- □ (C) HIV serologic test
- □ (D) Rapid plasma reagin
- □ (E) Rheumatoid factor
- □ (F) Sweat chloride
- □ (G) Tuberculin skin test

20 A 60-year-old farmer has a 15-year history of increasing dyspnea. On physical examination, his temperature is 37.6°C. A chest radiograph shows a bilateral increase in linear markings. Pulmonary function tests show reduced FVC with a normal FEV_1. A transbronchial lung biopsy specimen shows interstitial infiltrates of lymphocytes and plasma cells, minimal interstitial fibrosis, and small granulomas. What is the most likely cause of this clinical and pathologic picture?

- □ (A) Chronic inhalation of silica particles
- □ (B) Prolonged exposure to asbestos
- □ (C) Hypersensitivity to spores of actinomycetes
- □ (D) Infection with *Mycobacterium tuberculosis*
- □ (E) Auto-antibodies that react with alveolar basement membranes

21 A 20-year-old, previously healthy man is jogging one morning when he trips and falls to the ground. He suddenly becomes markedly short of breath. His jogging partner brings him to the emergency department where on examination there are no breath sounds audible over the right chest. A chest radiograph shows shift of the mediastinum from right to left. A right chest tube is inserted, and air rushes out. Which of the following types of obstructive lung disease is the most likely diagnosis?

- □ (A) Asthma
- □ (B) Bronchiectasis
- □ (C) Centriacinar emphysema
- □ (D) Chronic bronchitis
- □ (E) Distal acinar emphysema

□ (F) Panlobular emphysema

22 A 6-year-old child puts the contents of a bag of peanuts in his mouth and then takes a deep breath with the idea of blowing the peanuts out all over his sister. He aspirates a peanut during this maneuver. One day later, he has slight dyspnea. On physical examination, his temperature is 36.8°C, pulse is 70/min, respirations are 17/min, and blood pressure is 90/60 mm Hg. There are decreased breath sounds on auscultation and increased tympany on percussion over the right lower lung posteriorly. Chest CT scan shows a hemicircular area of density in the right lower lobe. Laboratory studies show a hemoglobin concentration of 13.6 g/dL and WBC count of 6175/mm^3. Gram stain of sputum shows normal flora. Which of the following complications has this child most likely developed?

□ (A) Bronchiectasis

□ (B) Resorption atelectasis

□ (C) Bronchopneumonia

□ (D) Pneumothorax

□ (E) Lung abscess

23 A 49-year-old man has sudden onset of severe lower abdominal pain with hematuria. He passes a ureteral calculus. Laboratory studies show that the calculus is composed of calcium oxalate. He is found to have a serum calcium concentration of 10.2 mg/dL, serum phosphorus level of 2.9 mg/dL, and serum albumin level of 4.6 g/dL. A chest radiograph shows a 7-cm hilar mass in the right lung. Chest CT scan shows prominent central necrosis in this mass. Which of the following neoplasms is most likely to be associated with these findings?

□ (A) Metastatic colonic adenocarcinoma

□ (B) Small cell anaplastic carcinoma

□ (C) Bronchioloalveolar carcinoma

□ (D) Squamous cell carcinoma

□ (E) Large-cell carcinoma

24 A 62-year-old man who has smoked one pack of cigarettes per day for the past 45 years has developed a severe cough with hemoptysis over the past month. He has experienced a 10-kg weight loss over the past year. On physical examination, he is afebrile. Laboratory studies show a serum Na^+ of 120 mmol/L; K^+, 3.8 mmol/L; Cl^-, 90 mmol/L; CO_2, 24 mmol/L; glucose, 75 mg/dL; creatinine, 1.2 mg/dL; calcium, 8.1 mg/dL; phosphorus, 2.9 mg/dL; and albumin, 4.2 g/dL. Which of the following findings is most likely to be seen on a chest radiograph?

□ (A) Bilateral fluffy infiltrates

□ (B) Bilateral upper lobe cavitation

□ (C) Diaphragmatic pleural calcified plaques

□ (D) Left pneumothorax

□ (E) Right middle lobe subpleural 2-cm nodule with hilar adenopathy

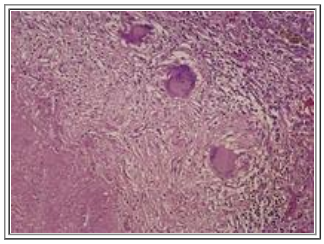
□ (F) Right perihilar 4-cm mass

□ (G) Right upper lung 3-cm nodule with air-fluid level

25 A 64-year-old man, who is a chain smoker, sees his physician because he had had a cough and a 5-kg weight loss over the past 3 months. Physical examination shows clubbing of the fingers. He is afebrile. A chest radiograph shows no hilar adenopathy, but there is cavitation within a 3-cm lesion near the right hilum. Laboratory studies are unremarkable except for a calcium level of 12.3 mg/dL, phosphorus concentration of 2.4 mg/dL, and albumin level of 3.9 g/dL. Bronchoscopy shows a lesion almost occluding the right main stem bronchus. A biopsy is performed. Based on the pathologist's report and further testing, including chest and abdomen CT and bone scans, the patient is told that a surgical

procedure with curative intent would be attempted. Which of the following neoplasms is most likely to be present in this patient?

- □ (A) Adenocarcinoma
- □ (B) Bronchioloalveolar carcinoma
- □ (C) Kaposi sarcoma
- □ (D) Large-cell carcinoma
- □ (E) Metastatic renal cell carcinoma
- □ (F) Non-Hodgkin lymphoma
- □ (G) Small-cell carcinoma
- □ (H) Squamous cell carcinoma



26 A 46-year-old woman goes to the physician for a routine health maintenance examination. On physical examination, there are no remarkable findings. Her body mass index is 22. She does not smoke. A tuberculin skin test is positive. A chest radiograph shows a solitary, 3-cm left upper lobe mass. The mass is removed at thoracotomy by wedge resection. The microscopic appearance of this lesion is shown in the figure. Which of the following is the most likely diagnosis?

- □ (A) Pulmonary hamartoma
- □ (B) Pulmonary infarction
- □ (C) *Mycobacterium tuberculosis* infection
- □ (D) Lung abscess
- □ (E) Primary adenocarcinoma

27 A 3-year-old boy has had a cough, headache, and slight fever for 5 days. His mother becomes concerned because he is now having increasing respiratory difficulty. On physical examination, his temperature is 37.8°C, pulse is 81/min, respirations are 25/min, and blood pressure is 90/55 mm Hg. On auscultation, there are inspiratory crackles, but no dullness to percussion or tympany. Respiratory syncytial virus is isolated from a sputum sample. Which of the following chest radiographic patterns is most likely to be present?

- □ (A) Lobar consolidation
- □ (B) Interstitial infiltrates
- □ (C) Large pleural effusions
- □ (D) Upper lobe cavitation
- □ (E) Hyperinflation
- □ (F) Hilar lymphadenopathy
- □ (G) Peripheral mass

28 A 35-year-old man comes to the nurse practitioner because of a 5-year history of episodes of wheezing and coughing.

The episodes are more common during the winter months, and he has noticed that they often follow minor respiratory tract infections. In the period between the episodes, he can breathe normally. There is no family history of asthma or other allergies. On physical examination, there are no remarkable findings. A chest radiograph shows no abnormalities. A serum IgE level and WBC count are normal. Which of the following is the most likely mechanism that contributes to the findings in this illness?

- □ (A) Accumulation of mast cells in airspaces after viral infections
- □ (B) Emigration of eosinophils into bronchi
- □ (C) Bronchial hyper-reactivity to virus-induced inflammation
- □ (D) Secretion of interleukin (IL)-4 and IL-5 by antiviral T cells
- □ (E) Hyper-responsiveness to inhaled spores of *Aspergillus*

29 A 78-year-old man has had increasing dyspnea without cough or increased sputum production for the past 4 months. On physical examination, he is afebrile. Breath sounds are reduced in all lung fields. A chest CT scan shows a dense, bright, right pleural mass encasing most of the left lung. Microscopic examination of a pleural biopsy specimen shows spindle and cuboidal cells that invade adipose tissue. Inhalation of which of the following pollutants is the most likely factor in the pathogenesis of this mass?

- □ (A) Asbestos
- □ (B) Bird dust
- □ (C) Silica
- □ (D) Cotton fibers
- □ (E) Coal dust
- □ (F) Ozone

30 An epidemiologic study is conducted in which individuals with chronic lung diseases undergo pulmonary function testing and blood gas analysis. One group is found to have normal FEV_1, decreased FVC, and normal Pco_2. In another group, FEV_1 is decreased more than FVC, the FEV_1/FVC ratio is 65%, and Pco_2 is increased. Both groups have increased bouts of pulmonary infections. Autopsy data are collected for the individuals whose underlying cause of death is pulmonary disease. Which of the following morphologic changes is most likely to be seen in both groups?

- □ (A) Marked medial thickening of pulmonary arterioles
- □ (B) Destruction of elastic tissue in alveolar walls
- □ (C) Fibrosis of alveolar walls
- □ (D) Hemorrhage in alveolar lumen
- □ (E) Hyaline membranes lining airspaces

31 A 35-year-old woman has experienced multiple bouts of severe necrotizing pneumonia with *Haemophilus influenzae, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Serratia marcescens* cultured from her sputum since childhood. She now has for weeks at a time a cough productive of large amounts of purulent sputum. On physical examination, there is dullness to percussion with decreased breath sounds over the right mid to lower lung fields. A chest radiograph shows areas of right lower lobe consolidation. A bronchogram shows marked dilation of right lower lobe bronchi. Which of the following mechanisms is the most likely cause of airspace dilation in this patient?

- □ (A) Unopposed action of neutrophil-derived elastase
- □ (B) Congenital weakness of supporting structures of the bronchial wall
- □ (C) Diffuse alveolar damage

□ (D) Destruction of bronchial walls by recurrent inflammation

□ (E) Damage to bronchial mucosa by major basic protein of eosinophils

32 A 56-year-old man with ischemic heart disease undergoes coronary artery bypass graft surgery under general anesthesia. Two days postoperatively, he experiences increasing respiratory difficulty with decreasing arterial oxygen saturation. On physical examination, he is afebrile. His heart rate is regular at 78/min, respirations are 20/min, and blood pressure is 135/85 mm Hg. The hemoglobin concentration has remained unchanged, at 13.7 g/dL, since surgery. After he coughs up a large amount of mucoid sputum, his condition improves. Which of the following is the most likely explanation of these findings?

□ (A) Resorption atelectasis

□ (B) Compression atelectasis

□ (C) Microatelectasis

□ (D) Contraction atelectasis

□ (E) Relaxation atelectasis

33 A 24-year-old man has had increasing dyspnea for the past 10 weeks. On physical examination, he is afebrile. There is dullness to percussion over the lungs posteriorly and decreased breath sounds. A chest radiograph shows large bilateral pleural effusions and widening of the mediastinum. Thoracentesis is performed on the left side and yields 500 mL of milky white fluid. Laboratory studies of the fluid show a high protein content; microscopy shows many lymphocytes and fat globules. What is the most likely diagnosis?

