Diseases of Cartilaginous and Noncartilaginous Airways

5

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Diseases of cartilaginous (large) and noncartilaginous (small) airways include various nonspecific inflammatory and destructive lesions. The diagnoses of these diseases are usually made clinically and rarely require biopsy. However, histologic abnormalities involving the airways are commonly encountered in lung biopsies, lobectomy specimens, lung explants, and autopsies, either as primary diagnoses or as secondary findings in other conditions. Table 5.1 lists the major disease categories discussed in this chapter.

Table 5.1 Major airway diseases

Large airway diseases
Asthma
Allergic bronchopulmonary aspergillosis
Bronchiectasis
Cystic fibrosis
Plastic bronchitis
Small airway diseases
Follicular bronchiolitis (discussed in Chap. 11)
Respiratory bronchiolitis
Constrictive bronchiolitis
Diffuse panbronchiolitis
Bronchiolitis not otherwise specified
Emphysema
Aspiration pneumonia

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Asthma

Asthma is a chronic relapsing inflammatory disorder characterized by hyperreactive airways and is usually diagnosed clinically. Changes of asthma (Figs. 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7 and 5.8) are usually incidental findings in transbronchial biopsies or surgical specimens removed for tumors or other lesions. Characteristic changes include goblet cell hyperplasia, thickened basement membrane, smooth muscle hyperplasia, and eosinophilic infiltrates. Although none of these changes is specific for asthma, recognizing the features of asthma may help in making correct diagnoses of other diseases commonly associated with asthma, such as eosinophilic pneumonia, eosinophilic granulomatosis with polyangiitis (Churg-Strauss disease), and allergic bronchopulmonary aspergillosis (ABPA). ABPA is distinguished by various combinations of eosinophilia that often take the form of eosinophilic pneumonia, mucoid impaction of bronchi characterized by histologically distinctive ("allergic") mucin, and bronchocentric granulomatosis.

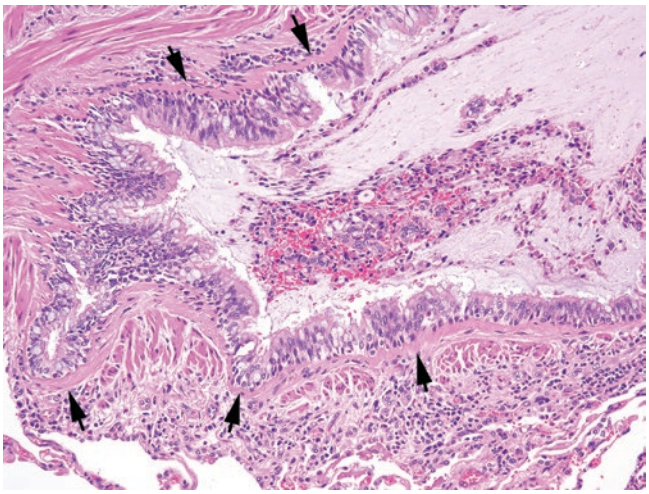

Fig. 5.2 Asthma. At higher magnification, the bronchial epithelium is remarkable for prominent goblet cell hyperplasia and thickened basement membrane (*arrows*). The bronchial wall shows smooth muscle hyperplasia and mild chronic inflammation. The lumen of the airway is almost completely occluded with a mucus plug

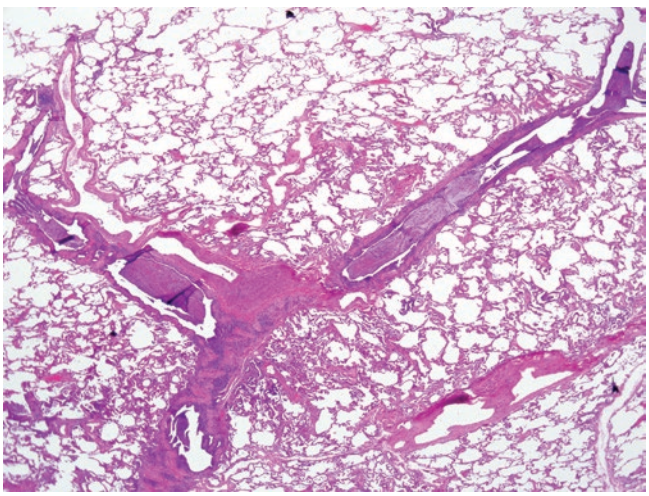

Fig. 5.1 Asthma. At low magnification, multiple airways are filled with mucus plugs. No significant inflammation is present. The lung parenchyma is normal

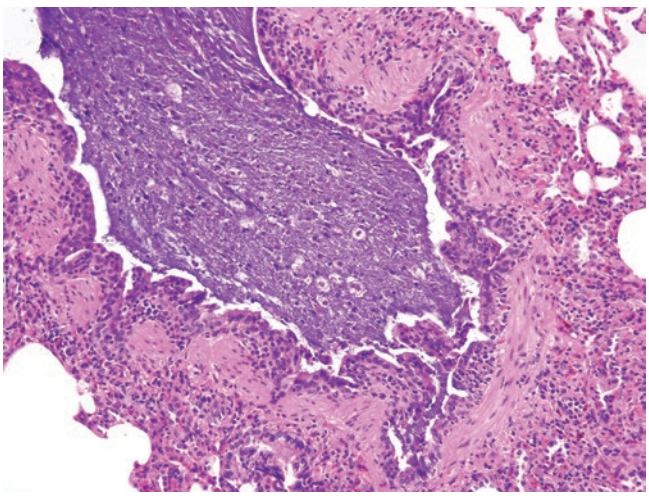

Fig. 5.3 Asthma. Another high-magnification photomicrograph showing an inflamed airway in a patient with asthma showing prominent smooth muscle hyperplasia, acute and chronic inflammatory infiltrates, and mucus plugging

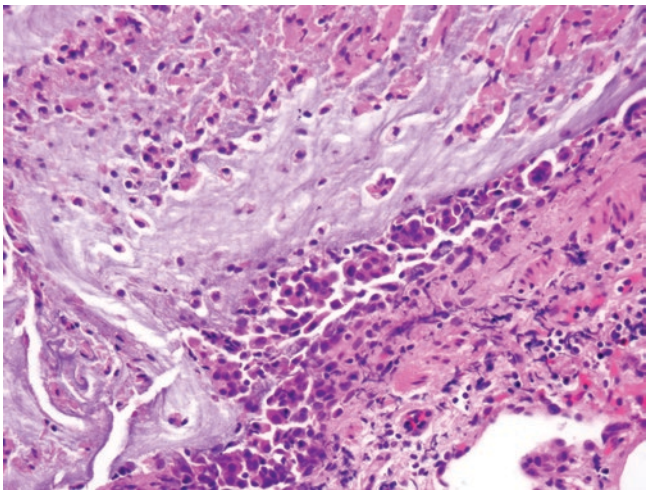

Fig. 5.4 Asthma. High-magnification view of mucus plug containing eosinophils and accompanied by epithelial necrosis

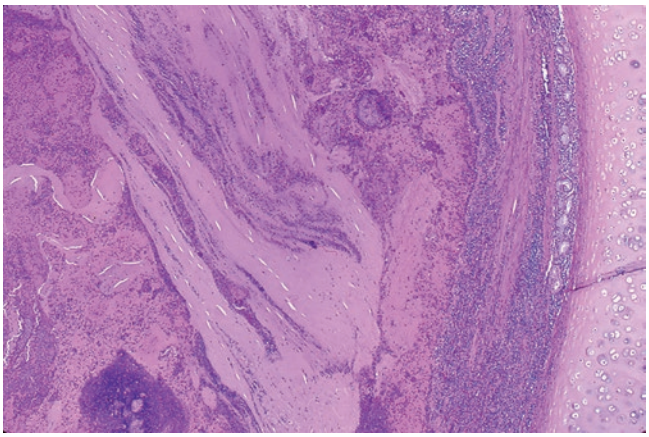

Fig. 5.6 Allergic bronchopulmonary aspergillosis associated with asthma. Low-magnification view of mucoid impaction of bronchi characterized by a dilated and inflamed cartilaginous airway impacted with allergic mucin. The allergic mucin contains layered cellular components in which eosinophils predominate within the lightly stained mucus

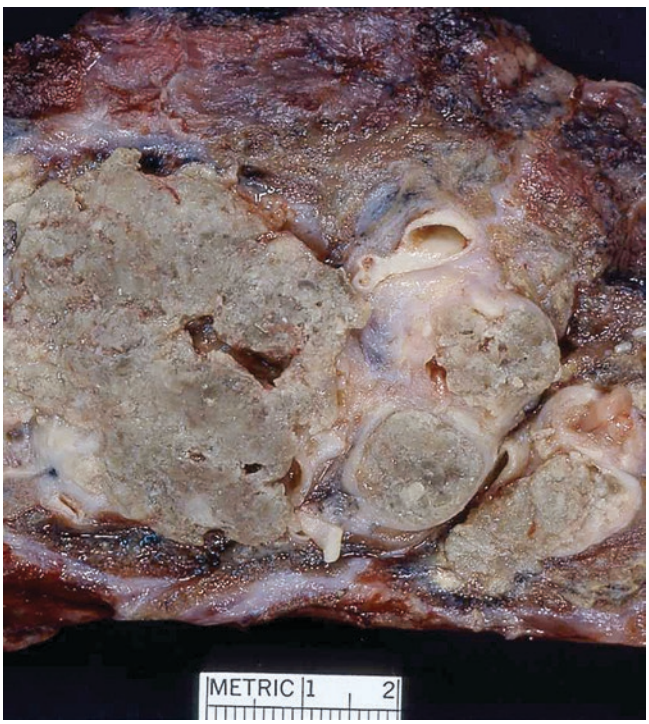

Fig. 5.5 Allergic bronchopulmonary aspergillosis associated with asthma. Gross photograph of a lobectomy specimen showing multiple dilated airways filled with green-gray, friable, desiccated mucus typical of mucoid impaction of bronchi

