Introduction

This chapter discusses six common entities of respiratory disease: obstructive and restrictive disorders of gas exchange, infectious and inflammatory diseases, immunologic disorders, vascular diseases of the lung, tumors of the lung and pleura, and miscellaneous other diseases of the respiratory tract.

Chronic Obstructive Lung Diseases

Chronic obstructive pulmonary disease (COPD) comprises a number of different respiratory diseases, with pathologic obstruction of pulmonary air flow as the common pathogenetic mechanism. Major examples of such diseases include chronic bronchitis, bronchiolitis and asthma, cystic fibrosis (CF), bronchiectasis, and α1-antitrypsin deficiency. COPD causes progressive and destructive emphysema and recurrent inflammation with destruction of lobular tissues and small vessels and finally may lead to cor pulmonale secondary to reduced intrapulmonary blood flow, pulmonary hypertension, and right heart insufficiency.

There are different types of emphysema, with a different extent of the lesion (centriacinar, panacinar, bullous) or different pathogenesis (acinar, paraseptal, interstitial). In radiology (and partly in pathology), the term lobular is used more commonly than acinar, although they are not completely congruent (acini being smaller units than lobes).

The pathophysiology of COPD as determined by spirometric function tests is defined by a normal or increased total lung capacity (TLC) and forced vital capacity (FVC) in combination with decreased forced expiratory volume (FEV). COPD follows either increased resistance to air flow (e.g., luminal narrowing of air ducts) or the loss of elastic recoil (passive widening of air spaces). The figures present gross features of the most common examples of COPD.
Fig. 3.1 Asthma bronchiale. (a) Note the cylindric bronchiectasis caused by chronic bronchitis. (b) Microscopy shows the typical eosinophilic cell infiltrate and sclerosis of the epithelial basement membrane. (c) COPD in this patient leads finally to bullous emphysema. Asthma bronchiale (AB) is a chronic lung disease with recurrent episodes of airflow obstruction caused by various inhaled antigens. The initial response consists of bronchospasm followed by a type I eosinophilic allergic (IgE type) reaction with sustained bronchoconstriction, increased vascular permeability, and secretion of highly viscous mucus. Causes of AB include exogenous allergic stimuli (e.g., pollen, hair, house dust), infectious organisms (e.g., influenza and parainfluenza virus, rhinovirus), drugs (e.g., nonsteroidal anti-inflammatory drugs, aspirin, β-adrenergic antagonists), occupational exposures (e.g., fur exposure by animal handlers, vegetable dusts, metal salts, pharmaceuticals, wood by woodworkers), and reactions induced by stress or exercise (e.g., nonspecific stimulation of sensitized persons by air temperature or dryness).
Fig. 3.2 Chronic exposure to “nontoxic” dusts (common air pollution, cigarette smoking, anthracosis) causes chronic bronchitis, emphysema, and COPD. The type of emphysema is usually centriacinar. Note the decreased consistency of the lung, with bulging and sunken-in parts (a); focal deposits of dust pigment (b); and centriacinar (centrilobular) pronounced emphysema (c). The pathogenesis consists of induction of either nonspecific inflammation or allergic sensitization (see Fig. 3.1). More extensive panacinar (panlobular) emphysema may develop either in the further course of exposure to these nontoxic dusts or ab initio by loss of alveolar septae in inherited diseases such as α1-antitrypsin deficiency.
Fig. 3.3 Interstitial emphysema (right lung), a form of localized emphysema, shows air bubbles resembling a string of pearls in interstitial tissue (arrows). It is caused by bronchoalveolar rupture secondary to high-pressure artificial respiration. Air may extend into the mediastinum and skin with compression of vessels and air spaces, causing severe respiratory and circulatory problems. Other localized emphysemas, such as paraseptal emphysema, may be caused by deposits of specific toxic substances (e.g., occupational exposure to chromium oxide). Irregular emphysema commonly develops around pulmonary scars of varying etiology.

Fig. 3.4 (a, b) CT images of lungs, showing centrilobular emphysema of differing intensity.

Fig. 3.5 A more extensive type, bullous (destructive) emphysema. Note the “clear” peripheral spaces. Bullous emphysema develops from the extension of centrilobular emphysema or from the aggravation of another localized emphysema, indicating long-term persistence of toxic exposures with inflammatory destruction of pulmonary tissue (especially elastic membranes, alveolar septae, and peribronchiolar tissues). Bullous emphysema is usually accompanied by pulmonary hypertension.
Fig. 3.6 CT scan of lungs with lower lobe panlobular emphysema. Note the “clear” spaces in the lower lobe regions.