□ (A) Bacterial pneumonia complicated by empyema

□ (B) Congenital heart disease

□ (C) Marfan syndrome with aortic dissection

□ (D) Micronodular cirrhosis

□ (E) Miliary tuberculosis

□ (F) Non-Hodgkin lymphoma

34 A 42-year-old man has had chronic sinusitis for several months. He now sees his physician because of malaise and a mild fever that has persisted for 3 weeks. On physical examination, his temperature is 37.9°C. On auscultation, a few crackles are heard over the lungs. Laboratory studies show serum urea nitrogen of 35 mg/dL; creatinine, 4.3 mg/dL; ALT, 167 U/L; AST, 154 U/L; and total bilirubin, 1.1 mg/dL. The C-ANCA titer is 1 : 256. A transbronchial lung biopsy is performed, and microscopic examination shows necrotizing capillaritis with mild intra-alveolar hemorrhage. A granuloma is seen within the wall of a necrotic small artery. Which of the following is the most likely diagnosis?

□ (A) Goodpasture syndrome

□ (B) Hypersensitivity pneumonitis

□ (C) Systemic lupus erythematosus

□ (D) Wegener granulomatosis

□ (E) Diffuse systemic sclerosis

35 For the past 6 years, a 45-year-old woman has had increasing respiratory difficulty that limits her activities. She does not smoke. On physical examination, she is afebrile and normotensive. Her lungs are hyperresonant. A chest radiograph shows flattening of the diaphragmatic leaves. Laboratory studies show the PiZZ phenotype of α_1-antitrypsin deficiency. Which of the following is most likely present in the lungs?

□ (A) Sarcoidosis

□ (B) Bronchiectasis

□ (C) Interstitial fibrosis

□ (D) Microatelectasis

□ (E) Panacinar emphysema

36 A clinical study is conducted in which patients who have undergone surgical procedures with intubation, mechanical ventilation, and general anesthesia are followed to determine the number and type of postoperative complications. The study group is found to have a higher incidence of pulmonary infections with leukocytosis and chest radiographs showing consolidation in the 2 weeks following their surgical procedure than patients who were not intubated and did not receive general anesthesia. Anesthesia is most likely to produce this effect via which of the following mechanisms?

□ (A) Decreased ciliary function

□ (B) Neutropenia

□ (C) Tracheal erosions

□ (D) Diminished macrophage activity

□ (E) Hypogammaglobulinemia

37 A 45-year-old man, a nonsmoker, has experienced a 3-kg weight loss over the past 3 months after the loss of his job. He recently developed a low-grade fever and cough with mucoid sputum production, and after 1 week, he noticed blood-streaked sputum. On physical examination, his temperature is 37.7°C. There are bilateral crackles in the left upper lobe on auscultation of the chest. Chest CT scan shows a 3-cm left upper lobe nodule with decreased attenuation centrally. Laboratory studies show hemoglobin, 14.5 g/dL; platelet count, 211,400/mm^3; and WBC count, 9890/mm^3 with 40% segmented neutrophils, 2% bands, 40% lymphocytes, and 18% monocytes. Which of the following findings in his sputum sample is most likely to be present?

□ (A) Acid-fast bacilli

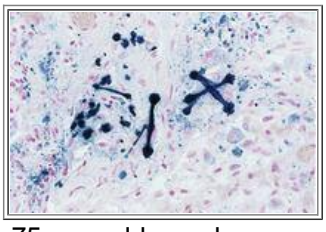
□ (B) Branching septate hyphae

□ (C) Charcot-Leyden crystals

□ (D) Foreign body giant cells

□ (E) Gram-negative bacilli

□ (F) Small dark neoplastic cells



38 A 75-year-old man has experienced increasing dyspnea for the past 4 years. On physical examination, he is afebrile, with a pulse of 70/min, respirations 20/min, and blood pressure 120/75 mm Hg. A chest radiograph shows increased interstitial markings, but no effusions. The right border of the heart and the pulmonary arteries are prominent. A transbronchial biopsy is performed; the figure shows the microscopic appearance with Prussian blue stain. Which of the following is the most likely diagnosis?

□ (A) Anthracosis

□ (B) Berylliosis

□ (C) Silicosis

□ (D) Calcinosis

□ (E) Asbestosis

39 A study is conducted of individuals who smoked at least one pack of cigarettes per day for 30 years. These individuals undergo pulmonary function testing, and a large subset is found to have decreased FEV_1, normal to decreased FVC, and FEV_1/FVC ratios less than 70%. All participants in the study are found to have an increased risk of pulmonary bacterial infections. They are found to have increasing hypoxemia over time. Autopsy data from the subset of individuals in the study with low FEV_1/FVC ratio who die of their underlying pulmonary disease are analyzed. Which of the following structures in the lungs is likely to be affected the most by the underlying disease?

□ (A) Alveolar sac

□ (B) Terminal bronchiole

□ (C) Alveolar duct

□ (D) Respiratory bronchiole

□ (E) Capillary

40 A 40-year-old man has had an increasing cough with hemoptysis for 2 weeks. On physical examination, his temperature is 38.2°C. A chest radiograph shows an area of consolidation in the right upper lobe. His condition improves with antibiotic therapy; however, the cough and hemoptysis persist for 2 more weeks. Chest CT scan shows right upper lung atelectasis. Bronchoscopic examination shows an obstructive mass filling the bronchus of the right upper lobe. Which of the following neoplasms is most likely to produce these findings?

□ (A) Hamartoma

□ (B) Adenocarcinoma

□ (C) Large-cell carcinoma

□ (D) Kaposi sarcoma

□ (E) Carcinoid tumor

41 A 12-year-old girl is brought to the physician because of a history of coughing and wheezing and repeated attacks of difficulty breathing. The attacks are particularly common in the spring. During an episode of acute respiratory difficulty, a physical examination shows that she is afebrile. Her lungs are hyperresonant, and a chest radiograph shows increased lucency of all lung fields. Laboratory tests show an elevated serum IgE level and peripheral blood eosinophilia. A sputum sample examined microscopically also has increased numbers of eosinophils. Which of the following histologic features is most likely to characterize the lung in this patient's acute condition?

□ (A) Dilation of respiratory bronchiole and distention of alveoli

□ (B) Dilation of bronchi with inflammatory destruction of walls

□ (C) Interstitial and alveolar edema with presence of hyaline membranes that line alveoli

□ (D) Thickening of bronchial epithelial basement membrane and hypertrophy of bronchial smooth muscle

□ (E) Patchy areas of consolidation surrounding bronchioles and neutrophilic exudate in affected alveoli

42 A 40-year-old man comes to the physician because of a 6-year history of increasing shortness of breath and weakness. On physical examination, he is afebrile and normotensive. A radiograph of the chest shows diffuse interstitial markings. Pulmonary function tests indicate diminished FVC, decreased diffusing capacity, and a normal FEV_1/FVC ratio. Which of the following sets of pathologic changes is most likely to be found in the lungs?

□ (A) Voluminous lungs with uniform dilation of airspaces distal to respiratory bronchioles

□ (B) Chronic inflammatory cells in bronchi with a marked increase in size of mucous glands

□ (C) Honeycomb lung with widespread alveolar septal fibrosis and hyperplasia of type II pneumocytes

□ (D) Chronic inflammation of bronchial walls with prominence of eosinophils

□ (E) Edematous, congested lungs with widespread necrosis of alveolar epithelial cells and prominent hyaline membranes

43 A clinical study is performed that includes patients who are hospitalized for more than 2 weeks and who were bedridden for more than 90% of that time. These patients undergo Doppler venous ultrasound examination of the lower extremities, blood gas testing, and radiographic pulmonary ventilation and perfusion scanning. A subset of patients is found who have abnormal ultrasound results suggestive of thrombosis, blood gas parameters with a lower Po_2, and pulmonary perfusion defects. Which of the following is most likely to be observed in the most patients in this subset?

□ (A) Sudden death

□ (B) Cor pulmonale

□ (C) Hemoptysis

□ (D) Dyspnea

□ (E) No symptoms

44 A 55-year-old man has experienced increasing respiratory difficulty for the past 18 months. He can no longer pass the yearly physical examination required to maintain active status as an airline pilot, the only occupation that he has ever had. There are no remarkable findings on physical examination. Pulmonary function tests show that FEV_1 is normal, but FVC is diminished. A chest radiograph shows diffuse interstitial disease, but no masses and no hilar adenopathy. The results of ANA and anti-DNA topoisomerase I antibody testing are negative. What is the most likely diagnosis?

□ (A) Scleroderma

□ (B) Goodpasture syndrome

□ (C) Silicosis

□ (D) Diffuse alveolar damage

□ (E) Idiopathic pulmonary fibrosis

45 A 54-year-old woman has had a mild fever with cough for the past week. Her symptoms gradually improve over the next 10 days. She then begins to have increasing fever, cough, shortness of breath, and malaise. On physical examination, her temperature is 37.9°C. There are inspiratory crackles on auscultation of the chest. A chest radiograph shows bilateral, patchy, small alveolar opacities. Chest CT scan shows small, scattered, ground-glass and nodular opacities. A transbronchial biopsy specimen shows polypoid plugs of loose fibrous tissue and granulation tissue filling bronchioles, along with a surrounding interstitial infiltrate of mononuclear cells. She receives a course of corticosteroid therapy, and her condition improves. Which of the following is the most likely diagnosis?

□ (A) Bronchiolitis obliterans with organizing pneumonia

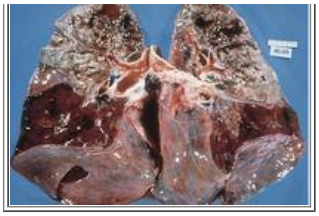
□ (B) Desquamative interstitial pneumonitis

□ (C) Diffuse alveolar damage

□ (D) Hypersensitivity pneumonitis

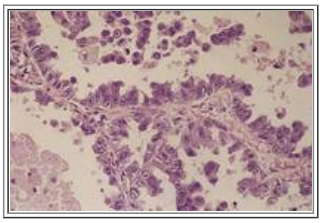
□ (E) Pulmonary alveolar proteinosis

□ (F) Wegener granulomatosis



46 A 56-year-old man has had fever, night sweats, and a 3-kg weight loss over the past 4 months. In the past month, he has had episodes of hemoptysis. He dies of respiratory failure and hypoxemia. The appearance of the lungs at autopsy is shown in the figure. Infection with which of the following organisms is most likely to have produced these findings?