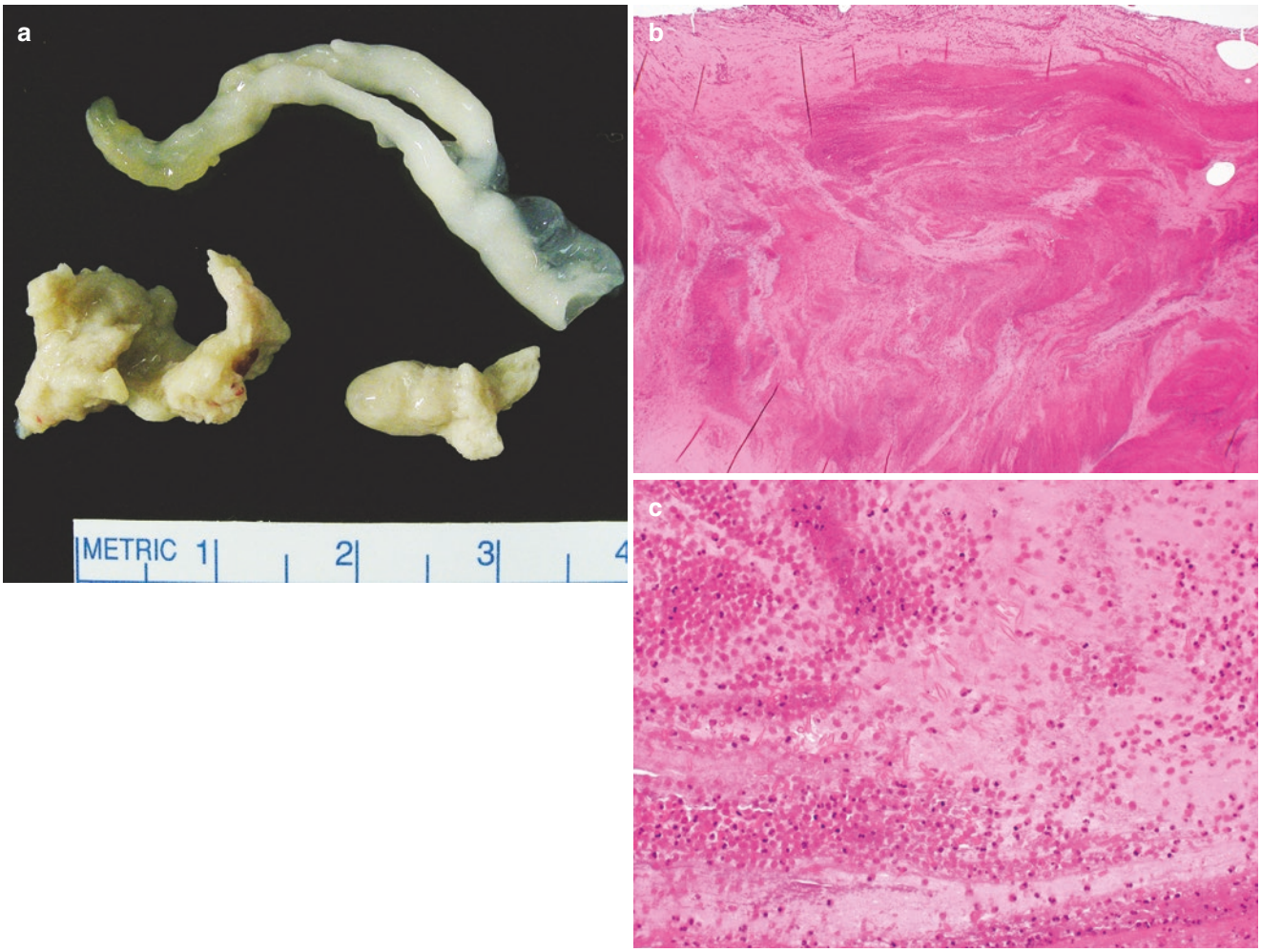

Fig. 5.7 Allergic mucin characteristic of mucoid impaction of bronchi (MIB) in allergic bronchopulmonary aspergillosis (ABPA). (**a**) Expectorated casts from a patient with MIB in ABPA. The gross appearance resembles plastic bronchitis (*see* Fig. 5.14); histologic features are helpful in distinguishing the two. (**b**) Low-magnification photomicrograph showing expectorated cast from a patient with ABPA. The alternating layers of inspissated mucus and degenerating eosinophils are characteristic of the allergic mucin that defines MIB in ABPA. (**c**) High-magnification photomicrograph of the allergic mucin illustrated in **b**, showing degenerating eosinophils and numerous Charcot-Leyden crystals, which are the breakdown products of eosinophilic granules

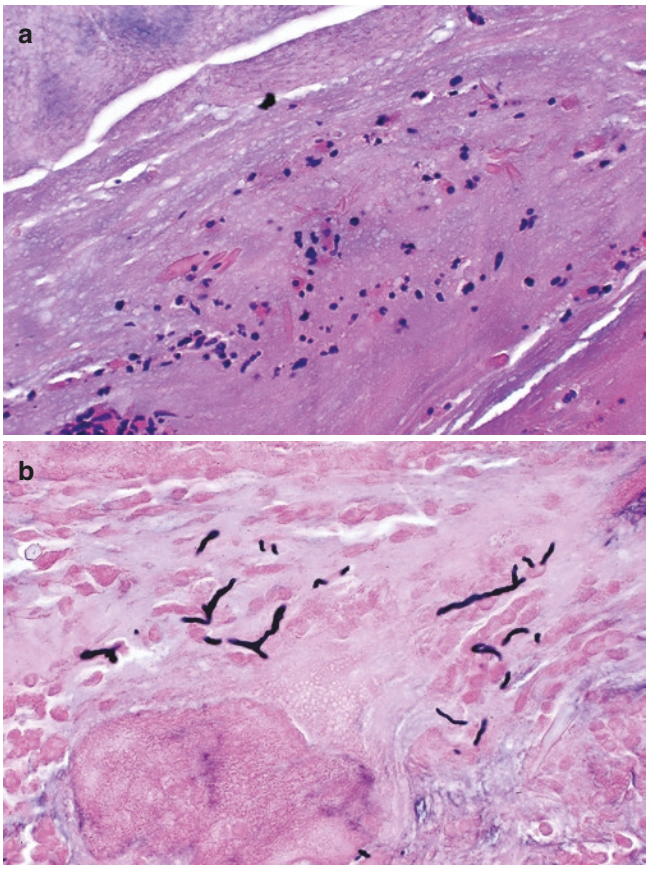

Fig. 5.8 Allergic mucin in allergic bronchopulmonary aspergillosis (ABPA) associated with asthma. (**a**) Another high-magnification view of allergic mucin with Charcot-Leyden crystals and degenerating eosinophils. (**b**) High-magnification view of Gomori methenamine silver (GMS) stained section showing fragmented, degenerating fungal hyphae in the allergic mucin from a patient with ABPA. The organisms are often rare in this condition and are largely limited to the allergic mucin without evidence of tissue invasion

Bronchiectasis

Bronchiectasis (Figs. 5.9, 5.10, 5.11, 5.12 and 5.13) is permanent dilation of bronchi and bronchioles, usually associated with necrotizing infections. Localized bronchiectasis is usually post-inflammatory following poorly treated or persistent pneumonia. The right middle lobe and lingula are especially susceptible to localized bronchiectasis (middle lobe syndrome). Obstruction caused by tumors or aspirated foreign bodies may lead to localized post-obstructive bronchiectasis. Diffuse bilateral bronchiectasis is most commonly associated with cystic fibrosis.

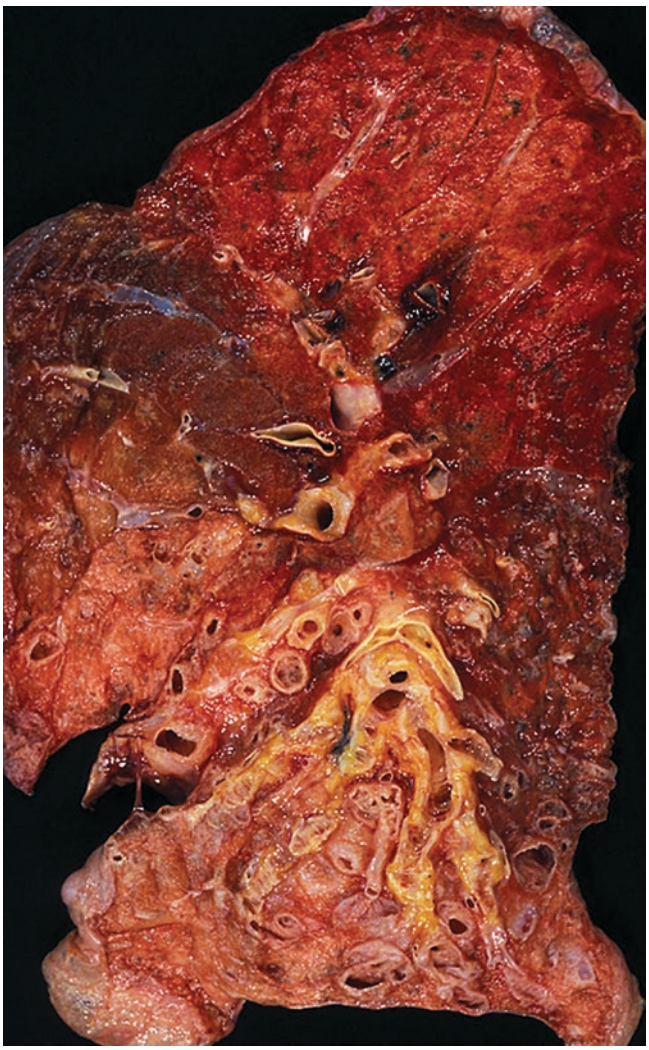

Fig. 5.9 Localized bronchiectasis. Gross photograph of a surgical specimen showing localized bronchiectasis. Dilated bronchi and associated bronchopneumonia and scarring are seen in the lower lobe, extending almost to the pleural surface. The bronchi and lung parenchyma in the upper lobe are normal

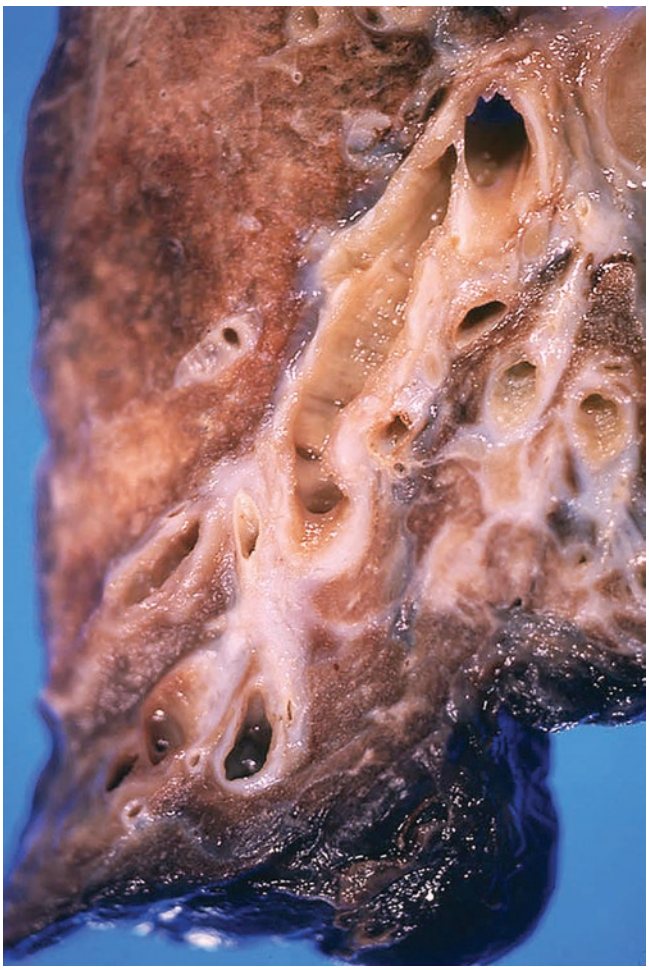

Fig. 5.10 Localized bronchiectasis. A close-up photograph of another resection specimen showing dilated bronchi with a characteristic corrugated mucosal surface