Fig. 3.7 Paraseptal emphysema affects subpleural lobules and thus has a peripheral location. It is thought to be associated with smoking and has upper lobe predominance, but other toxic inhalants (e.g., fumes, air pollution) may also account for this type of emphysema.
**Fig. 3.8** Different types of emphysema in thin sections of the lung. (a) Centriacinar emphysema. (b) Panacinar emphysema. (c) Bullous emphysema. Information on etiology and pathogenesis may be found in the legends for the preceding figures.
Fig. 3.9 Lung in mucoviscidosis (fibrocystic disease; CF) showing severe bronchiectasis with mucous plugging (a, b). A microscopic overview (c) shows severe overproduction of mucus (red parts in glands, double arrow) as well as bronchiectasis (single arrows) and mucous plugging. CF is an autosomal recessive disorder with deficient exocrine functions or glands in a number of organs, including the pancreas, liver, lungs, small intestines, and others. The disease results from a genetic defect of the CF transmembrane conductance regulator (CFTR) protein, which is responsible for regulating the function of the chloride channel. It most often affects white children, with an incidence of about 1 in 2,500 births. Pathologically, CF is responsible for chronic bronchiolitis and bronchitis with severe mucous plugging and bronchial cyst formation. Chronic pancreatitis and secondary biliary cirrhosis are among other complications.
Fig. 3.10 Similar bronchiectases and COPD may be caused by a hereditary deficiency of α₁-antitrypsin, a circulating glycoprotein produced in the liver and responsible for inhibiting proteases including trypsin, chymotrypsin, elastase, thrombin, and various bacterial proteases. Note bullous emphysema and focal interstitial fibrosis (a), as well as striking bronchiectasis and mucoid metaplasia of the bronchial epithelium (b). α₁-Antitrypsin deficiency in the lung decreases the inhibition of neutrophil elastase and thus will cause emphysema. In the liver, it is associated with the development of cirrhosis.

Fig. 3.11 Mucoviscidosis (CF) in a young male. Note in this chest radiograph distinct upper lobe predilection of bronchiectasis in CF. In more advanced disease, lesions will become more widespread, involving the lobes diffusely.
Fig. 3.12 Four CT scans of the patient in Fig. 3.11, showing progression. In the 1950s, pathologist Lynne Reid classified the extent of bronchiectasis in CF as tubular (a), varicose (b), and cystic (c, d) in progressive order of bronchial disruption.
Chronic Restrictive Lung Diseases

Restrictive pulmonary diseases (RPDs) include a number of disorders that have in common a progressive limitation of respiratory expansion of the lungs. Both acute and chronic forms are defined: Acute RPDs include adult respiratory distress syndrome (ARDS) and acute hypersensitivity pneumonitis, whereas chronic RPDs include idiopathic pulmonary fibrosis (IPF), sarcoidosis, collagen vascular diseases affecting the lung (see the section on Immunologic Diseases), and pneumoconioses. Chronic diseases progress to extensive pulmonary fibrosis with honeycombing, and (as with COPD) pulmonary hypertension and cor pulmonale may develop. Spirometric function tests in RPDs show significantly reduced respiratory compliance (reduced FVC with normal or reduced FEV).

Fig. 3.13  Adult respiratory distress syndrome: voluminous lung with a glistening, fleshy cut surface (a, b). Microscopy shows alveolar and interstitial edema, hyaline membrane formation (c), and (depending on the duration of the lesion) increasing interstitial inflammatory infiltration with fibrogenesis (see also “shock lung” in Fig. 3.64). ARDS is the clinical term for diffuse alveolar damage (DAD) resulting from alveolar epithelial and endothelial damage of various etiologies. Among the etiopathogenetic processes leading to DAD are circulatory shock of any kind, infections (e.g., bacterial septicemia, certain viruses), aspiration, and certain drugs (e.g., oxygen, toxic gases, cytotoxic drugs, heroin). Leakage of proteinaceous fluid into the alveolar space, accompanied by destruction of type I pneumocytes, will initiate fibrin-rich precipitates in alveoli (hyaline membranes) and alveolar walls, with subsequent proliferation of type II pneumocytes and an inflammatory reaction. In patients who survive the acute phase, defective recovery usually leads to interstitial (and partly alveolar) fibrosis.
Idiopathic pulmonary fibrosis (interstitial lung disease, idiopathic interstitial pneumonias) with varying alveolar and interstitial inflammatory infiltrates, progressive interstitial fibrosis, secondary hypertensive vascular disease, and a final stage with honeycombing of the lungs. Note the fleshy gross appearance of the lungs in earlier stages (a), with various microscopic interstitial infiltrates (b–d) and gross honeycombing at the end stage (e). For further subclassification, see Table 3.1. The etiology of these diseases is inhomogeneous, as demonstrated by the large variety of terms in use. In many cases, these diseases appear to be autoimmune, either primary or secondary in the course of other systemic autoimmune disorders, but frequently the etiology remains obscure. These disorders are grouped together because of similar clinical manifestations, including severe shortness of breath, diffuse abnormalities of lung mechanics and gas exchange, and diffuse abnormalities in chest radiographs and CT scans, as well as similar clinical outcomes.
Fig. 3.15 Portable anteroposterior supine image from an intubated intensive care unit patient with diffuse alveolar opacities, as seen in ARDS (e.g., DAD). The patient also has a feeding tube and a left internal jugular catheter with its tip in the superior vena cava (SVC). The alveolar opacities obscure the heart borders, diaphragm, and costophrenic sulci. ARDS is really a clinical diagnosis that may occur in septicemia, hemodynamic shock, circulating toxins, trauma, and many other disorders.