- □ (A) *Candida albicans*
- □ (B) *Coccidioides immitis*
- □ (C) Influenza A
- □ (D) *Klebsiella pneumoniae*
- □ (E) *Legionella pneumophila*
- □ (F) *Mycobacterium tuberculosis*
- □ (G) *Mycoplasma pneumoniae*
- □ (H) *Nocardia asteroides*



47 A 57-year-old woman comes to her physician because she has had a cough and pleuritic chest pain for the past 3 weeks. On physical examination, she is afebrile. Some crackles are audible over the left lower lung on auscultation. A chest radiograph shows an ill-defined area of opacification in the left lower lobe. After 1 month of antibiotic therapy, her condition has not improved, and the lesion is still visible radiographically. CT-guided needle biopsy of the left lower lobe of the lung is performed, and the specimen has the histologic appearance shown in the figure. Which of the following neoplasms is most likely to be present in this patient?

- □ (A) Adenocarcinoma
- □ (B) Bronchioloalveolar carcinoma
- □ (C) Hamartoma
- □ (D) Large-cell carcinoma
- □ (E) Mesothelioma
- □ (F) Metastatic breast carcinoma
- □ (G) Squamous cell carcinoma

48 A 65-year-old man worked in a shipyard for 10 years, and then he worked for 5 years for a company that installed fire-retardant insulation. He experienced increasing dyspnea for several years and eventually died of progressive respiratory failure with hypoxemia. At autopsy, a firm, tan mass encased the left lung. Within the lung parenchyma adjacent to the mass, many ferruginous bodies were identified on microscopic examination. Which of the following findings is most likely to have been seen on a chest radiograph?

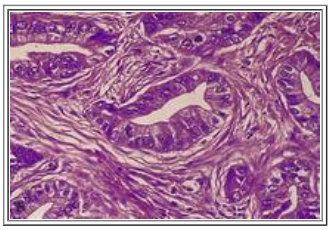
- □ (A) Bilateral fluffy infiltrates

□ (B) Bilateral upper lobe cavitation

□ (C) Diaphragmatic pleural calcified plaques

□ (D) Left main bronchus, 1.5-cm endobronchial mass

□ (E) Right middle lobe bronchial dilation



49 A 60-year-old woman has had a chronic nonproductive cough for 4 months along with loss of appetite and a 6-kg weight loss. She does not smoke. On physical examination there are no remarkable findings. Her chest radiograph shows a right peripheral subpleural mass. A fine-needle aspiration biopsy is performed, and she undergoes a right lower lobectomy. The microscopic appearance of the lesion is shown in the figure. She receives therapy directed at epithelial growth factor receptor (EGFR) and remains symptom-free for the next 10 years. Which of the following neoplasms did she most likely have?

□ (A) Adenocarcinoma

□ (B) Bronchial carcinoid

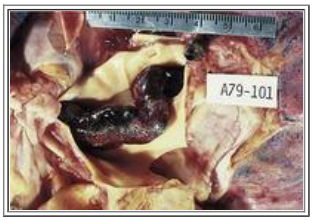
□ (C) Bronchioloalveolar carcinoma

□ (D) Hamartoma

□ (E) Large-cell carcinoma

□ (F) Small-cell anaplastic carcinoma

□ (G) Squamous cell carcinoma



50 A 68-year-old woman had a cerebral infarction and was hospitalized for 3 weeks. Her condition improved, and she was able to get up and move about with assistance. A few minutes after walking to the bathroom, she experienced sudden onset of severe dyspnea. Despite resuscitative measures, she died 30 minutes later. The major autopsy finding is shown in the figure. Which of the following is the most likely mechanism for sudden death in this patient?

□ (A) Atelectasis

□ (B) Hemorrhage

□ (C) Acute right-sided heart failure

□ (D) Bronchoconstriction

□ (E) Edema

51 A 61-year-old woman has experienced increasing dyspnea and a nonproductive cough for 5 months. On physical examination, her temperature is 37.7°C. A chest radiograph shows prominent hilar lymphadenopathy with reticulonodular infiltrates bilaterally. A transbronchial biopsy is performed, and the microscopic findings include interstitial fibrosis and

small, noncaseating granulomas. One granuloma contains an asteroid body in a giant cell. The medical history indicates that she smoked cigarettes for 10 years, but stopped 5 years ago. Which of the following is the most likely cause of her illness?

- □ (A) Delayed hypersensitivity response to an unknown antigen
- □ (B) Immune complexes formed in response to inhaled antigens
- □ (C) Diffuse alveolar damage
- □ (D) Smoke inhalation for many years
- □ (E) Infection with atypical mycobacteria

52 A 62-year-old man is a smoker with a 10-year history of cough productive of copious mucopurulent sputum. Over the past 6 months, he has developed progressive dyspnea. Physical examination shows bilateral pedal edema and a soft but enlarged liver. A chest radiograph shows bilateral pleural effusions and a prominent heart border on the right side. Arterial blood gas values are Po_2, 60 mm Hg; Pco_2, 55 mm Hg; pH, 7.31; and HCO_3^-, 28 mEq/L. The patient is intubated and placed on a ventilator, and he requires increasing amounts of oxygen. He dies 6 days later. At autopsy, which of the following microscopic findings is most likely to be characteristic of his underlying pulmonary disease?

- □ (A) Infiltrates of eosinophils
- □ (B) Extensive interstitial fibrosis
- □ (C) Granulomas in bronchovascular distribution
- □ (D) Carcinoma filling lymphatic spaces
- □ (E) Hypertrophy of bronchial submucosal glands

53 A 25-year-old woman has had progressive dyspnea and fatigue for the past 2 years. On physical examination, she has pedal edema, jugular venous distention, and hepatomegaly. Lung fields are clear on auscultation. Chest CT scan shows right heart enlargement. Cardiac catheterization is performed, and the pulmonary arterial pressure is increased, without gradients across the pulmonic valve, and no shunts are noted. A transbronchial biopsy is performed, and microscopic examination shows plexiform lesions of peripheral pulmonary arteries, with striking smooth muscle hypertrophy causing marked luminal narrowing. A mutation in a gene encoding for which of the following is most likely to cause her pulmonary disease?

- □ (A) Bone morphogenetic receptor 2 (BMPR2)
- □ (B) Fibrillin-1
- □ (C) Lysyl hydroxylase
- □ (D) Endothelin
- □ (E) Atrial natriuretic factor
- □ (F) Renin
- □ (G) Endothelial nitric oxide synthetase (eNOS)

54 A 30-year-old man is hospitalized after a motor vehicle accident in which he sustains blunt trauma to the chest. On physical examination, there are contusions to the right side of the chest, but no lacerations. Within 1 hour after the accident, he develops sudden difficulty breathing and marked pain on the right side. Vital signs now show that he is afebrile; his pulse is 80/min, respirations are 23/min, and blood pressure is 100/65 mm Hg. Breath sounds are not audible, and there is tympany to percussion on the right side. Which of the following radiographic findings is most likely to be present?

- □ (A) Large bilateral pleural effusions on chest radiograph
- □ (B) High probability of pulmonary embolus on ventilation/perfusion scan

□ (C) Extensive centrilobular emphysema on chest CT scan

□ (D) Right rib fractures with pneumothorax on chest radiograph

□ (E) Bilateral patchy infiltrates on chest radiograph

55 A pharmaceutical company is designing pharmacologic agents to treat the recurrent bronchospasms characteristic of bronchial asthma. Several agents that are antagonistic of various mediators of bronchoconstriction are tested for efficacy in reducing the frequency and severity of acute asthmatic episodes. An antagonist of which of the following mediators is most likely to be effective in the early, acute phase of bronchial asthma?

□ (A) Complement C3a and C3b

□ (B) Platelet-activating factor

□ (C) Interleukin-5

□ (D) Leukotrienes C_4 and E_4

□ (E) Histamine

□ (F) Tumor necrosis factor and interleukin-1

56 A 59-year-old woman visits her physician because of shortness of breath that has worsened over the past 2 months. On physical examination, she is afebrile. There are diffuse rales on auscultation, with dullness to percussion up to the mid lung fields. A chest radiograph shows bilateral pleural effusions, with effusions on the right greater than those on the left. Thoracentesis yields 700 mL of fluid from the right pleural cavity. The fluid is clear and slightly yellow-tinged. A cell count performed on the fluid shows 1/mm^3 WBCs and 12/mm^3 RBCs. What is the most probable cause of these findings?

□ (A) Metastatic adenocarcinoma

□ (B) Congestive heart failure

□ (C) Systemic lupus erythematosus

□ (D) Chronic renal failure

□ (E) Mediastinal malignant lymphoma

57 A 40-year-old woman has never smoked and works as a file clerk at a university that designates all work areas as “nonsmoking.” She goes to the physician for a routine health maintenance examination. On physical examination, there are no remarkable findings. A routine chest radiograph shows a 3-cm, sharply demarcated mass in the left upper lobe of the lung. Fine-needle aspiration of the mass is attempted, but the pathologist performing the procedure remarks, “This is like trying to biopsy a ping-pong ball.” No tissue is obtained. Thoracotomy with wedge resection is performed. On sectioning, the mass has a firm, glistening, bluish white cut surface. A culture of the mass yields no growth. Which of the following terms best describes this mass?

□ (A) Adenocarcinoma

□ (B) Hamartoma

□ (C) Large-cell carcinoma

□ (D) Mesothelioma

□ (E) Non-Hodgkin lymphoma

□ (F) Squamous cell carcinoma

58 One day after moving into a new apartment, a 25-year-old man experiences acute onset of fever, cough, dyspnea, headache, and malaise. The symptoms subside over several days when he visits a friend in another city. On the day of his return, he visits the physician. There are no remarkable findings on physical examination. A chest radiograph also is

unremarkable. Which of the following is most likely to produce these findings?

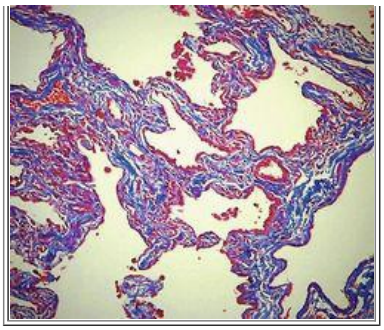
- □ (A) Antigen-antibody complex formation
- □ (B) Attachment of antibodies to basement membrane
- □ (C) Formation of mycolic acid
- □ (D) Generation of prostaglandins
- □ (E) Release of histamine
- □ (F) Release of leukotrienes
- □ (G) Toxic injury to type I pneumocytes

59 A 20-year-old man has had a mild fever with nonproductive cough, headache, and myalgia for the past week. He goes to the physician, who records a temperature of 37.9°C and notes erythema of the pharynx. Diffuse crackles are heard on auscultation of the lungs. A chest radiograph shows bilateral extensive patchy infiltrates. A sputum Gram stain shows normal flora. Cold agglutinin titer is elevated. He receives a course of erythromycin therapy, and his condition improves. Infection with which of the following organisms is most likely to produce these findings?