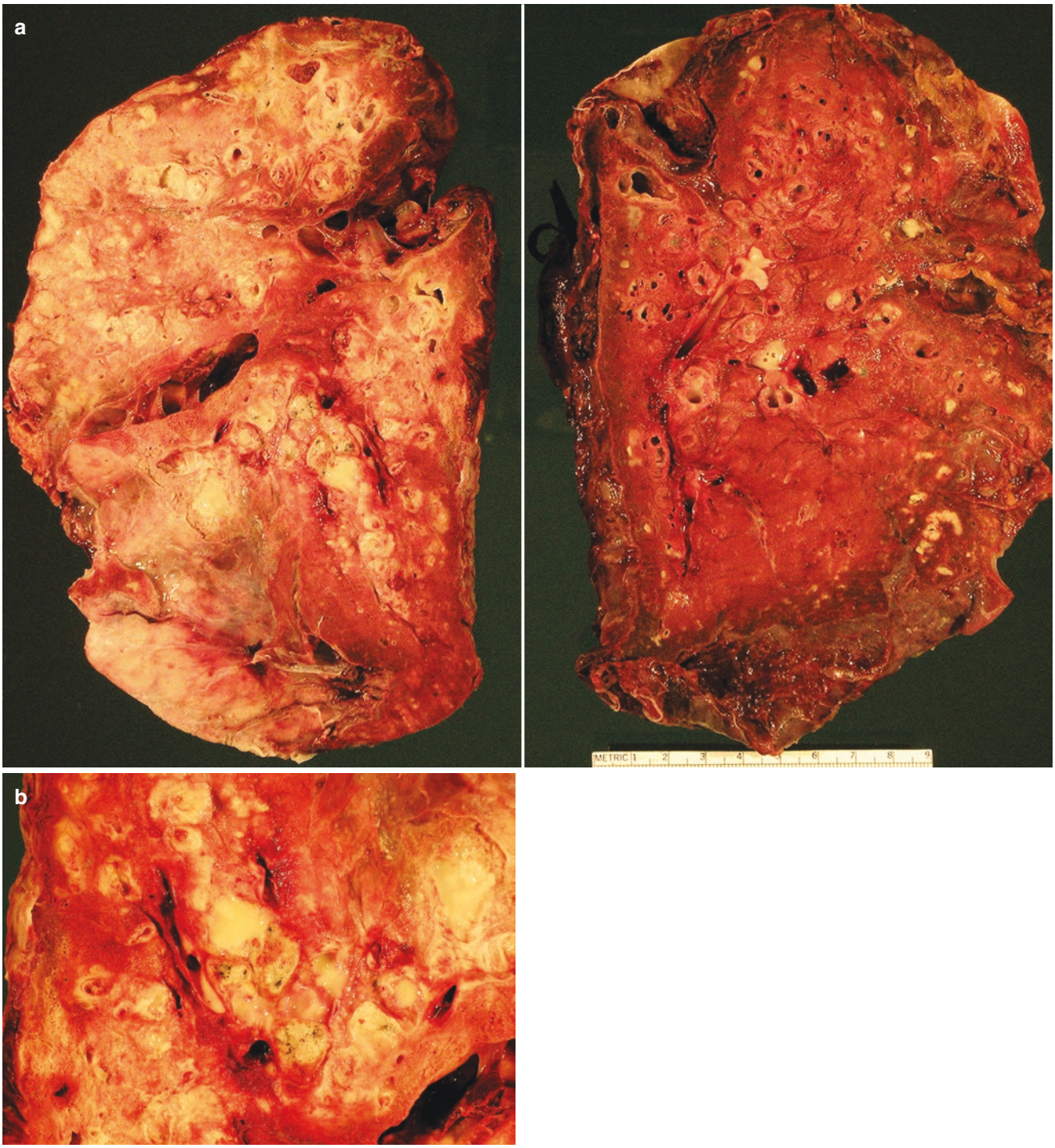

Fig. 5.11 Diffuse bronchiectasis. (**a**) Gross photograph of explanted lungs from a patient with cystic fibrosis. The cut surface shows diffusely dilated bronchi, some of which are filled with purulent exudates. (**b**) A close-up view showing the dilated bronchi filled with purulent exudates. There is also prominent peribronchial fibrosis and scarring, with very limited intervening normal lung parenchyma

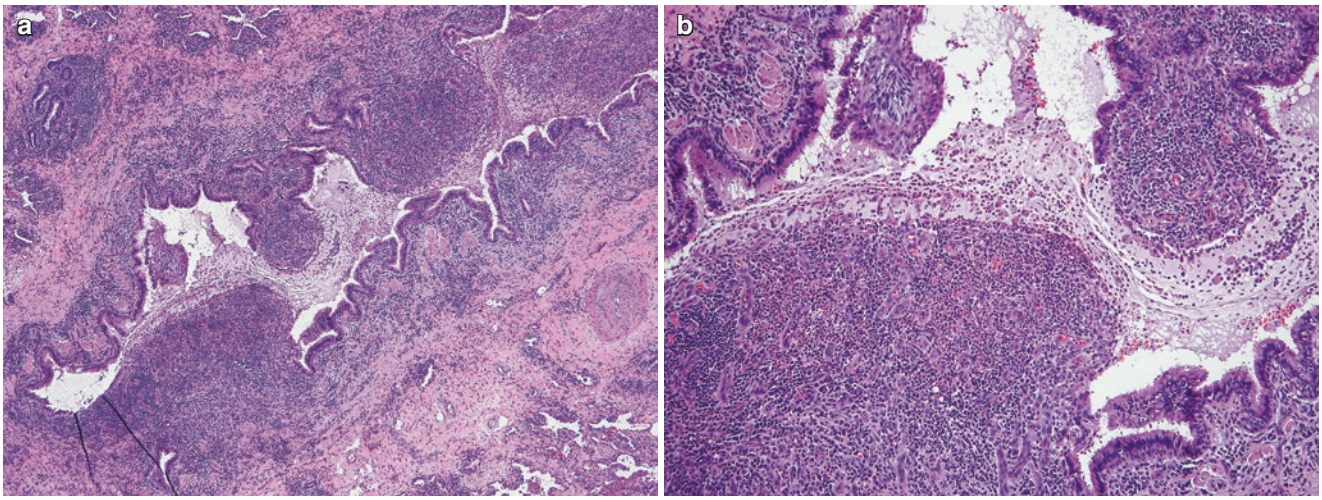

Fig. 5.12 Bronchiectasis. (**a**) Low-magnification photomicrograph showing a dilated bronchus with prominent acute and chronic inflammation with lymphoid aggregates and scarring of more distal peribronchial lung tissue. The integrity of the bronchial wall has been destroyed by inflammation and fibrosis, with an incomplete smooth muscle layer and attenuation of cartilage. (**b**) A higher-magnification photomicrograph shows focal necrosis of the lining respiratory epithelium with tufts of granulation tissue that are common and contribute to the risk of hemoptysis in these patients

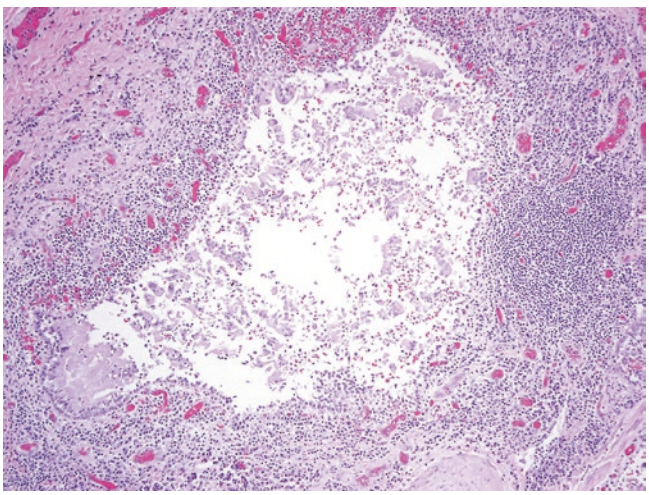

Fig. 5.13 Bronchiectasis. A photomicrograph showing another example of bronchiectasis in which there is severe acute and chronic inflammation with extensive necrosis of respiratory epithelium, peribronchial fibrosis, and an incomplete smooth muscle layer. The lumen contains sloughed epithelial cells and neutrophils

Plastic Bronchitis

Plastic bronchitis (Figs. 5.14 and 5.15) is a rare condition in which casts form in the tracheobronchial tree, causing potentially life-threatening airway obstruction and asphyxiation. It has been reported mainly in children with congenital heart diseases, especially in those patients who underwent corrective surgical procedures. Other associated conditions include infections, cystic fibrosis, and sickle cell disease. In rarely reported sporadic adult patients, the etiology is unknown. The expectorated bronchial casts grossly resemble the mucus plugs of mucoid impaction in patients with allergic bronchopulmonary aspergillosis (ABPA); however, the casts in plastic bronchitis are mainly made up of fibrin with variable numbers of mononuclear inflammatory cells rather than the allergic mucin typical of ABPA.

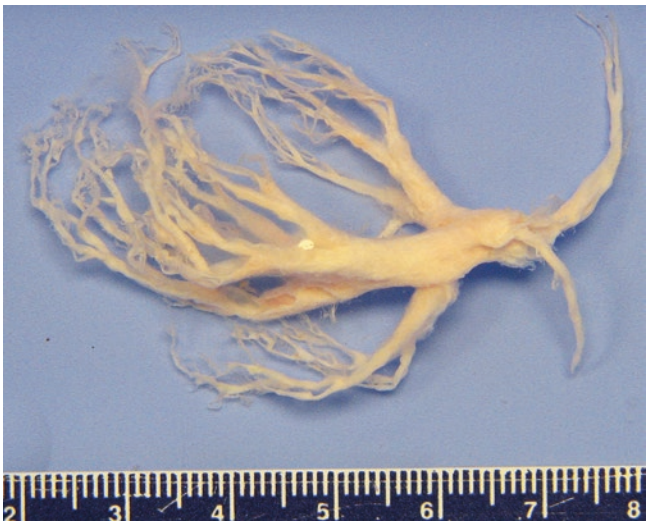

Fig. 5.14 Plastic bronchitis. Gross photograph of an expectorated bronchial cast resembling a tree with branches. The size and shape of the casts may vary from small segmental casts to large casts filling the entire tracheobronchial tree of a lung

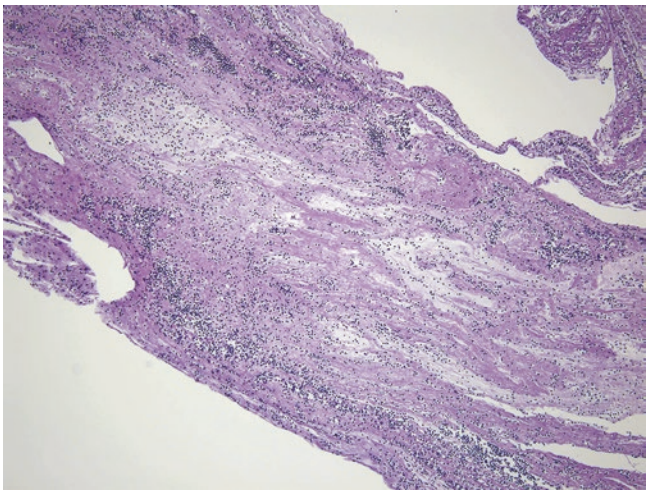

Fig. 5.15 Plastic bronchitis. Low-magnification photomicrograph of an expectorated cast showing a combination of fibrin and small lymphocytes

Respiratory Bronchiolitis

Respiratory bronchiolitis (RB) (Figs. 5.16, 5.17, 5.18 and 5.19) is a lesion that is present in almost all current (and many former) smokers in whom it usually represents an incidental finding of limited clinical and physiologic significance beyond corroborating a smoking history. It may remain for a prolonged period (years) after a patient stops smoking. The characteristic feature is clusters of lightly pigmented macrophages situated within the lumens of distal airways and peribronchiolar air spaces. The pigment is finely granular and usually stains positive with a Prussian blue iron stain, but it lacks the coarse refractile granules more characteristic of bleeding-associated hemosiderin. On rare occasions, this lesion may cause a syndrome of mild restrictive lung disease referred to as respiratory bronchiolitis/interstitial lung disease (RBILD) (*see* Chap. 6).

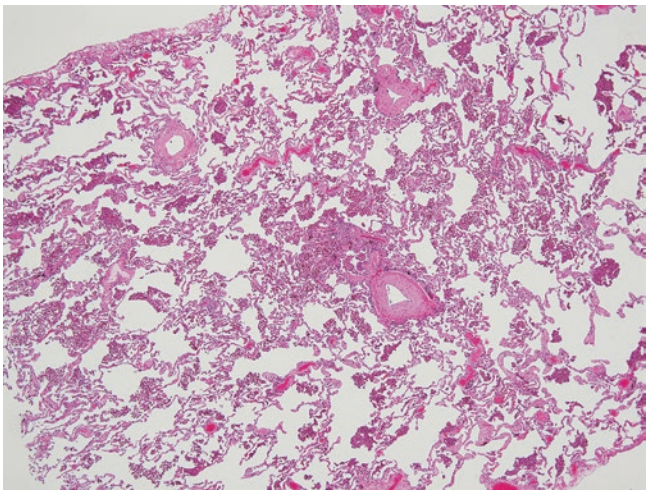

Fig. 5.16 Respiratory bronchiolitis. Low-magnification photomicrograph of respiratory bronchiolitis in a patient with RBILD. Lightly pigmented alveolar macrophages are clustered within the lumina of bronchioles and spill into adjacent air spaces

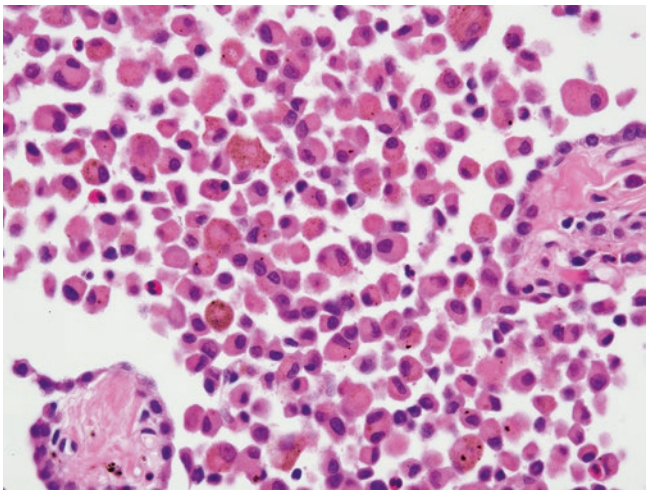

Fig. 5.18 Respiratory bronchiolitis. High-magnification photomicrograph showing the finely granular brown pigment typical of respiratory bronchiolitis. Occasional eosinophils are often present but should not be numerous

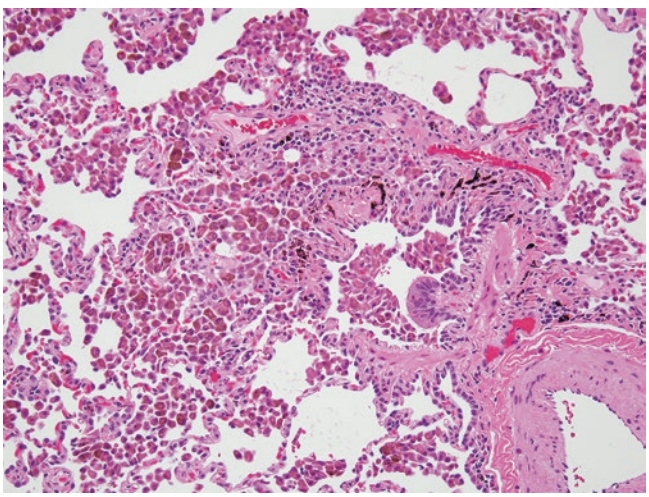

Fig. 5.17 Respiratory bronchiolitis. High-magnification photomicrograph from the same biopsy illustrated in Fig. 5.16 showing finely granular brown (smoker's) pigment in the cytoplasm of alveolar macrophages

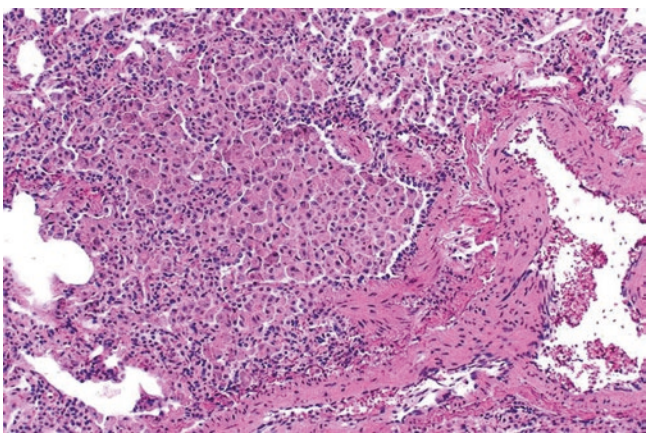

Fig. 5.19 Respiratory bronchiolitis. Another example showing a confluent aggregate of pigmented macrophages filling the entire lumen of the respiratory bronchiole and extending into adjacent alveolar spaces

Constrictive (Obliterative) Bronchiolitis

Constrictive (obliterative) bronchiolitis (Figs. 5.20, 5.21, 5.22, 5.23 and 5.24) is a rare small airway disease that is most commonly encountered in lung or stem-cell transplant recipients in whom it is a manifestation of chronic rejection or graft-versus-host disease, respectively. Other less common causes include infections, drug toxicities, connective tissue diseases (rheumatoid arthritis), and diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH). In rare patients it may be a form of idiopathic small airway disease. Patients usually are first seen with severe cough and dyspnea. Pulmonary function tests show obstructive changes. Over-inflation and air-trapping are the usual findings radiologically. The disease is progressive in most patients.

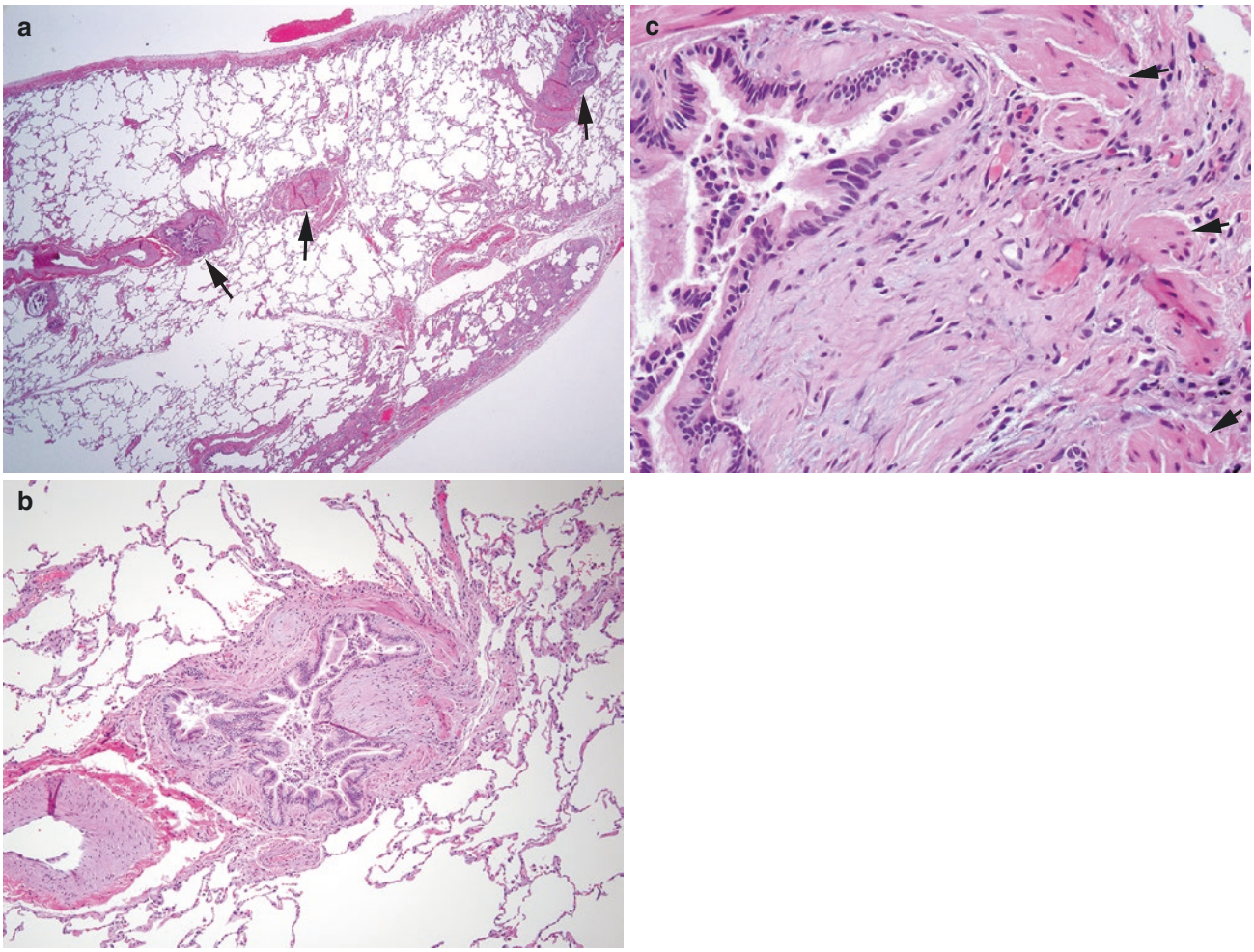

Fig. 5.20 Constrictive bronchiolitis. (**a**) Low-magnification photomicrograph of a lung wedge biopsy showing largely unremarkable alveolar lung parenchyma. A few bronchioles (*arrows*) have thickened walls, a feature that is inconspicuous and easily overlooked at this magnification. (**b**) Intermediate-magnification view showing a narrowed lumen caused by subepithelial fibrosis. (**c**) High-magnification photomicrograph illustrating prominent fibroblast proliferation in a collagenous and myxoid stroma situated between the respiratory epithelium and the smooth muscle layer (*arrows*)

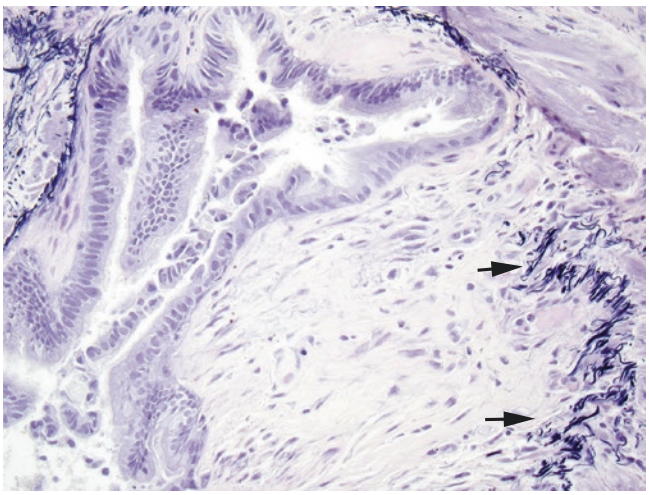

Fig. 5.21 Constrictive bronchiolitis. High-magnification photomicrograph of an elastic tissue stain highlights the fibrosis that separates the respiratory epithelium from the subepithelial elastic layer (*arrows*)

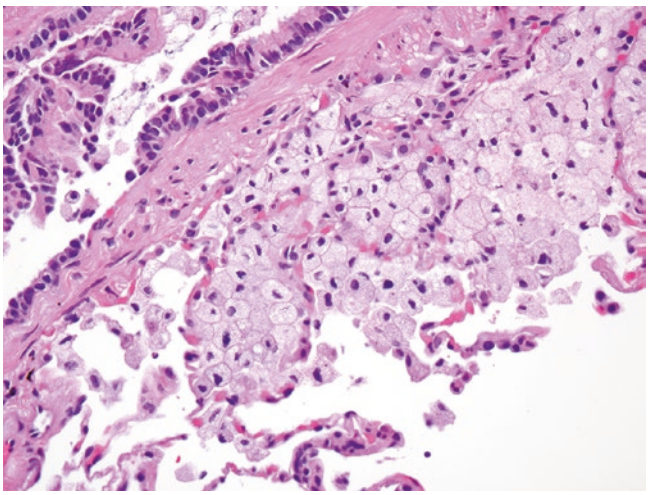

Fig. 5.23 Constrictive bronchiolitis. High-magnification photomicrograph showing the accumulation of foamy macrophages in peribronchiolar alveolar spaces, a common nonspecific finding indicating small airway obstruction