- □ (A) *Legionella pneumophila*
- □ (B) *Mycobacterium fortuitum*
- □ (C) *Mycoplasma pneumoniae*
- □ (D) *Nocardia asteroides*
- □ (E) Respiratory syncytial virus

60 A 26-year-old woman from East Asia developed a fever with chills over the past 4 days. Yesterday, she had increasing shortness of breath and a nonproductive cough. On physical examination, her temperature is 38.6°C. A chest radiograph shows right lower lobe infiltrates. Laboratory studies show hemoglobin, 13.4 g/dL; hematocrit, 40.2%; platelet count, 78,400/mm^3; and WBC count, 3810/mm^3 with 77% segmented neutrophils, 2% bands, 5% lymphocytes, and 16% monocytes. Over the next 2 days, she has increasing respiratory distress requiring intubation and mechanical ventilation. A repeat chest radiograph shows worsening bilateral infiltrates. Her oxygen saturation has decreased to 90%. Infection with which of the following is most likely to have caused this patient's illness?

- □ (A) Coronavirus
- □ (B) Cytomegalovirus
- □ (C) Ebola virus
- □ (D) Herpes simplex virus
- □ (E) HIV
- □ (F) Paramyxovirus
- □ (G) Respiratory syncytial virus



61 A 63-year-old man has had worsening dyspnea with a nonproductive cough for the past 9 months. On physical examination, he is afebrile and normotensive. His heart rate is 77/min and regular. On auscultation of the chest, diffuse dry crackles are heard in all lung fields. There are no other significant physical findings. A chest radiograph shows irregular opacifications throughout both lungs. The figure shows a transbronchial biopsy specimen colored with trichrome stain. Laboratory studies include negative serologic tests for ANA, anti-DNA topoisomerase I, ANCA, and anticentromere antibody. Despite glucocorticoid therapy, his condition does not improve, and he dies 2 years later. What is the most likely diagnosis?

- □ (A) Acute respiratory distress syndrome
- □ (B) Goodpasture's syndrome
- □ (C) Idiopathic pulmonary fibrosis
- □ (D) Sarcoidosis
- □ (E) Scleroderma
- □ (F) Wegener granulomatosis

62 A 26-year-old woman with postpartum sepsis is afebrile on antibiotic therapy, but she has had worsening oxygenation over the past 3 days. Her chest x-ray shows scattered bilateral pulmonary opacifications. A ventilation perfusion scan shows areas of mismatch. This process is developing from upregulation of nuclear factor kappa-B that promotes interleukin-8 and tumor necrosis factor release, with damage to endothelium and type I cells. Which of the following microscopic findings is most likely to be present in her lungs?

- □ (A) Alveolar hyaline membranes
- □ (B) Arterial plexiform lesions
- □ (C) Interstitial fibrosis
- □ (D) Lymphocytic infiltrates
- □ (E) Respiratory bronchiolar destruction

63 A 46-year-old man has had increasing dyspnea with nonproductive cough for the past year. On physical examination he is afebrile and has clubbing of digits. Pulmonary function testing reveals a mild restrictive abnormality along with reduced diffusing capacity of carbon monoxide. A transbronchial biopsy is performed and microscopic examination shows numerous alveolar macrophages, plump epithelial cells, mild interstitial fibrosis, and loss of respiratory bronchioles. Lamellar bodies and iron pigment are present within these macrophages. Which of the following is the most likely etiology for his pulmonary disease?

- □ (A) Atopy
- □ (B) Cigarette smoking
- □ (C) Ciliary dyskinesia
- □ (D) Mold spores
- □ (E) Silica dust

64 An epidemiologic study shows that a highly pathogenic strain of influenza A virus with the antigenic type H5N1 that normally causes disease in birds has been increasingly found to cause influenza in humans. Unlike other strains of influenza A virus, the H5N1 virus is associated with a 60% mortality rate. The enhanced pathogenicity of this avian flu virus is primarily due to mutation in its genome that enables it to do which of the following?

- □ (A) Elicit a weak cytotoxic T cell response
- □ (B) Enter many types of host cells
- □ (C) Escape inactivation by macrophages
- □ (D) Infect CD4+ T cells.
- □ (E) Spread from humans to humans

ANSWERS

1 **(A)** Silica crystals incite a fibrogenic response after ingestion by macrophages. The greater the exposure and the longer the time of exposure, the greater is the lung injury. Silica is a major component of sand, which contains the mineral quartz. The small silica crystals are inhaled, and their buoyancy allows them to be carried to alveoli. There, they are ingested by macrophages, which secrete cytokines that recruit other inflammatory cells and promote fibrogenesis. Tobacco smoke leads to loss of lung tissue and emphysema, not to fibrosis. Ozone, a component of smog, has no obvious pathologic effects. Particulate matter, such as wood dust, is mainly screened out by the mucociliary apparatus of the upper airways. Carbon monoxide readily crosses the alveolar walls and binds avidly to hemoglobin, but does not injure the lung directly.

BP7 271–272, 468BP8 498–499PBD7 732–735PBD8 698–699

2 **(A)** This patient has a lung abscess that most likely resulted from aspiration, which can occur in individuals with a depressed cough reflex or in neurologically impaired individuals (e.g., owing to acute alcoholism, anesthesia, or Alzheimer disease). Aspiration into the right lung and the lower lobe is more common because the main stem bronchus to the left lung is more acutely angled. Bacterial organisms are most likely to produce abscesses. The most common pathogen is *Staphylococcus aureus,* but anaerobes such as *Bacteroides, Peptococcus,* and *Fusobacterium* spp. also may be implicated. These anaerobes normally are found in the oral cavity and are readily aspirated. The purulent, liquefied center of the abscess can produce the radiographic appearance of an air-fluid level. Tuberculosis can produce granulomatous lesions with central cavitation that may be colonized by *Aspergillus,* although not over a few days. Nocardial and actinomycotic infections often lead to chronic abscesses without significant liquefaction and affect immunocompromised individuals. Cytomegalovirus, *Pneumocystis,* and cryptococcal infections are seen in immunocompromised individuals and do not typically form abscesses. *Candida* pneumonia is rare.

BP7 495–496BP8 515PBD7 747, 752–753PBD8 716–717

3 **(B)** This patient's disease meets the clinical definition of chronic bronchitis. He has had persistent cough with sputum production for at least 3 months in 2 consecutive years. Chronic bronchitis is a disease of smokers and individuals living in areas of poor air quality, which explains the chronic cough with mucoid sputum production. This patient's episodes of bronchoconstriction set off by viral infections suggest, however, a superimposed element of nonatopic asthma. Cor pulmonale leads to pleural effusions, not to bronchoconstriction. Emphysema and chronic bronchitis can overlap in clinical and pathologic findings, but significant bronchoconstriction is not a feature of emphysema. Bronchiectasis results in airway dilation from bronchial wall inflammation with destruction. Hypersensitivity pneumonitis is marked by features of a restrictive lung disease, sometimes with dyspnea, but without mucus production.

BP7 463–464BP8 488–489PBD7 721–723PBD8 687–688

4 **(A)** This patient has findings associated with right and left heart failure. The left-to-right shunt produced by the atrial septal defect leads to increased pulmonary arterial pressure, thickening of the pulmonary arteries, and increased pulmonary vascular resistance. Eventually, the shunt may reverse, which is known as the Eisenmenger complex. Pulmonary fibrosis can be caused by diseases such as pneumoconioses, collagen vascular diseases, and granulomatous diseases. Pulmonary vasculitis may be seen with immunologically mediated diseases, such as Wegener granulomatosis. Granulomatous inflammation does not occur from increased pulmonary arterial pressure. An infarction of the lung can occur with pulmonary embolism.

BP7 477–478BP8 506–507PBD7 743–745PBD8 707

5 **(C)** Although *Pneumocystis jiroveci* pneumonia can be seen with various acquired and congenital immunodeficient states (mainly those affecting cell-mediated immunity), it is most often associated with AIDS and is diagnostic of AIDS in HIV-infected individuals. Diabetics are most prone to contract bacterial infections. Patients with autoimmune disease may have cytopenias that predispose to infection, and if they are treated with immunosuppressive drugs, various infections are possible. Likewise, patients with sarcoidosis treated with corticosteroid therapy may have opportunistic infections. A patient with severe combined immunodeficiency is susceptible to *P. jiroveci* pneumonia, but it is unlikely that without treatment such a patient would have survived to age 40 years. Pulmonary emphysema predisposes to pulmonary infections, mainly caused by bacterial organisms.

BP7 497–498BP8 525–526PBD7 361, 747, 756PBD8 720

6 **(D)** The figure shows a pleura-based "red infarct" typical of pulmonary thromboembolism that affects patients who are immobilized in the hospital, such as patients with congestive heart failure. The source of the emboli is usually thrombi within pelvic or leg veins affected by phlebothrombosis. The bronchial arterial supply of blood is sufficient to produce hemorrhage, but insufficient to prevent infarction. Patients with underlying cardiac or respiratory diseases that compromise pulmonary circulation are at greater risk of infarction if thromboembolism does occur. Infarction is not a complication of smoking in patients with emphysema or asthma. HIV infection increases the risk of pulmonary infections, but not of infarction. The small emboli from the small vegetations of nonbacterial thrombotic endocarditis are unlikely to produce infarction. Vasculitis of the lung typically involves arterioles, capillaries, or venules of insufficient size to produce a grossly apparent infarction. Pneumoconioses with restrictive lung disease produce pulmonary fibrosis but not a compromised vasculature or infarction.

BP7 476BP8 505PBD7 742–743PBD8 706

7 **(B)** The productive cough suggests an alveolar exudate with neutrophils, and the course is compatible with an acute infection. Bacterial organisms should be suspected. Pneumococcus is the most likely agent to be cultured in individuals acquiring a pneumonia outside of the hospital, and particularly when a lobar pneumonic pattern is present, as in this case. The atypical pneumonia of *Mycoplasma* does not produce purulent sputum, unless there is a secondary bacterial infection, which is a common complication of viral and *Mycoplasma* pneumonias. Cryptococcal and mycobacterial infections typically produce granulomatous disease. *Candida* pneumonia is rare, but may occur in immunocompromised patients. *Pneumocystis* pneumonia is seen in immunocompromised patients and is unlikely to produce a lobar pattern of infection. Nocardiosis also is seen in immunocompromised patients and produces chronic abscessing inflammation.

BP7 479–482BP8 509–511PBD7 747–750PBD8 711–714

8 **(F)** The solitary fibrous tumor, or localized benign mesothelioma, of pleura is a rare neoplasm that appears as a pedunculated mass. There is no relationship to asbestos exposure or other environmental pathogens. Bronchioloalveolar carcinomas are peripheral (but intraparenchymal) masses with atypical epithelial cells growing along the framework of the lung. A hamartoma is a peripheral intraparenchymal mass with a significant component of fibrous connective tissue and usually with cartilage present. Hodgkin lymphoma is more likely to involve lymph nodes in the mediastinum. A malignant mesothelioma forms a pleural mass that is not circumscribed; the cells are atypical and cytokeratin positive. Metastases are typically multiple and often produce bloody effusions.