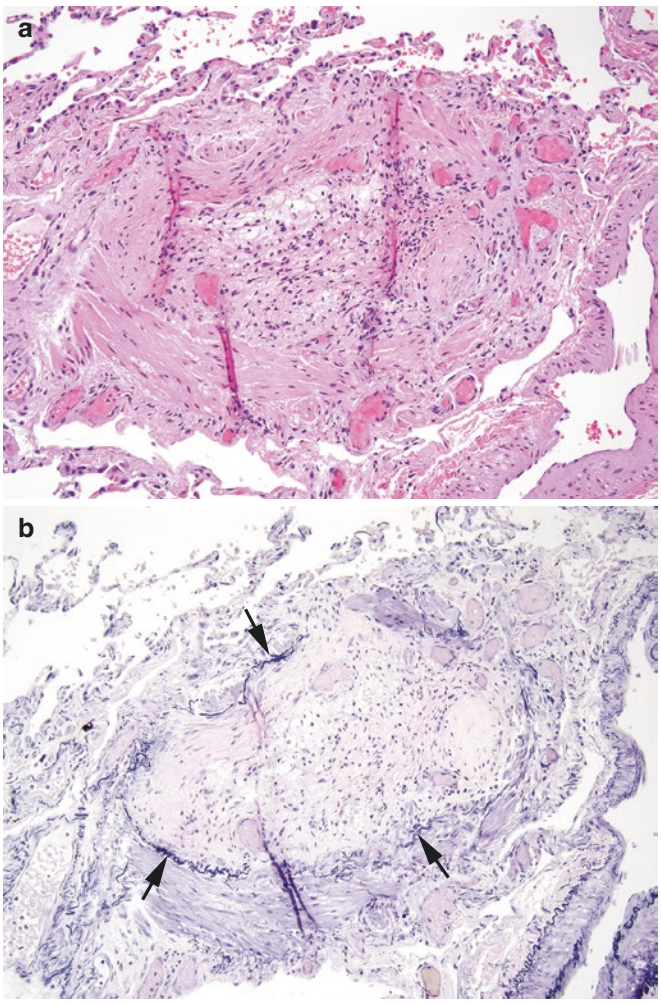

Fig. 5.22 Constrictive bronchiolitis. (**a**) High-magnification photomicrograph of bronchiole illustrated in Fig. 5.20a. The lumen of the bronchiole is completely obliterated by fibrosis with a scant infiltrate of inflammatory cells, including foamy histiocytes. The bronchiole is recognizable by its residual smooth muscle layer and the adjacent small muscular pulmonary artery. (**b**) An elastic stain highlights the residual elastic layer (*arrows*) of the obliterated bronchiole

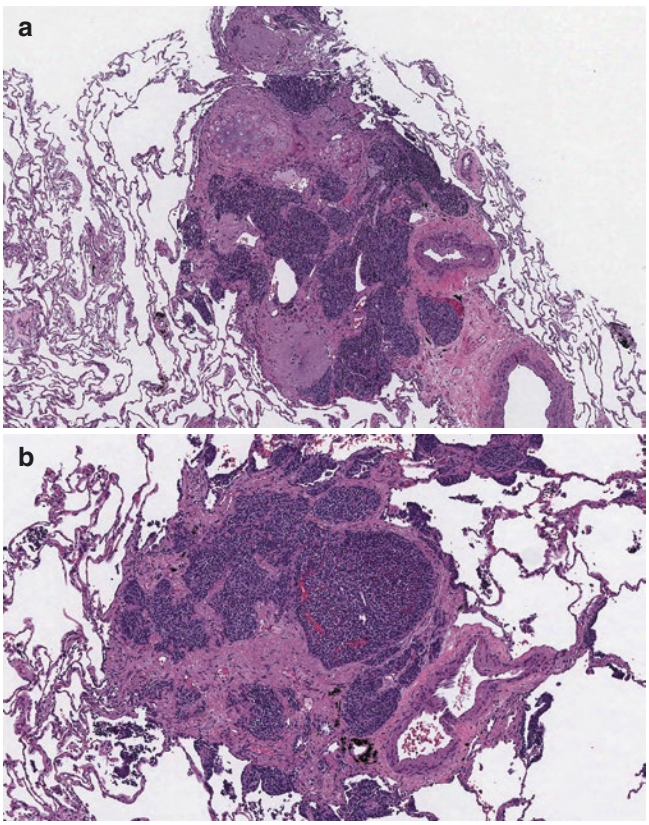

Fig. 5.24 Diffuse neuroendocrine cell hyperplasia (multiple carcinoid tumorlets) with constrictive bronchiolitis. (**a**) Low-magnification photomicrograph showing a carcinoid tumorlet in a cartilaginous airway with an obliterated lumen from a patient who had never smoked. Mosaic attenuation on a high-resolution computed tomography scan and airflow limitation on pulmonary function studies were found. (**b**) Low-magnification photomicrograph of the same lung biopsy showing an obliterated bronchiolar lumen associated with a carcinoid tumorlet

Diffuse Panbronchiolitis

Diffuse panbronchiolitis (Figs. 5.25, 5.26 and 5.27) is a rare form of chronic bronchiolitis involving mainly the respiratory bronchioles with a striking infiltrate of foamy macrophages. Diffuse panbronchiolitis occurs primarily in Japan, although rare examples have been reported in Western countries. Extended therapy with macrolide antibiotics has significantly improved the prognosis of this potentially fatal condition. The diagnosis should be made only in the appropriate clinical setting, given that similar histologic findings have been reported in other conditions.

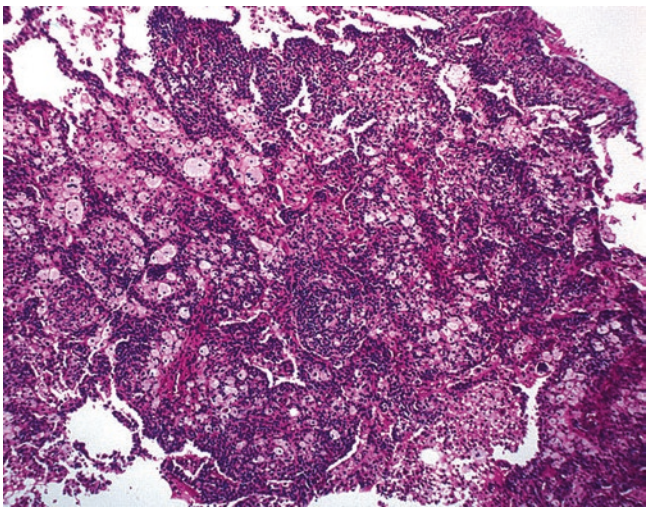

Fig. 5.25 Diffuse panbronchiolitis. Photomicrograph showing a characteristic combination of peribronchiolar inflammation rich in lymphocytes accompanied by a striking accumulation of foamy macrophages in the peribronchiolar interstitium

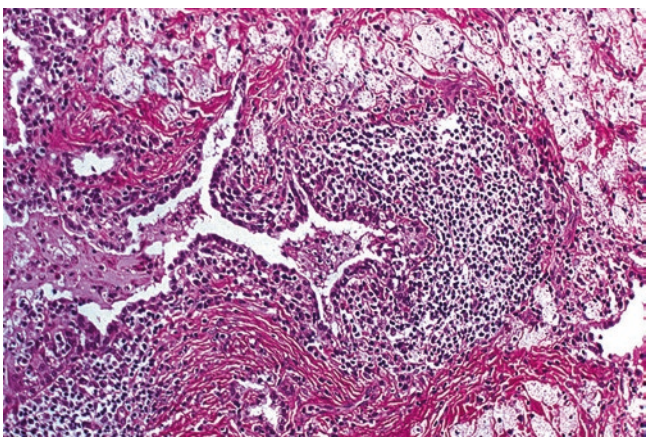

Fig. 5.26 Diffuse panbronchiolitis. High-magnification view of another bronchiole showing a chronic bronchiolitis in which lymphocytes predominate and large numbers of foamy macrophages expand the wall of the bronchiole and extend into adjacent alveolar septa

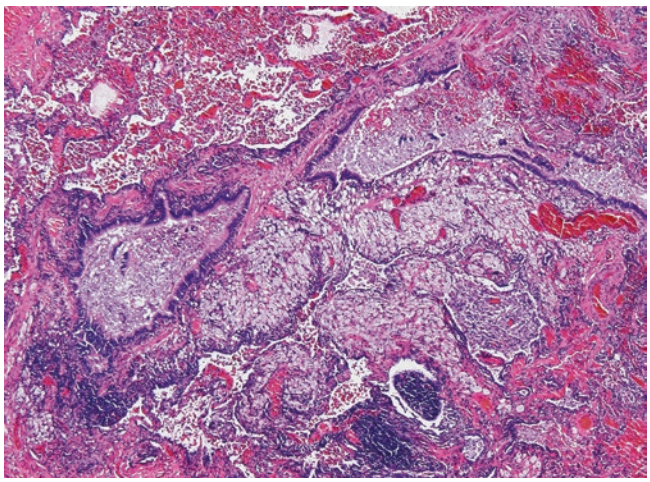

Fig. 5.27 Diffuse panbronchiolitis-like changes in a patient with sequestration. This low- magnification photomicrograph shows histologic findings typical of diffuse panbronchiolitis but in a patient with an intralobar sequestration, illustrating that histology by itself is insufficient to establish the diagnosis of diffuse panbronchiolitis

Bronchiolitis, NOS

Bronchiolitis, not otherwise specified (NOS) (Figs. 5.28, 5.29, 5.30 and 5.31), is sometimes encountered in patients without evidence of infection, bronchiectasis, underlying systemic disease, or other potential causes for primary airway disease. Patients with unexplained bronchiolitis may or may not have evidence of physiologically significant airflow limitation. Various combinations of acute and chronic inflammation are exquisitely localized to small airways with minimal extension into adjacent lung parenchyma. Inflammation of bronchiole walls may be accompanied by luminal inflammatory exudates, bronchiolectasis, and/or mucostasis. Acute bronchiolitis is commonly caused by bacterial infections, including classic *Mycoplasma* pneumonia. Chronic bronchiolitis may be accompanied by a distinctive combination of peribronchiolar fibrosis and extension of hyperplastic columnar respiratory epithelium onto fibrotic alveolar septa, a combination of findings referred to as *peribronchiolar metaplasia*. Peribronchiolar metaplasia may also occur in patients with other forms of diffuse parenchymal lung disease, including usual interstitial pneumonia and hypersensitivity pneumonia.

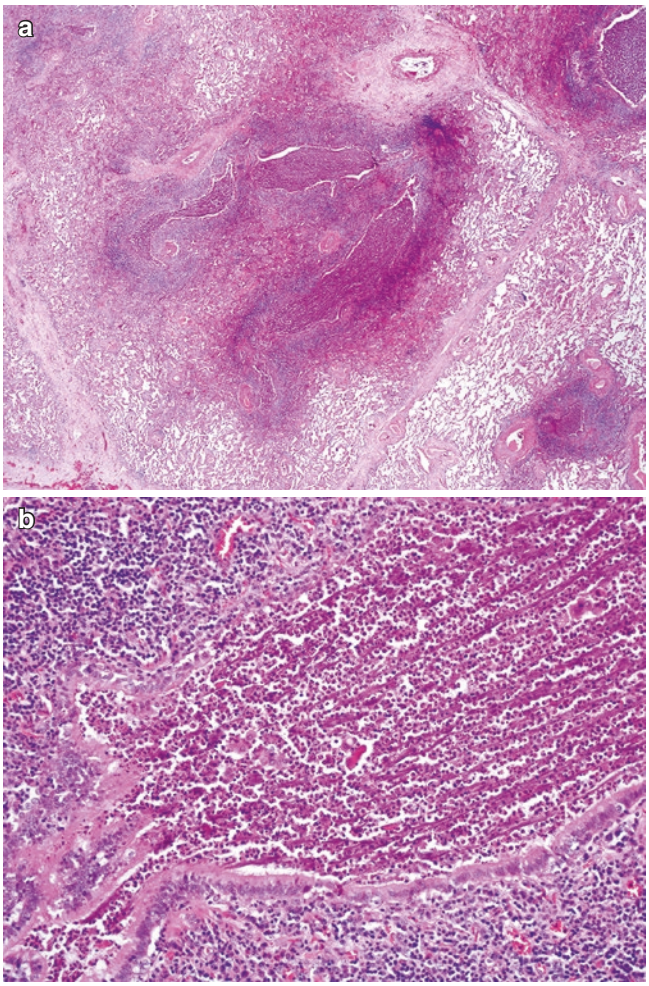

Fig. 5.28 Acute bronchiolitis caused by bacterial infection. (**a**) Low-magnification photomicrograph showing an acute inflammatory exudate distending bronchiole lumina with an acute and chronic inflammatory infiltrate expanding bronchiolar walls. The inflammation is exquisitely localized to the airways, leaving the surrounding lung parenchyma uninvolved. (**b**) High-magnification photomicrograph showing an acute suppurative inflammatory infiltrate distending the bronchiolar lumina. Chronic inflammation predominates in the bronchiole wall. A tissue Gram stain demonstrated bacterial cocci

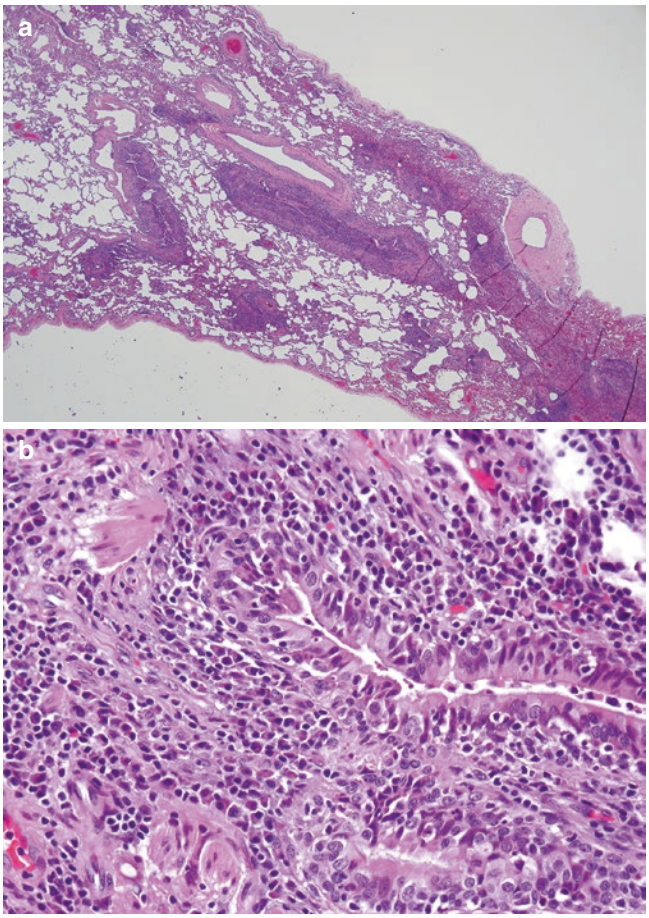

Fig. 5.29 Chronic bronchiolitis, NOS in a patient with systemic lupus erythematosus. (**a**) Low-magnification photomicrograph showing an inflammatory reaction involving the bronchioles without extending into the adjacent lung parenchyma. (**b**) At high magnification, the inflammatory infiltrate is composed of lymphocytes and plasma cells

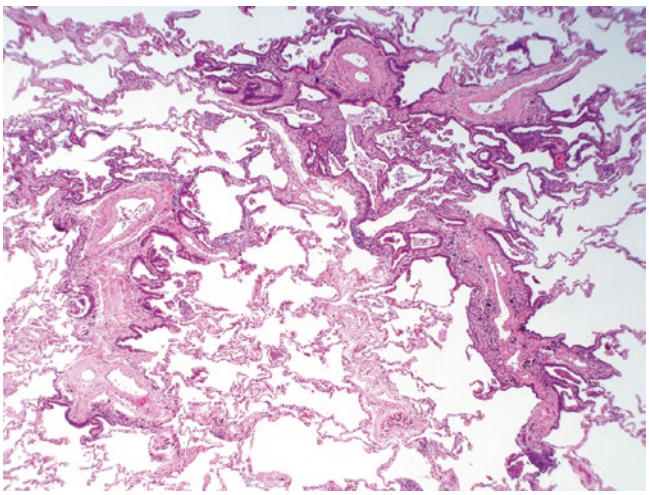

Fig. 5.30 Peribronchiolar metaplasia in chronic bronchiolitis, NOS. Photomicrograph showing chronic bronchiolitis accompanied by fibrosis that extends into peribronchiolar interstitium accompanied by hyperplasia of columnar respiratory epithelial cells. This is a relatively nonspecific manifestation of chronic small airway injury that can occur in a variety of contexts, including in patients with underlying hypersensitivity pneumonia and usual interstitial pneumonia. Occasionally peribronchiolar metaplasia occurs in isolation in patients with mild restrictive lung disease in whom there is no radiologic or histologic evidence of other forms of diffuse lung disease, a circumstance referred to as *peribronchiolar metaplasia-interstitial lung disease*

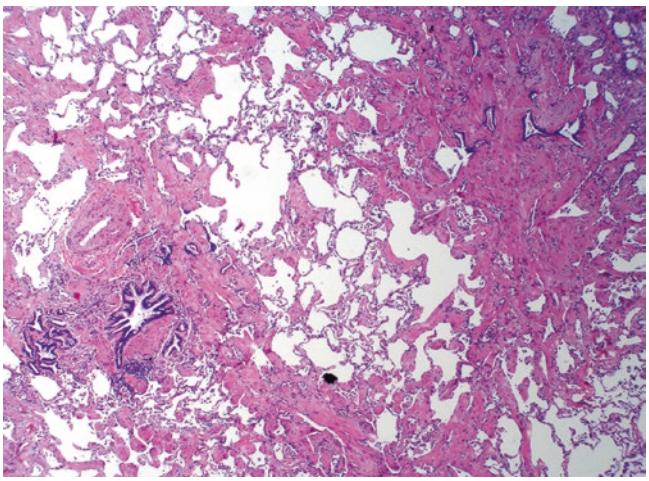

Fig. 5.31 Chronic bronchiolitis, NOS. Low-magnification photomicrograph showing the prominent smooth muscle hyperplasia sometimes associated with chronic small airway injury of any cause, including chronic bronchiolitis, NOS

Emphysema

Emphysema (Figs. 5.32, 5.33, 5.34, 5.35, 5.36 and 5.37) is defined as permanent enlargement of air spaces distal to terminal bronchioles accompanied by destruction of the walls without significant fibrosis. Emphysema is classified into three subtypes: centriacinar (centrilobular), distal acinar (paraseptal), and panacinar subtypes. Centrilobular emphysema shows a predilection for the upper lobes, is usually smoking-related, and is the most common subtype. Panacinar emphysema is associated with alpha-1 antitrypsin deficiency and tends to involve both upper and lower lung zones. Distal acinar emphysema, also commonly referred to as paraseptal emphysema, mainly involves paraseptal and subpleural parenchyma and may cause bullae and/or pleural blebs affiliated with spontaneous pneumothorax. Diagnosis of emphysema is usually based on clinical and radiologic features. Surgical specimens in which emphysema is encountered include lung resected for tumors, pleural bleb resections, and explanted lungs.

Placental transmogrification is an unusual pattern of parenchymal fragmentation seen in severe bullous emphysema, including rare examples of localized giant bullous emphysema presenting as enlarging unilocular cysts.

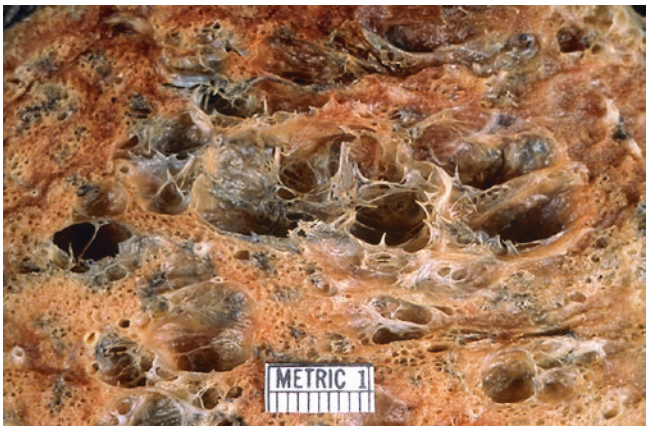

Fig. 5.32 Centrilobular emphysema. Gross photograph showing the cut surface of lung with enlarged air spaces distributed in a centrilobular fashion, leaving relatively spared parenchyma between emphysematous spaces and interlobular septa. No significant fibrosis is seen

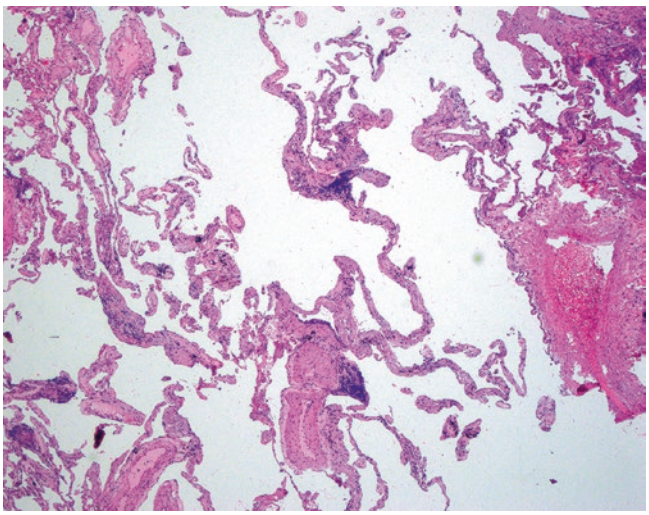

Fig. 5.33 Centrilobular emphysema. Low-magnification photomicrograph showing centrilobular emphysema characterized by enlarged air spaces and alveolar wall destruction

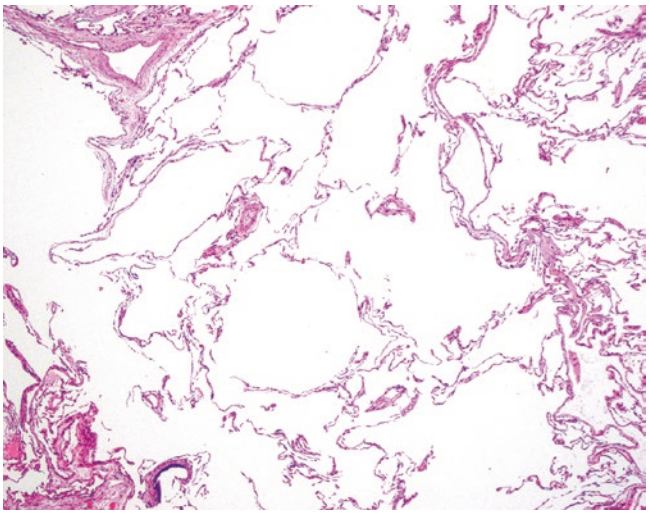

Fig. 5.34 Panacinar emphysema. Low-magnification photomicrograph showing panacinar emphysema characterized by diffusely enlarged air spaces. The alveolar walls are thin and fragmented