PBD7 768PBD8 732–733

9 **(C)** Asthma, particularly extrinsic (atopic) asthma, is driven by a type I hypersensitivity response. The Charcot-Leyden crystals represent the breakdown products of eosinophil granules. The Curschmann spirals represent the whorls of sloughed surface epithelium in the mucin. There can be inflammatory cells in the sputum with bronchiectasis and chronic bronchitis, although without eosinophils as a major component. Foreign body aspiration may result in inflammation, but without eosinophils. Inflammation is not a component of emphysema. There is mechanical pharyngeal obstruction with obstructive sleep apnea, but without bronchoconstriction or inflammation.

BP7 455–458BP8 489–492PBD7 723–727PBD8 688–692

10 **(B)** The patient's findings are predominantly those of an obstructive lung disease—emphysema—with a centrilobular pattern of predominantly upper lobe involvement. Smoking is a major cause of this disease. The inflammation that can accompany smoking leads to increased neutrophil elaboration of elastase and elaboration of macrophage elastase that is not inhibited by the antiprotease action of α_1-antitrypsin. This results in a loss of lung tissue, not fibrogenesis. Fibrogenesis is typical of restrictive lung diseases, such as pneumoconioses that follow inhalation of dusts. α_1-Antitrypsin deficiency is uncommon and leads to a panlobular pattern of emphysema. Abnormal chloride ion transport is a feature of

cystic fibrosis, which leads to widespread bronchiectasis. Dynein arms are absent or abnormal in Kartagener syndrome, which leads to bronchiectasis. Macrophage recruitment and activations by interferon-γ released from T cells is a feature of chronic inflammatory conditions and pneumoconioses.

BP7 458–462BP8 485PBD7 717–720PBD8 684–686

11 **(G)** Most *Mycobacterium tuberculosis* infections are asymptomatic and subclinical. Active disease is uncommon, although a preceding illness or poor living conditions increase the risk. Calcifications and cavitation are complications most often seen after reinfection or reactivation of tuberculosis infections in adults. Lymphadenopathy or subpleural granuloma formation is more frequent in primary tuberculosis infections. A diffuse reticulonodular pattern suggests miliary tuberculosis. Extensive opacification is unlikely to occur in mycobacterial disease.

BP7 488–489BP8 516–521PBD7 381–386, 747PBD8 367–372, 717

12 **(E)** The extensive pulmonary involvement with emphysema suggests the panlobular form, which can be worse in the lower lobes. The major antielastase is α_1-antitrypsin deficiency, which is an inherited disease. Individuals with atopy are more likely to develop asthma, which has transient air trapping, not emphysema. The *CFTR* gene mutations lead to cystic fibrosis and widespread pulmonary bronchiectasis. Smoking increases inflammation with neutrophils releasing proteases, mainly in upper lobes, producing the centriacinar pattern of emphysema. Prior infection with tuberculosis may result in upper lobe cavitation, not emphysema.

BP7 459–460BP8 485PBD7 718–720PBD8 684

13 **(E)** The patient has the acquired form of pulmonary alveolar proteinosis (PAP), an uncommon condition of unknown etiology characterized by autoantibodies against granulocyte-macrophage colony-stimulating factor (GM-CSF). Ten percent of PAP cases are congenital secondary to mutations in the GM-CSF gene. Both forms of PAP have impaired surfactant clearance by alveolar macrophages. α_1-Antitrypsin deficiency leads to panlobular emphysema. *CFTR* gene mutations lead to cystic fibrosis and widespread bronchiectasis. AntiDNA topoisomerase I antibodies are seen in diffuse scleroderma, which produces interstitial fibrosis. Anti–glomerular basement membrane antibody is present in Goodpasture syndrome with extensive alveolar hemorrhage. Neutrophilic myeloperoxidase is a form of antineutrophil cytoplasmic autoantibody seen in Wegener granulomatosis.

PBD7 741PBD8 705

14 **(G)** This patient has features of Cushing syndrome, a paraneoplastic syndrome resulting from ectopic corticotropin production (most often from a pulmonary small-cell carcinoma), which drives the adrenal cortices to produce excess cortisol. Small-cell carcinomas are aggressive tumors that tend to metastasize early. Even when they appear to be small and localized, they are not or will not remain so. Surgery is not an option for these patients. They are treated as if they have systemic disease; some chemotherapy protocols afford benefit for 1 year or more, but cure is uncommon. Adenocarcinomas and large-cell carcinomas tend to be peripheral neoplasms in the lung, and they are less likely to produce a paraneoplastic syndrome. Bronchial carcinoids tend to be small and are not likely to produce paraneoplastic effects; rarely, they produce carcinoid syndrome. Renal cell carcinomas have been associated with Cushing syndrome, but the typical pattern of metastases is multiple nodules in both lungs. Non-Hodgkin lymphomas rarely occur in the lung, are not associated with smoking, and do not produce Cushing syndrome. Squamous cell carcinomas can be central and occur in smokers, but they are more likely to produce hypercalcemia.

BP7 504BP8 534PBD7 763–764PBD8 728

15 **(D)** The clinical and morphologic picture is that of acute respiratory distress syndrome (ARDS). ARDS is characterized by diffuse alveolar damage, which is initiated in most cases by injury to capillary endothelium by neutrophils and macrophages. Leukocytes aggregate in alveolar capillaries and release toxic oxygen metabolites, cytokines, and eicosanoids. The damage to the capillary endothelium allows leakage of protein-rich fluids. Eventually, the overlying alveolar epithelium also is damaged. Reduced surfactant production causes respiratory distress syndrome with hyaline membrane disease in newborns. ARDS and disseminated intravascular coagulation (DIC) can complicate septic shock, but DIC is not the cause of ARDS. Aspiration of bacteria causes bronchopneumonia. Release of fibrogenic cytokines is an important cause of chronic diffuse pulmonary fibrosis.

BP7 466–468BP8 481–483PBD7 715–716PBD8 680–682

16 **(C)** The patient has Goodpasture syndrome. Renal and pulmonary lesions are produced by an antibody directed against an antigen common to the basement membrane in glomerulus and alveolus. This leads to a type II hypersensitivity

reaction. C-ANCA and P-ANCA are best known as markers for various forms of systemic vasculitis. The anti-DNA topoisomerase I antibody is a marker for scleroderma. Antimitochondrial antibody is associated with primary biliary cirrhosis. ANA is used as a general screening test for various autoimmune conditions, typically collagen vascular diseases such as systemic lupus erythematosus.

BP7 473–474BP8 507–508PBD7 745–746PBD8 709–710

17 **(B)** These findings point to an obstructive lung disease, such as emphysema, which occurs from airway narrowing or from loss of elastic recoil. Adenocarcinomas, similar to other primary lung tumors, typically involve one lung and do not produce small airway disease. Diffuse alveolar damage is an acute restrictive lung disease. Chronic pulmonary embolism does not affect FVC because the airways are not affected, but there is a ventilation/perfusion mismatch. Sarcoidosis is a form of chronic restrictive lung disease. Pneumoconioses produce a restrictive pattern of lung disease with all lung volumes decreased, low FVC, and normal FEV_1/FVC ratio.

BP7 458–462BP8 484–486PBD7 717–719PBD8 686–687

18 **(C)** This patient has Horner syndrome as a result of cervical sympathetic ganglion involvement by invasive carcinoma. Such a tumor in this location with these associated findings is called a Pancoast tumor. Infectious processes such as pneumonia are unlikely to impinge on structures outside the lung. Bronchiectasis destroys bronchi within the lung. Sarcoidosis can result in marked hilar adenopathy with a mass effect, but involvement of the superior cervical ganglion is unlikely. Likewise, tuberculosis is a granulomatous disease that can lead to hilar adenopathy, although usually without destruction of extrapulmonary tissues.

BP7 503BP8 532PBD7 763–764PBD8 728–729

19 **(G)** These findings represent the so-called Ghon (or primary) complex, consisting of a small subpleural granuloma with extensive hilar nodal caseating granulomas. The Ghon complex is a feature of primary tuberculosis, which is most often a subclinical disease of younger individuals. Individuals who are immunocompromised, such as HIV-infected patients, do not mount a good granulomatous response and have more extensive poorly formed granulomas, dissemination of tuberculosis, or both. Patients with cystic fibrosis and an elevated sweat chloride level (more often elevated in children than in adults) develop widespread bronchiectasis with infection by bacterial agents, particularly *Pseudomonas aeruginosa* and *Burkholderia cepacia*. Anticentromeric antibody is characteristic of limited scleroderma, which does not have significant pulmonary involvement, in contrast to diffuse scleroderma. ANA is present in many autoimmune diseases, mainly in systemic lupus erythematosus, with pleuritis and pleural effusions. The rapid plasma reagin test is used to diagnose syphilis, which does not have significant pulmonary disease. Rheumatoid nodules may be seen in rheumatoid arthritis; these can be subpleural, but patients typically have arthritis.

BP7 487BP8 519PBD7 381–386PBD8 370

2 0 **(C)** This patient has “farmer's lung,” which is a form of hypersensitivity pneumonitis caused by inhalation of actinomycete spores. These spores contain the antigen that incites the hypersensitivity reaction. Because type III (early) and type IV immune hypersensitivity reactions are involved, granuloma formation can occur. The disease abates when the patient is no longer exposed to the antigen. Chronic exposure can lead to more extensive interstitial lung disease. Silicosis can produce a restrictive lung disease with fibrosis, but there are nodules of fibrosis that develop over years with minimal inflammation. Asbestosis is another pneumoconiosis that also can produce interstitial fibrosis over many years, and the risk of neoplasia is increased. Pulmonary tuberculosis can produce granulomas, but the pattern would be miliary, and it is unlikely that it would continue for 15 years. Antibodies directed against pulmonary basement membrane are a feature of Goodpasture syndrome, which mainly produces pulmonary hemorrhage.

BP7 472–473BP8 503PBD7 733, 739PBD8 703

21 **(E)** Distal acinar (paraseptal) emphysema is localized, beneath pleura typically in an upper lung lobe, and may occur in an area of fibrosis or scar formation. Although the lesions are usually less than 2 cm in diameter, they are prone to rupture with minor trauma, leading to pneumothorax. They can be a cause for spontaneous pneumothorax in young adults. Centriacinar emphysema arises in respiratory bronchioles and is seen in smokers. Panacinar (panlobular) emphysema involves most of the lung lobule and can be seen in all lobes; α_1-antitrypsin deficiency is the most likely antecedent. Asthma results from bronchoconstriction with air trapping, but is not likely to be complicated by pneumothorax. Bronchiectasis results from inflammation with destruction of bronchi; hemoptysis is the most likely complication, not pneumothorax. Chronic bronchitis is unlikely to produce a bronchopleural fistula with pneumothorax.

BP7 460–461BP8 485–486PBD7 718–719PBD8 684

22 **(B)** Complete obstruction of a bronchus can result in resorption of air and localized atelectasis. Obstruction by a foreign body can lead to localized bronchiectasis, but this takes weeks to months to develop. Distal to an obstruction, bronchopneumonia can develop, which can lead to a lung abscess. Fever with leukocytosis would be typical, however. Pneumothorax is unlikely because local obstruction does not produce enough air trapping to cause an air leak, particularly in a normal child's lung.