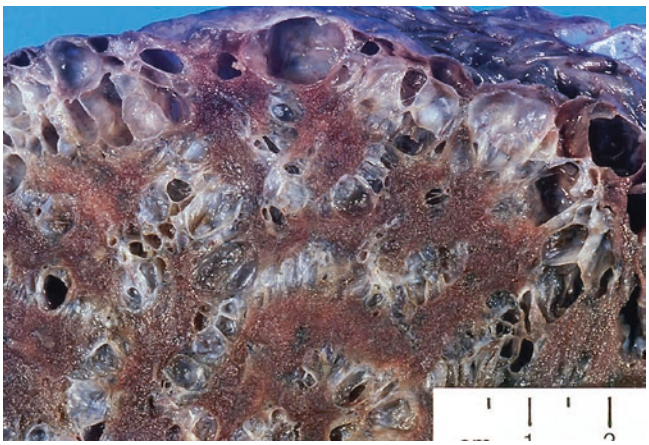

Fig. 5.35 Distal acinar (paraseptal) emphysema. Gross photograph showing the cut surface of the lung with striking distal acinar emphysema characterized by paraseptal and subpleural bullae and blebs

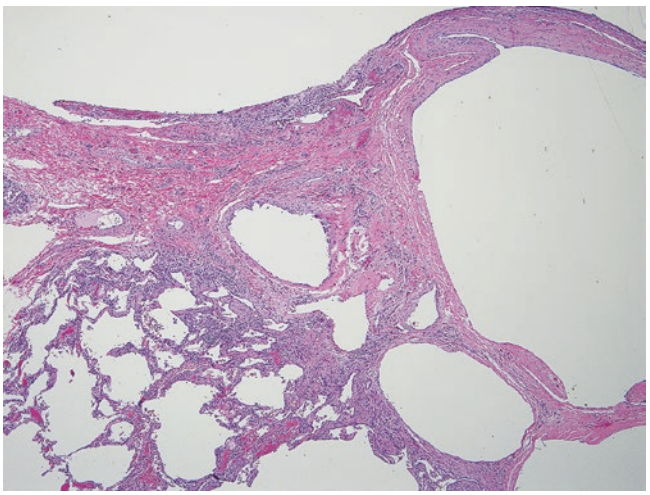

Fig. 5.36 Pleural blebs in distal acinar (paraseptal) emphysema. Low-magnification view of pleural blebs containing air collection within the visceral pleura resulting from rupture of subpleural alveoli and dissection of air into the pleural connective tissue. Fibrosis and chronic inflammation are commonly seen associated with pleural blebs. The immediately adjacent subpleural parenchyma also shows enlarged air spaces

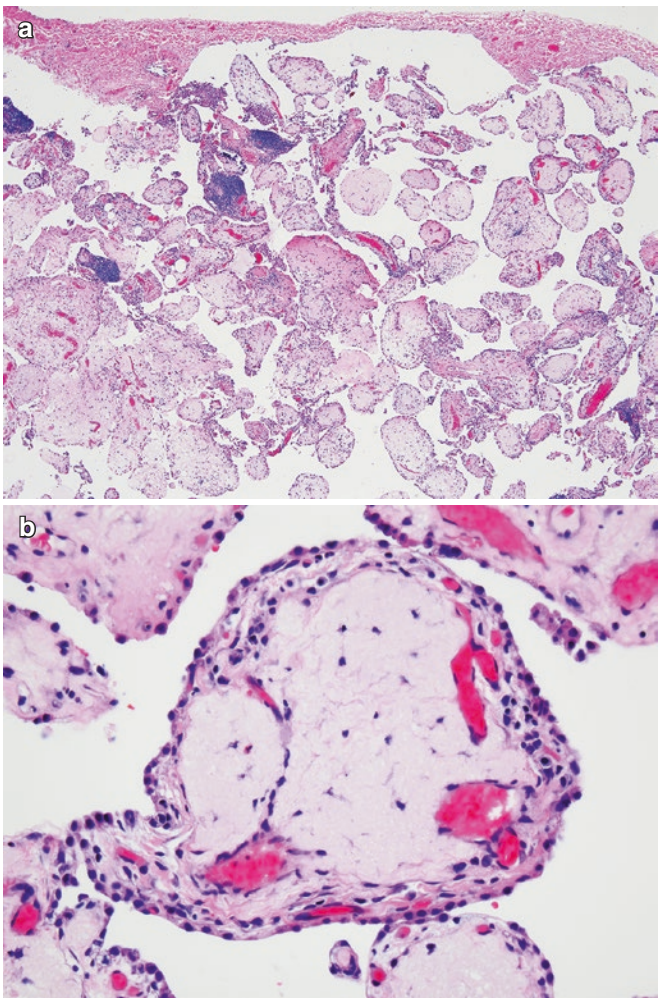

Fig. 5.37 Placental transmogrification in severe emphysema. (**a**) A large emphysematous bulla contains fragmented alveolar walls in which the interstitium is expanded by a combination of inflammation, fibrosis, and stromal mucins, resulting in papillary structures superficially resembling placental villi. (**b**) High-magnification photomicrograph showing fibrovascular cores lined by hyperplastic alveolar pneumocytes resembling placental chorionic villi

Aspiration Pneumonia

Aspiration pneumonia (Figs. 5.38, 5.39, 5.40, 5.41, 5.42, 5.43 and 5.44) caused by foreign material aspiration may present acutely as necrotizing bacterial bronchopneumonia or chronically with mild symptoms and pulmonary nodules or infiltrates. The latter presentation in patients without obvious risk factors for aspiration may raise the clinical suspicion of tumors and atypical infections. Granulomas and organizing pneumonia are commonly seen in aspiration pneumonia. The key to the diagnosis is the presence of foreign material. The aspirated foreign material varies in appearance and in amount. The most commonly encountered aspirated material is degenerated vegetable matter, followed by inert fillers (excipients) common in oral medications, including microcrystalline cellulose and crospovidone, and rarely degenerated skeletal muscle.

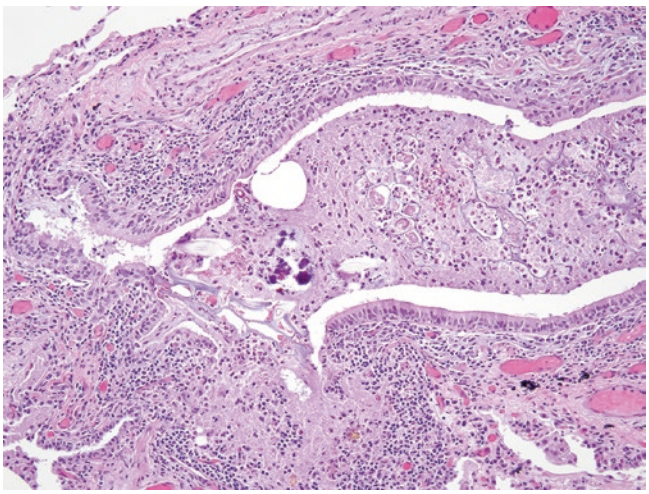

Fig. 5.38 Aspiration pneumonia. Photomicrograph showing degenerated vegetable matter within the bronchiolar lumen associated with a suppurative and fibrinous exudate. No granuloma or giant-cell reaction is present in this example

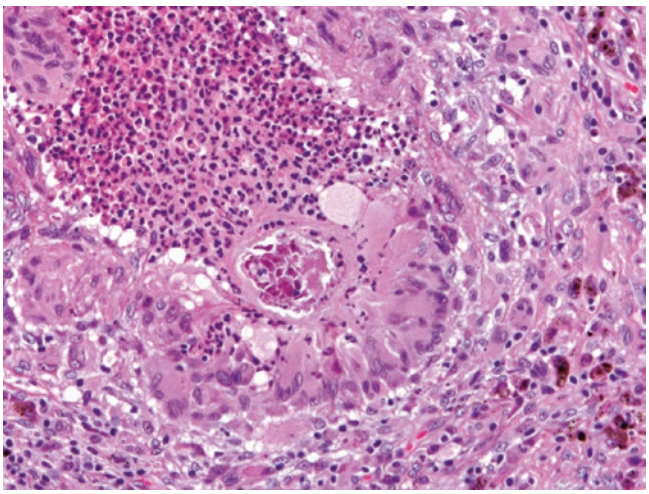

Fig. 5.40 Aspiration pneumonia. High-magnification photomicrograph showing degenerated vegetable matter associated with suppurative granulomatous inflammation

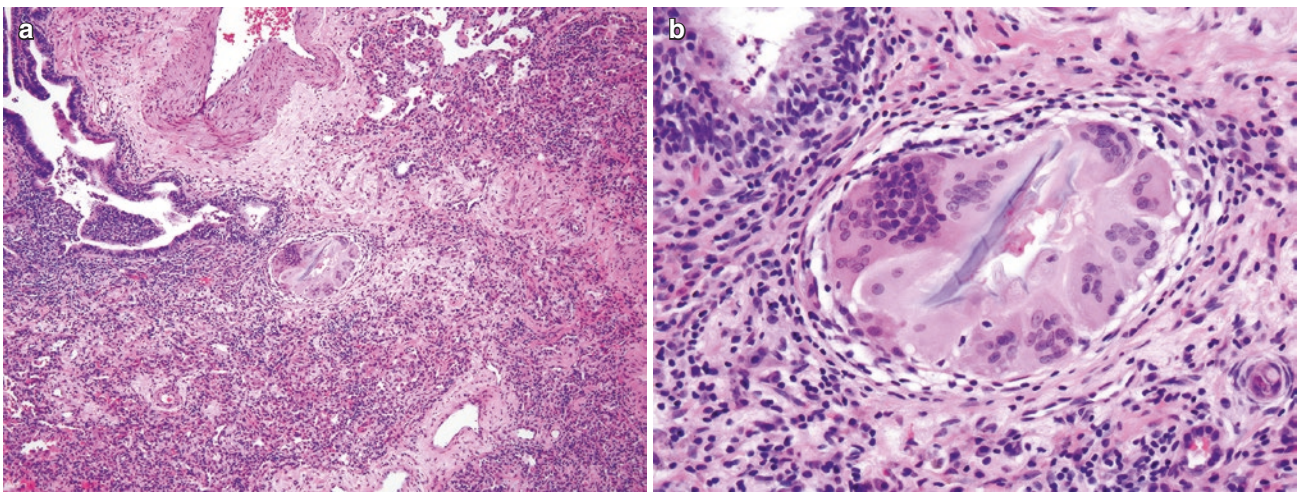

Fig. 5.39 Aspiration pneumonia. (**a**) Low-magnification photomicrograph showing bronchiolocentric chronic and granulomatous inflammation. (**b**) High-magnification view of granuloma composed of multiple giant cells surrounding aspirated vegetable matter

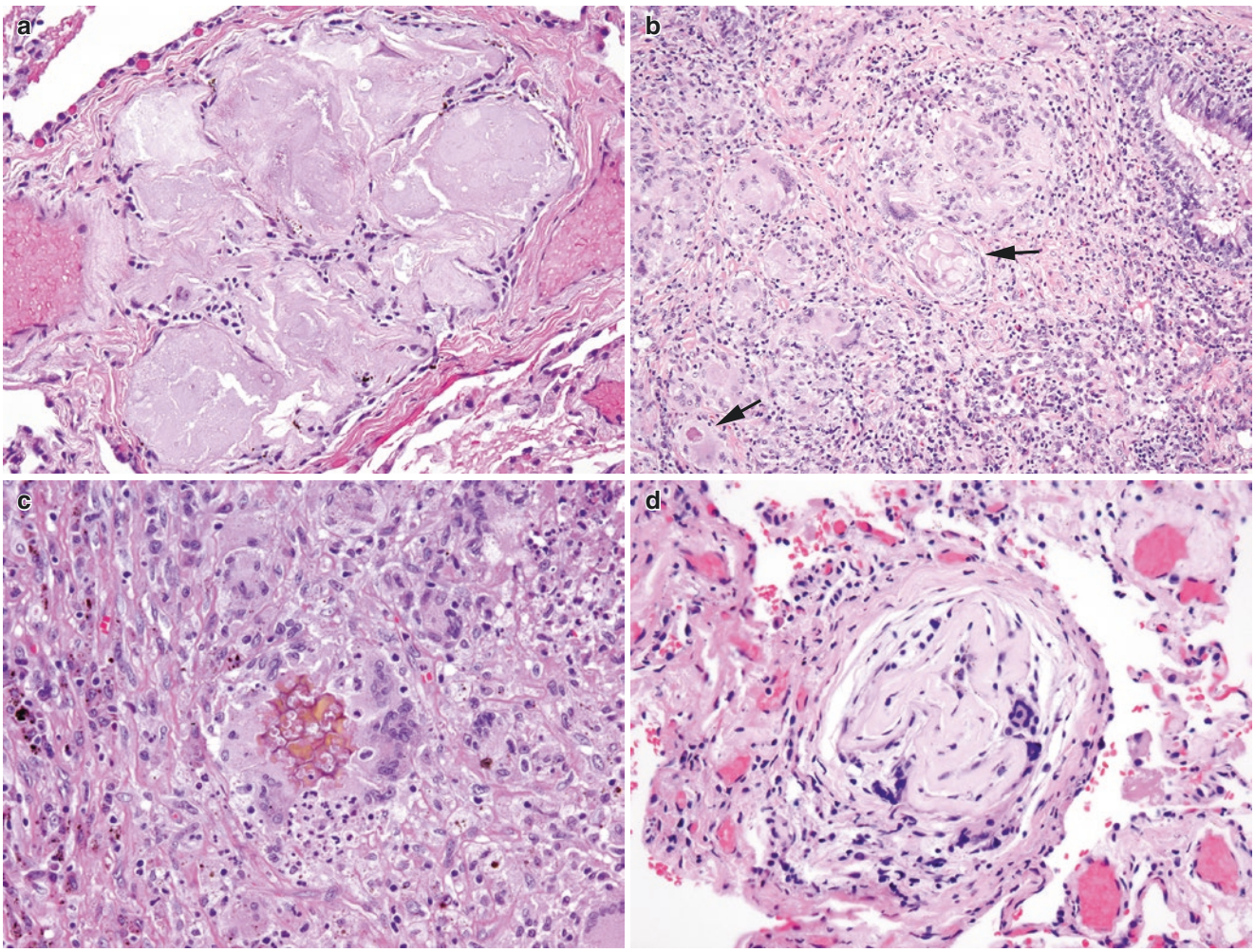

Fig. 5.41 Aspiration pneumonia showing multiple forms of degenerated vegetable matter. (**a**) High-magnification view showing multifaceted large eosinophilic particles lacking internal structures that are situated within the peribronchiolar interstitium and surrounded by a thin rim of histiocytes. (**b**) Another high-power view showing round eosinophilic structures (*arrows*) within multinucleated giant cells. (**c**) High-magnification photomicrograph showing brown amorphous matter within a giant cell. (**d**) High-power view showing collapsed, curved, elongated eosinophilic structures superficially resembling hyalinized blood vessels with an associated giant-cell reaction in peribronchiolar interstitium

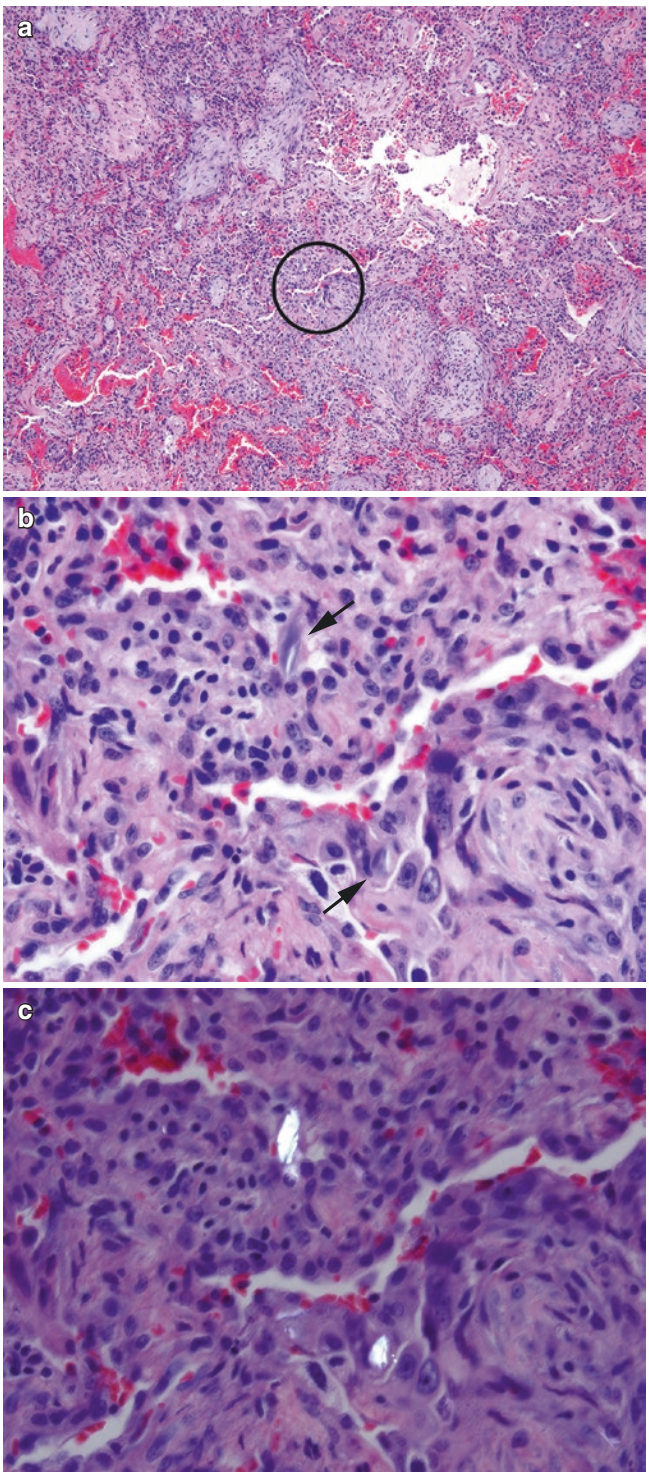

Fig. 5.42 Aspiration pneumonia. (**a**) Low-magnification photomicrograph showing changes of organizing pneumonia characterized by polypoid fibroblast plugs filling up air spaces. Organizing pneumonia is a common finding in aspiration and should prompt a search for other features that might establish aspiration as a likely etiology. (**b**) High-magnification view of the circled area in **a** showing pale-gray crystalline material (*arrows*) characteristic of microcrystalline cellulose, a common inert filler (excipient) in oral medications. (**c**) Microcrystalline cellulose is strongly birefringent when viewed with polarized light

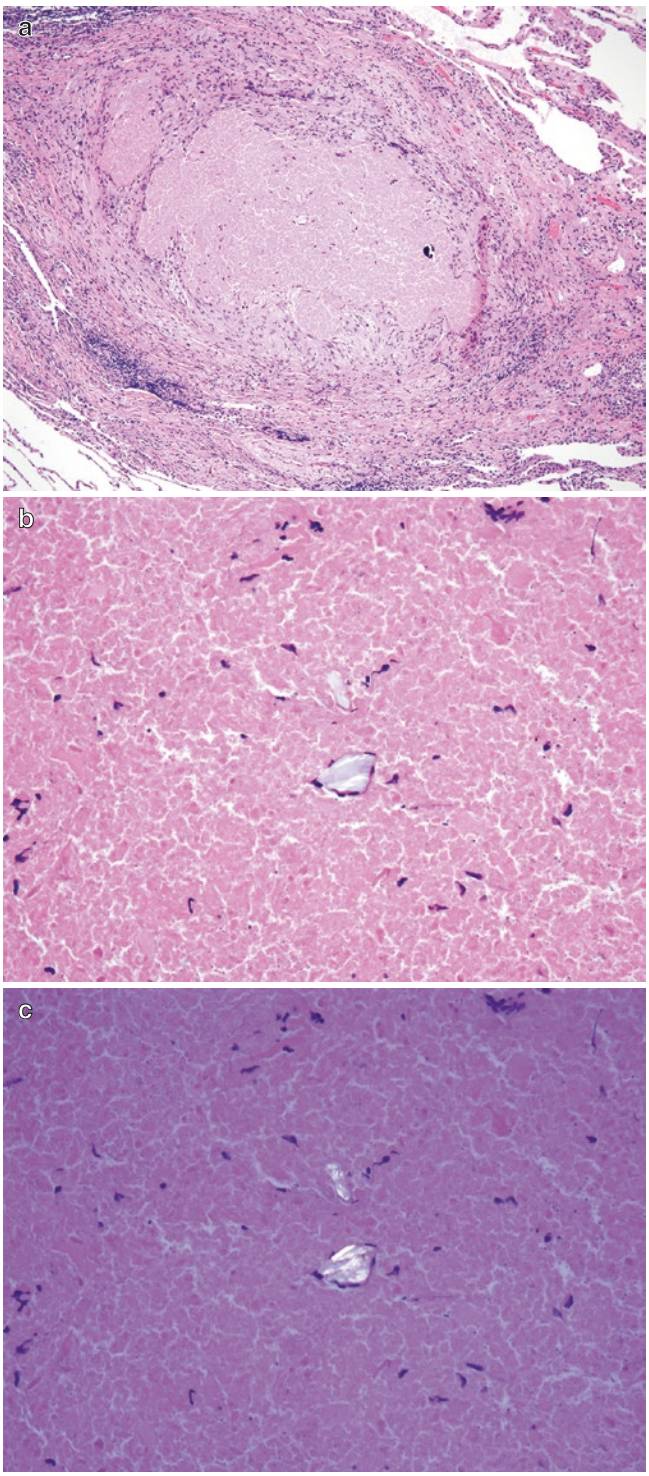

Fig. 5.43 Aspiration pneumonia. (**a**) Low-magnification photomicrograph showing necrotizing granulomatous inflammation centered on an airway ("bronchocentric granulomatosis"). (**b**) Higher magnification of the necrotic center demonstrates pale-gray particulates of microcrystalline cellulose. (**c**) The microcrystalline cellulose shows strong birefringence when viewed with polarized light

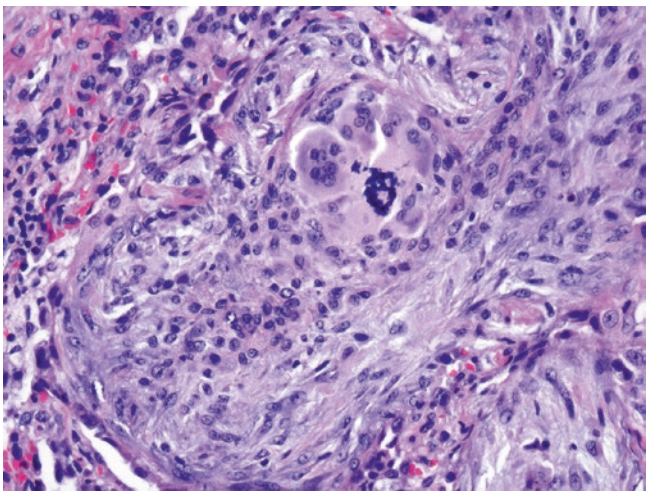

Fig. 5.44 Aspiration pneumonia. High-magnification photomicrograph showing a combination of granulomatous inflammation and organizing pneumonia associated with deeply basophilic, coral-like material consistent with crospovidone, another common filler in oral medications

Suggested Readings

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