BP7 454BP8 480–481PBD7 713–714PBD8 679

23 **(D)** Most paraneoplastic syndromes involving lung carcinomas are associated with small-cell anaplastic (oat cell) carcinomas, but hypercalcemia is an exception. Most commonly, it is caused by squamous cell carcinoma. Metastatic disease also can lead to hypercalcemia when bone metastases are present, but metastases to the lung usually manifest as multiple masses, not one large mass. Bronchioloalveolar carcinomas are uncommon and are not often associated with hormone-like factor production. Large-cell carcinomas do not commonly cause a paraneoplastic syndrome.

BP7 206, 504BP8 534PBD7 763–764PBD8 728–729

24 **(F)** The patient probably has a small-cell anaplastic (oat cell) carcinoma of the lung, which is most likely to produce a paraneoplastic syndrome with the syndrome of inappropriate secretion of antidiuretic hormone. Oat cell cancers tend to be central masses, and they are strongly associated with smoking. Fluffy infiltrates suggest an infectious process. Upper lobe cavitation suggests secondary tuberculosis. Diaphragmatic pleural plaques can be a feature of pneumoconioses, particularly asbestosis. Pneumothorax is most likely to occur from chest trauma, not from a neoplasm. A subpleural nodule with hilar adenopathy is the classic Ghon complex of primary tuberculosis, which is unlikely to manifest with hemoptysis. An air-fluid level suggests liquefaction in an abscess.

BP7 499, 503BP8 530–533PBD7 759–762PBD8 726–727

25 **(H)** Of all lung cancers, squamous cell carcinoma is the one most likely to produce paraneoplastic hypercalcemia, and there is a strong association with smoking. These tumors also can undergo central necrosis—hence a cavity may form. Localized squamous cell carcinomas, in contrast to small-cell carcinomas, may be cured by surgery. Adenocarcinomas, bronchioloalveolar carcinomas, and large-cell carcinomas tend to produce peripheral masses and generally are not associated with paraneoplastic syndromes. Kaposi sarcoma involving visceral organs is most often seen in association with AIDS, and it is often multifocal. Renal cell carcinomas may be associated with hypercalcemia, but metastases usually appear as multiple masses (although of all metastatic tumors, renal cell carcinoma is most likely to produce solitary metastases). Non-Hodgkin lymphomas generally do not have paraneoplastic effects; they are uncommon in the lung and are not associated with smoking. Small-cell carcinomas are never localized enough for curative surgery (they are usually detected at an advanced stage), although they often produce various paraneoplastic syndromes, but not hypercalcemia.

BP7 500–501, 504BP8 531–534PBD7 759–763PBD8 725–726

26 **(C)** The figure shows pink, amorphous tissue at the lower left, representing caseous necrosis. The rim of the granuloma has epithelioid cells and Langhans giant cells. Caseating granulomatous inflammation is most typical of *Mycobacterium tuberculosis* infection. A hamartoma is a benign neoplastic process, and the mass is composed of pulmonary tissue elements, including cartilage and bronchial epithelium. A pulmonary infarct should have extensive hemorrhage. A lung abscess would have an area of liquefactive necrosis filled with tissue debris and neutrophils. A carcinoma may have central necrosis, not caseation, and there would be atypical, pleomorphic cells forming the mass.

BP7 484–486BP8 516–519PBD7 381–386PBD8 367–372

27 **(B)** Respiratory syncytial virus pneumonia is most common in children, and it can occur in epidemics. Viral, chlamydial, and mycoplasmal pneumonias are most often interstitial, without neutrophilic alveolar exudates. The diagnosis is often presumptive because culture is difficult and expensive. Lobar consolidation is more typical of a bacterial process, such as can be seen in *Streptococcus pneumoniae* infection. Pleural effusions can be seen in pulmonary inflammatory processes, but they are most pronounced in heart failure. Cavitation is most likely to complicate secondary tuberculosis in adults. Hyperinflation can accompany bronchoconstriction in asthma. Marked lymphadenopathy is more characteristic of chronic processes, such as granulomatous diseases or metastases. A mass lesion suggests a neoplasm or granuloma, not a viral infection.

BP7 483BP8 511, 536PBD7 347, 747PBD8 349, 714–715

28 **(C)** This history is typical of nonatopic, or intrinsic, asthma. There is no family history of asthma, no eosinophilia, and a normal serum IgE level. The fundamental abnormality in such cases is bronchial hyperresponsiveness (i.e., the threshold of bronchial spasm is intrinsically low). When airway inflammation occurs after viral infections, the bronchial muscles spasm, and an asthmatic attack occurs. Such bronchial hyperreactivity also may be triggered by inhalation of air pollutants, such as ozone, sulfur dioxide, and nitrogen dioxide. Accumulation of mast cells and eosinophils is typical of atopic asthma. Secretion of interleukin (IL)-4 and IL-5 by type 2 helper T cells also occurs in cases of allergic asthma. Bronchopulmonary aspergillosis refers to colonization of asthmatic airways by *Aspergillus,* which is followed by development of additional IgE antibodies.

BP7 457–458BP8 490PBD7 723–727PBD8 688

29 **(A)** The patient has a malignant mesothelioma. This is a rare tumor even in individuals with a history of asbestos exposure. The tumor appears decades after exposure. Bronchogenic carcinoma is more common in individuals with asbestos exposure, particularly when there is a history of smoking. Bird dust can lead to hypersensitivity pneumonitis. Silicosis is typified by interstitial fibrosis and causes a slight increase in the risk of bronchogenic carcinoma. Inhalation of cotton fibers (byssinosis) leads to symptoms related to bronchoconstriction. Coal dust inhalation can lead to marked anthracosis, but without a significant risk of lung cancer. Ozone and nitrogen oxides in smog can cause acute respiratory discomfort, but are not known to be promoters of neoplasia.

BP7 504–505BP8 536PBD7 735, 768–770PBD8 733–734

30 **(A)** Changes associated with pulmonary hypertension are characteristic of restrictive and obstructive lung diseases. This explains the occurrence of cor pulmonale and right-sided congestive heart failure in patients with chronic obstructive pulmonary disease (e.g., emphysema) or with pneumoconiosis. In both cases, the pulmonary vascular bed is reduced to increase pulmonary arterial pressures. Destruction of elastic tissue in alveolar walls is seen in emphysema, and fibrosis of alveolar walls occurs in restrictive lung diseases. Alveolar hemorrhage is not a feature of restrictive or obstructive lung disease. Hyaline membranes are seen in diffuse alveolar damage (acute respiratory distress syndrome), which has characteristics of an acute restrictive lung disease.

BP7 477–478BP8 506–507PBD7 743–745PBD8 707–709

31 **(D)** This patient has a typical history of bronchiectasis. In this condition, irreversible dilation of bronchi results from inflammation and destruction of bronchial walls after prolonged infections or obstruction. Serious bouts of pneumonia can predispose to bronchiectasis. Unopposed action of elastases damages the elastic tissue of alveoli, giving rise to emphysema. Chondromalacia weakening the bronchial wall is rare. Diffuse alveolar damage is an acute condition that gives rise to acute respiratory distress syndrome. Bronchial mucosal damage by eosinophils occurs in bronchial asthma. It does not cause destruction of the bronchial wall.

BP7 464–465BP8 493PBD7 727–728PBD8 692–693

32 **(A)** Resorption atelectasis is most often the result of a mucous or mucopurulent plug obstructing a bronchus. It can occur postoperatively, or it may complicate bronchial asthma. Compression atelectasis results from accumulation of air or fluid in the pleural cavity, which can happen with a pneumothorax, hemothorax, or pleural effusion. Microatelectasis can occur postoperatively, in diffuse alveolar damage, and in respiratory distress of the newborn from loss of surfactant. Contraction atelectasis occurs when fibrous scar tissue surrounds the lung. Relaxation atelectasis is a synonym for compression atelectasis.

BP7 454BP8 480–481PBD7 713–714PBD8 679

33 **(F)** The pleural fluid findings are typical of chylothorax, which is uncommon but distinctive. Disruption of the thoracic duct in the posterior chest is most likely to cause chylothorax, and malignant neoplasms, such as a high-grade non-Hodgkin lymphoma, are most likely to do this. An empyema is composed of pus formed from neutrophilic exudation and would appear cloudy and yellow. Congenital heart disease can lead to congestive heart failure with a serous effusion. Aortic dissection is an acute condition that can produce a hemothorax. Cirrhosis is more likely to be associated with ascites or liver failure with hypoalbuminemia leading to hydrothorax. Miliary tuberculosis is seen as a reticulonodular pattern on a chest radiograph; tuberculosis may produce hemorrhagic effusions.

BP7 505–506BP8 535PBD7 766–767PBD8 732

34 **(D)** Vasculitis is a key feature of Wegener granulomatosis. Although multiple organs can be affected, the lung and kidney are most often involved. The C-ANCA test result is often positive, whereas a positive P-ANCA result suggests

microscopic polyangiitis. Renal and pulmonary disease may be present in Goodpasture syndrome; there may be a positive result for anti–glomerular basement membrane antibody, but no C-ANCA or P-ANCA positivity. In hypersensitivity pneumonitis, an initial type III hypersensitivity response is followed by a type IV response, and renal disease is not expected. In systemic lupus erythematosus, renal disease is far more likely than pulmonary disease, and C-ANCA or P-ANCA positivity is not expected. Of the collagen vascular diseases, systemic sclerosis is more likely to produce significant pulmonary disease, but hemoptysis is not a prominent feature, and the C-ANCA result is unlikely to be positive.

BP7 351–352, 474BP8 508PBD7 535, 539, 541, 746–747PBD8 516–517, 709

35 **(E)** Lack of the anti-elastase activity of α_1-antitrypsin promotes damage to the pulmonary elastic tissue, resulting in loss of structures throughout lung acini and causing panacinar emphysema. There is irreversible dilation of respiratory bronchioles to terminal alveoli. This dilation is more pronounced in the lower lobes of the lung, where greater perfusion occurs. Sarcoidosis is a granulomatous, mainly interstitial disease. Bronchiectasis results from chronic and destructive inflammation of bronchi. Interstitial fibrosis results from inhalation of injurious dusts (e.g., silica, asbestos) or from lung injury in collagen vascular diseases. Microatelectasis can occur postoperatively or with loss of surfactant in diffuse alveolar damage.

BP7 461BP8 484–485PBD7 719–720PBD8 684–686

36 **(A)** The anesthetic gases tend to reduce the ciliary function of the respiratory epithelium that lines the bronchi. The mucociliary apparatus helps clear organisms that are inhaled into the respiratory tree. The anesthetic gases and drugs do not typically result in marrow failure with neutropenia. The subglottic tracheal region, where the cuff of the endotracheal tube is located, can become eroded, but this is more likely to occur when intubation is prolonged for weeks. Macrophage function is not significantly affected by anesthesia. The levels of γ-globulins in serum are not reduced by the effects of anesthesia.

BP7 479BP8 510PBD7 727, 747PBD8 710

37 **(A)** The patient has a “coin lesion” on imaging of his lungs, which could be an infectious granuloma, a neoplasm, or a hamartoma. His fever suggests infection, and the CT finding of decreased central attenuation in the nodule suggests necrosis in a neoplasm or caseous necrosis in a granuloma. The lymphocytosis and monocytosis are consistent with tuberculosis. Nonsmokers are unlikely to develop primary lung neoplasms, and adenocarcinoma is the most common in that setting. Smokers are most likely to develop squamous cell carcinomas and small-cell anaplastic carcinomas. Individuals who are immunocompromised are most likely to develop fungal infections, particularly with *Aspergillus* that has branching septate hyphae. Charcot-Leyden crystals form from eosinophil granules in individuals with allergic asthma. Foreign body giant cells can be seen with lipid pneumonias. Gram stain is most useful for determining which bacterial organisms may be present, and gram-negative bacilli such as the Enterobacteriaceae produce acute pneumonias and abscesses with neutrophilia.

BP7 488–490BP8 522PBD7 381–386PBD8 718, 730

38 **(E)** The ferruginous bodies shown in the figure are long, thin crystals of asbestos that have become encrusted with iron and calcium. The inflammatory reaction incited by these crystals promotes fibrogenesis and resultant pneumoconiosis. Anthracosis is a benign process seen in city dwellers as a consequence of inhaled carbonaceous dust. Berylliosis is marked by noncaseating granulomas. Silica crystals are not covered by iron and tend to result in formation of fibrous nodules (silicotic nodules). Calcium deposition may occur along alveolar walls when the serum calcium level is high (metastatic calcification).

BP7 272–274, 468BP8 499–500PBD7 735–736PBD8 700

39 **(D)** Centrilobular emphysema results from damage to the central or proximal part of the lung acinus, with dilation that primarily affects the respiratory bronchioles. There is relative sparing of the distal acinar structures (alveolar ducts and alveolar sacs). In panacinar emphysema, the lung lobule is involved from the respiratory bronchiole to the terminal alveoli. In paraseptal emphysema, the distal acinus is involved.

BP7 459–460BP8 485–486PBD7 718–720PBD8 684

40 **(E)** Most pulmonary carcinoids are central obstructing masses involving a bronchus. These neuroendocrine tumors have unpredictable behavior, but many are resectable and follow a benign course. They typically manifest with hemoptysis and the consequences of bronchial obstruction. In this case, the pneumonia in the right upper lobe probably resulted from obstruction to drainage caused by the tumor. A hamartoma is an uncommon but benign pulmonary lesion that also is

located peripherally. Adenocarcinomas are common lung tumors, but are typically peripheral. Large-cell carcinomas are typically large, bulky, peripheral masses. Kaposi sarcoma can involve the lung in some patients with AIDS, and the tumor often has a bronchovascular distribution, but obstruction is uncommon.

BP7 504BP8 534–535PBD7 764–765PBD8 729–730

41 **(D)** This child has atopic asthma, a type I hypersensitivity reaction in which there are presensitized, IgE-coated mast cells in mucosal surfaces and submucosa of airways. Contact with an allergen results in degranulation of the mast cells, with release of mediators, such as leukotrienes, histamine, and prostaglandins, which attract leukocytes, particularly eosinophils, and promote bronchoconstriction. The characteristic histologic changes in the bronchi result from the inflammation. Dilation of the respiratory bronchiole is a feature of centrilobular emphysema. Bronchial dilation with inflammatory destruction is a feature of bronchiectasis. Hyaline membranes are seen with acute diffuse alveolar damage. Neutrophilic exudates with consolidation are seen in pneumonic processes, typically from bacterial infections.

BP7 455–457BP8 490–492PBD7 723–727PBD8 688–692

42 **(C)** The spirometric data suggest a restrictive lung disease process. The progressive pulmonary interstitial fibrosis of a restrictive lung disease such as a pneumoconiosis eventually can lead to dilation of remaining airspaces, giving a “honeycomb” appearance. The loss of lung tissue with emphysema also leads to airspace dilation, but without alveolar wall fibrogenesis. The increase in mucous glands with chronic bronchitis leads to copious sputum production, but not fibrogenesis. Eosinophilic infiltrates suggest atopic asthma, an episodic disease without fibrogenesis. Hyaline membranes, edema, inflammation, and focal necrosis are features of diffuse alveolar damage (acute respiratory distress syndrome) in the acute phase; if patients survive for weeks, diffuse alveolar damage may resolve to honeycomb change.

BP7 468BP8 483–484PBD7 728–729PBD8 696–697

43 **(E)** The findings in this study suggest pulmonary thromboembolism, and most pulmonary emboli are small and clinically silent. Sudden death may occur with large emboli that occlude the main pulmonary arteries. Cor pulmonale can result from repeated embolization with reduction in the pulmonary vascular bed. Hemoptysis with pulmonary embolism is uncommon, although it may occur when a hemorrhagic infarction results from thromboembolism. Dyspnea can occur with medium to large emboli.

BP7 475–477BP8 504–506PBD7 742–743PBD8 706–707

44 **(E)** This patient has chronic restrictive lung disease. The cause of many slowly progressive cases of restrictive lung disease is unknown. These cases must be distinguished from cases with identifiable causes, such as infection, collagen vascular disease, drug use, and pneumoconioses. Scleroderma may produce a progressive restrictive lung disease, but there are usually other manifestations involving the skin, and the ANA test result typically is positive. Goodpasture syndrome is a rare cause of sudden onset of severe hemoptysis. Silicosis is a progressive interstitial disease, but the patient's occupation as a pilot would tend to exclude exposure to dusts. Diffuse alveolar damage is an acute form of interstitial disease.

BP7 468BP8 495PBD7 729–731PBD8 693–694

4 5 **(A)** Bronchiolitis obliterans with organizing pneumonia, also called cryptogenic organizing pneumonia, is an uncommon, nonspecific reaction to a lung injury, such as an infection or toxic exposure. Desquamative interstitial pneumonitis (DIP) is an uncommon smoking-related interstitial disease in which monocytes gather together to form intra-alveolar macrophages; DIP is not related to idiopathic pulmonary fibrosis. Diffuse alveolar damage is an acute condition complicating an underlying lung injury; there is damage to alveolar capillary walls, followed by exudate with hyaline membrane formation. Hypersensitivity pneumonitis is a type III (and type IV) hypersensitivity response to an inhaled allergen. Pulmonary alveolar proteinosis is a rare idiopathic condition in which there are gelatinous alveolar proteinaceous exudates. Wegener granulomatosis is a form of vasculitis with pulmonary capillaritis.

BP7 475BP8 496PBD7 731, 767PBD8 696, 720

4 6 **(F)** The figure shows a prominent upper lobe cavitation in the tan-to-white caseating granulomas, typical of reactivation-reinfection tuberculosis in adults. *Candida* is a rare cause of lung infection. Coccidioidomycosis can produce granulomatous disease, but it is much less common than tuberculosis. Influenza viral infections have mainly interstitial mononuclear inflammation. The bacterial organisms listed, including *Legionella* and *Klebsiella,* are more likely to produce a bronchopneumonia with alveolar neutrophilic exudates. *Mycoplasma* infection produces mainly interstitial mononuclear inflammation. Nocardiosis of the lung appears mainly as chronic abscessing inflammation.

BP7 488–490BP8 520–521PBD7 381-386PBD8 369–372

47 **(B)** Bronchioloalveolar carcinoma is a peripheral tumor that can mimic pneumonia. Most of these tumors are well differentiated. Adenocarcinomas and large-cell carcinomas also are peripheral, but the former tend to produce a localized mass, whereas cells of the latter are large and pleomorphic and form sheets; sometimes it is difficult to distinguish among them. Hamartomas are uncommon, very slow-growing, benign peripheral masses composed of cartilage, epithelial cells, and fibrous connective tissue with blood vessels. Mesotheliomas almost always occur in the setting of prior asbestos exposure; they are large pleural masses. Metastases tend to appear as multiple nodules. Squamous cell carcinomas occasionally can be peripheral (although most are central) and are composed of pink, polygonal cells that have intercellular bridges. If well differentiated, squamous cell carcinomas show keratin pearls.

BP7 502BP8 531–534PBD7 760–762PBD8 725–727

48 **(C)** This patient is at occupational risk of asbestos exposure. The inhaled asbestos fibers become encrusted with iron and appear as the characteristic ferruginous bodies with iron stain. The firm, tan mass encasing the pleura is most likely a malignant mesothelioma. Asbestosis more commonly gives rise to pleural fibrosis and interstitial lung disease, similar to other pneumoconioses. This is seen grossly as a dense pleural plaque, which often is calcified. Asbestosis can give rise to bronchogenic carcinoma, especially in smokers. Fluffy infiltrates suggest an infectious process. Upper lobe cavitation suggests secondary tuberculosis. An endobronchial mass could be a carcinoid tumor, which is not related to asbestosis. Focal bronchial dilation is a pattern seen in bronchiectasis, which is most often a complication of recurrent or chronic infection.

BP7 272–274, 468BP8 499–500PBD7 735–737PBD8 699–701

49 **(A)** Cancers that arise in non-smokers are pathogenetically distinct from those that occur in smokers. They frequently have *EGFR* mutations and almost never have *KRAS* mutations. Most are adenocarcinomas. 25% of lung cancers worldwide occur in non-smokers. Primary adenocarcinomas in the lung tend to be small, peripheral masses that are amenable to surgical excision and have a better overall prognosis than other forms of lung cancer. Overall, far more metastatic adenocarcinomas involve the lung than do primary adenocarcinomas. Bronchial carcinoids are uncommon endobronchial lesions. Bronchioloalveolar carcinomas are peripheral masses with a distinctive microscopic appearance of neoplastic cells proliferating along the alveolar and bronchiolar framework. Hamartomas are small, peripheral masses that contain benign epithelial and connective tissue elements. Large cell carcinomas are too poorly differentiated to be called adenocarcinomas or squamous cell carcinomas. The most common cancers in smokers are small cell anaplastic and squamous cell carcinomas.

BP7 502BP8 529–533PBD7 758–761PBD8 724–729

50 **(C)** The patient had a saddle pulmonary thromboembolus. Sudden death occurs from hypoxemia or from acute cor pulmonale with right-sided heart failure. Because the airways are not obstructed, the lungs do not collapse, and there is no bronchoconstriction. With such an acute course, there is not enough time for a hemorrhagic pulmonary infarction to occur. Edema is not a feature of thromboembolism.

BP7 476BP8 504–506PBD7 742–743PBD8 706–707

51 **(A)** The clinical and morphologic features strongly suggest sarcoidosis. This granulomatous disease has an unknown cause, but the presence of granulomas and activated T cells in the lungs indicates a delayed hypersensitivity response to some inhaled antigen. Lung involvement, occurring in about one third of cases, may be asymptomatic or may lead to restrictive lung disease. Hypersensitivity pneumonitis is an immune complex disease that is triggered by inhaled allergens. This form of lung disease is characterized by acute dyspneic episodes. There can be granulomas in the lung, but lymph node enlargement is not seen. Diffuse alveolar damage is an acute lung injury seen in acute respiratory distress syndrome. Smoking causes chronic bronchitis and emphysema. Atypical mycobacteria cause caseating granulomas, as does *Mycobacterium tuberculosis*.

BP7 470–472BP8 501–502PBD7 737–739PBD8 701–703

52 **(E)** This patient had chronic bronchitis complicated by pulmonary hypertension and cor pulmonale. There are few characteristic microscopic features of chronic bronchitis, so it is mainly defined clinically by the presence of a persistent cough with sputum production for at least 3 months in at least 2 consecutive years. Increased eosinophils are characteristic of bronchial asthma, which is an episodic disease unlikely to cause cor pulmonale. Chronic bronchitis does not lead to diffuse pulmonary fibrosis. Granulomatous disease is more typical of sarcoidosis or mycobacterial infection.

Lymphangitic metastases may fill lymphatic spaces and produce a reticulonodular pattern on a chest radiograph, but patients tend not to live long with such advanced cancer.

BP7 463–464BP8 488–489PBD7 722–723, 744PBD8 687–688

53 **(A)** The finding of pulmonary hypertension in a young individual without any known pulmonary or cardiac disease is typical for primary pulmonary hypertension. The increased pulmonary arterial pressure leads to right heart hypertrophy. The large pulmonary arteries show atherosclerosis; the arterioles show plexogenic arteriopathy with a tuft of capillary formations producing a network, or web, that spans the lumens of dilated thin-walled arteries. BMPR2, a cell surface protein belonging to the TGF-β receptor superfamily, causes inhibition of vascular smooth muscle cell proliferation and favors apoptosis. In the absence of BMPR2 signaling, smooth muscle proliferation occurs, and pulmonary hypertension ensues. Inactivating germline mutations in the *BMPR2* gene are found in 50% of the familial (primary) cases of pulmonary hypertension and in 26% of sporadic cases. None of the other molecules listed regulate pulmonary arterial wall structure. Fibrillin-1 gene mutation occurs in Marfan syndrome. Lysyl hydroxylase is required for cross-linking collagen, and its loss gives rise to one form of Ehlers-Danlos syndrome. Endothelin and endothelial nitric oxide control vascular caliber. Renin and atrial natriuretic factor regulate sodium and water homeostasis, plasma volume, and systemic arterial pressure.

BP7 767BP8 506–507PBD7 743–745PBD8 707–709

54 **(D)** Blunt trauma to the chest can lead to rib fracture. The sharp bone can penetrate the pleura and produce an air leak, resulting in pneumothorax. Although pulmonary embolus and pneumonia are possible complications in hospitalized patients, they would not occur this quickly. Edema and hydrothorax are unlikely from trauma alone; hemorrhage is more likely. Although pneumothorax can complicate rupture of a bulla in emphysema, this is more likely to occur in paraseptal emphysema than in centrilobular emphysema.

BP7 506BP8 535PBD7 767–768PBD8 732

55 **(D)** The early, acute phase of bronchial asthma is triggered by release of chemical mediators, whereas the late phase is mediated by recruited inflammatory cells and the cytokines they release. Among the early-phase mediators, the leukotrienes C_4, D_4, and E_4 promote intense bronchoconstriction and mucin production. Montelukast is an agent that binds to cysteinyl leukotriene (CysLT) receptors on mast cells and eosinophils to block the lipoxygenase pathway of arachidonic acid metabolism, which generates the leukotrienes. Prostaglandin D_2 also is a bronchoconstrictor, but its role is less well defined than that of leukotrienes. C3a increases vascular permeability, and C3b acts as an opsonin. Platelet-activating factor (PAF) increases vascular permeability and aids in histamine release from platelet granules. Interleukin (IL)-5, along with PAF, is chemotactic for neutrophils. Histamine acts during the early acute phase of type I hypersensitivity reactions, but is far less potent, and antihistaminic agents are not useful for treating asthma. It has very little role in chronic bronchial asthma, when the late-phase reaction takes over. Tumor necrosis factor and IL-1 mediate fever and induce acute-phase responses with neutrophilia, adrenocorticotropic hormone release, and hypotension.

BP7 457BP8 491PBD7 717, 726PBD8 689–690

56 **(B)** Congestive heart failure is far more common than the other listed conditions. The cell count and appearance indicate a transudate. Lymphoma may lead to chylothorax, and carcinomas involving the pleura tend to produce blood-tinged fluid. Systemic lupus erythematosus and renal failure tend to produce effusions with more protein or cells.

BP7 505BP8 535PBD7 766–767PBD8 731–732

57 **(B)** Hamartomas are uncommon benign peripheral lesions of the lung. They are composed of benign-appearing epithelial cells and connective tissue, typically with a large component of cartilage. They are induced in the differential diagnosis of a “coin lesion” (a Susan B. Anthony dollar, not a real silver dollar) that also includes carcinoma and granuloma. Adenocarcinoma is the most common primary lung malignancy in nonsmokers, and it can manifest as a coin lesion, but it is composed of gland-forming, malignant cells without cartilage. It tends to be peripheral, making surgical resection an option in many cases. Large cell carcinomas also are more likely to be peripheral, but they tend to be larger masses. Malignant mesothelioma is a rare neoplasm, even in individuals who have been exposed to asbestos, and it arises on the pleura. Primary non-Hodgkin lymphomas of the lung are uncommon. Some squamous cell carcinomas can be peripheral, but they are most likely to occur in individuals who smoke.

BP7 167–168BP8 528PBD7 765PBD8 730

58 **(A)** The patient has hypersensitivity pneumonitis, with acute symptoms that occur soon after exposure to an antigen, often actinomycetes or fungi (molds) growing in air conditioners. The symptoms improve when the patient leaves the

environment where the antigen is located. The pulmonary pathologic changes are usually minimal, with interstitial mononuclear infiltrates. This type of hypersensitivity pneumonitis is called “farmer's lung”; inhaling actinomycetes in moldy hay can cause this illness. It is mainly a type III hypersensitivity reaction, but with more chronic exposure to the antigen, there may be a component of type IV hypersensitivity with granulomatous inflammation. Attachment of antibody to basement membrane occurs in Goodpasture syndrome. Mycolic acid is a component of the cell wall of mycobacteria, and infections with these organisms are chronic, not episodic. Prostaglandins are produced by the cyclooxygenase pathway of arachidonic acid metabolism during acute inflammation and mediate pain and vasodilation. Histamine release is characteristic of a type I hypersensitivity reaction that more typically occurs in allergic disease. Leukotrienes are important mediators in asthma. A toxic injury is more typical of inhalation of a toxic gas, such as sulfur dioxide (so-called silo-filler's disease).

BP7 472–473BP8 503PBD7 739PBD8 703–704

59 **(C)** The patient has “primary atypical pneumonia” caused by *Mycoplasma pneumoniae,* a cell wall–deficient organism that is difficult to culture. Often, a diagnosis is made empirically. The findings are similar to those of other viral infections, and serologic testing shows the specific organism. *Legionella* can produce an extensive pneumonia with neutrophilic alveolar exudates, and the organisms are difficult to show—they may be revealed by Dieterle silver stain. *Mycobacterium fortuitum* is a rare infection that is most likely to be seen in very ill or immunocompromised individuals. Nocardiosis produces chronic abscessing inflammation; it is seen mostly in immunosuppressed individuals. Respiratory syncytial virus is typically an infection of early childhood.

BP7 482–484BP8 513–514PBD7 346, 349, 751PBD8 714–715

60 **(A)** The patient has severe acute respiratory syndrome, which is caused by a strain of coronavirus that is much more virulent than the coronaviruses known to be associated with the “common cold.” Cytomegalovirus is seen in immunocompromised patients and often involves multiple organs. Ebola virus is virulent and does not cause specific respiratory findings. Herpes simplex virus is a very rare cause of pneumonia, even in immunocompromised patients. HIV does not directly cause lung disease; however, HIV causes AIDS, which is associated with many pulmonary infections. Respiratory syncytial virus causes acute respiratory illness in young children.

BP7 481BP8 514PBD8 716

61 **(C)** Idiopathic pulmonary fibrosis leads to progressive restrictive lung disease. An unknown antigen incites the T_H2 inflammatory process with activated macrophage release of cytokines such as fibroblast growth factor and TGF-β1. TGF-β1 down-regulates telomerase activity and leads to epithelial cell apoptosis. TGF-β1 diminishes caveolin-1, a protein that inhibits fibrosis. Acute respiratory distress syndrome follows acute lung injury in very ill patients, typically patients in an intensive care unit. Goodpasture's syndrome is characterized by diffuse pulmonary hemorrhage. Sarcoidosis is marked by granulomatous inflammation. In this case, scleroderma is less likely because of the negative serologic test result. Wegener granulomatosis produces necrotizing granulomatous inflammation, and the ANCA test often is positive.

BP7 469–470BP8 494–495PBD7 729–731PBD8 694–695

62 **(A)** She has acute lung injury with development of diffuse alveolar damage, clinically known as acute respiratory distress syndrome (ARDS). Inciting sepsis, trauma, or other form of lung injury lead to a vicious cycle of inflammation with ongoing damage, mainly through the action of neutrophils. Plexiform lesions are characteristic for pulmonary hypertension. Though ARDS may eventually proceed to fibrosis, most patients do not survive that long. Lymphocytic infiltrates may be seen with infections such as viral pneumonias or immune-mediated lung diseases. Destruction of respiratory bronchioles is a feature of centrilobular emphysema.

BP7 466–468BP8 481–483PBD7 715–716PBD8 680–682

63 **(B)** He has desquamative interstitial pneumonitis (DIP), one form of smoking-related interstitial lung disease. Most cases abate with cessation of smoking and corticosteroid therapy. Atopy is classically related to asthma, an acute obstructive pulmonary process. One form of primary ciliary dyskinesia is Kartagener syndrome, which leads to bronchiectasis from ongoing inflammation with infection. Inhalation of mold spores produces farmer's lung — hypersensitivity pneumonitis. Inhalation of silicates leads to pulmonary fibrosis over years, but without large numbers of macrophages.

BP8 504PBD7 740PBD8 704

64 **(B)** The antigenic drift of influenza viruses, by altering their hemagglutinin (H) and neuraminidase (N) genes, allows

them to escape host antibodies. Cleavage of influenza viral hemagglutinin by host proteases is essential for the virus to enter cells. The less virulent influenza viruses are cleaved by proteases that are mainly localized to the lung and hence the disease is limited to the lungs. H5N1 virus has much broader tissue tropism because its hemagglutinin can be cleaved by proteases present in many tissues. Host responses to flu virus, such as a cytotoxic T cell response or macrophage engulfment, are not the major determinant of pathogenicity. Selective infection of CD4+ T cells is a propensity of HIV. Currently avian flu cannot be spread from human to human—but should that happen there would be an avian flu pandemic.

BP8 514PBD7 751–752PBD8 715