Table 3.1 Classification of idiopathic pulmonary fibrosis

| Feature                  | NSIP  | UIP   | DIP   | AIP   | LIP   | COP   |
|--------------------------|-------|-------|-------|-------|-------|-------|
| Interstitial inflammation|       |       |       |       |       |       |
| Prominent                | Scant | Scant | Scant | Scant | Scant | Prominent |
| Interstitial fibrosis    |       |       |       |       |       |       |
| Collagen                 | Variable, diffuse | Patchy | Variable, diffuse | No | Yes, diffuse | No |
| Fibroblast foci          | Occasional | No | No | Yes, diffuse | No | No |
| BOOP                     | Occasional, focal | Occasional, focal | No | Occasional, focal | No | Prominent |
| Alveolar macrophages     | Occasional, patchy | Occasional, patchy | Yes, diffuse | No | Patchy | No |
| Hyaline membranes        | No | No | No | Yes, focal | No | No |
| Honeycombing             | Rare | Yes | No | No | Sometimes | No |

From Leslie and Wick [1]

AIP acute interstitial pneumonitis, BOOP bronchiolitis obliterans with organizing pneumonitis, COP cryptogenic organizing pneumonitis, DIP desquamative interstitial pneumonitis, LIP lymphocytic interstitial pneumonitis, NSIP nonspecific interstitial pneumonitis, UIP usual interstitial pneumonitis
Fig. 3.16 (a–d) Four axial CT images of honeycombing, showing the classic patterns of usual interstitial pneumonitis (UIP): peripheral, subpleural thin-walled air cysts with basal distribution and traction bronchiectasis. If the etiology of honeycombing is unknown (as it is in 70% of cases), it is called idiopathic pulmonary fibrosis. The remaining 30% of UIP patterns are associated with asbestosis, collagen vascular disease such as scleroderma, rheumatoid arthritis and lupus erythematosus, chemotherapeutic drug toxicities, chronic hypersensitivity pneumonitis, or end-stage sarcoid. IPF, a type of chronic fibrosing interstitial pneumonitis, results from recurrent focal injury of the alveolar wall epithelium and abnormal wound healing.
Systemic diffuse (miliary) sarcoidosis causing restrictive lung disease. The appearance features voluminous lungs with multiple miliary white nodules throughout the parenchyma (a, b, surface; c, cut surface). Microscopy shows typical noncaseating, epithelioid cell granulomas (d) with asteroid and Schaumann bodies (e) in multinucleated giant cells. Granulomas successively progress to fibrosis (nodular and interstitial). Sarcoidosis is a systemic granulomatous disease of yet unknown etiology, with the lungs being the most frequently affected organ. Lymph nodes, skin, brain, and eyes are also commonly affected. The disease is characterized by an abnormal accumulation and activity of CD4 T helper lymphocytes, suggesting a certain abnormal immune reaction to an exogenous stimulus (e.g., a defect of T-suppressor cell function?). Sarcoidosis is most frequent among Scandinavian populations, but it affects all races and both sexes.
Fig. 3.17 (continued)

Miner’s lung. Occupational exposure to dusts (coal dust and other types) causes COPD progressing to RLD. (a) Note the extensive deposits of black dust in the lung, with extensive focal scarring. (b, c) Microscopy shows extensive scarring related to pigment deposits and surrounding (local) emphysema. For further subclassification, see Table 3.2.
### Table 3.2 Clinical and pathologic features of pneumoconioses

| Entity                                      | Clinical appearance          | Pathologic changes                                                                 |
|---------------------------------------------|------------------------------|----------------------------------------------------------------------------------|
| Coal miner’s lung Black lung disease        |                              | Diffusely distributed, small focal anthracosilicosis, initially centriacinar and peribronchiolar with many carbon-laden macrophages and perifocal emphysema. Extent of fibrosis depends on admixture of quartz |
| Silicosis                                   |                              | Alveolar lipoproteinosis and progressive diffuse interstitial fibrosis secondary to inhalation of small, particulate silica crystals (e.g., after sand blasting) |
| Nodular silicosis                            |                              | Multiple growing silicotic nodules, usually 2 mm to 1 cm in diameter; fibrosing granulomas with concentric fibrous layering, some anthracotic pigment, small slitlike spaces, and needle-shaped crystalline spicules on polarization; perifocal emphysema |
| Nodular silicosis (common)                  |                              | Multiple growing silicotic nodules, usually 2 mm to 1 cm in diameter; fibrosing granulomas with concentric fibrous layering, some anthracotic pigment, small slitlike spaces, and needle-shaped crystalline spicules on polarization; perifocal emphysema |
| Progressive massive silicosis               |                              | Multiple silicotic granulomas up to 10 cm in diameter, both lungs involved, massive and rapidly progressive fibrosis |
| Asbestosis and asbestos-related diseases     |                              | Alveolitis with progressive interstitial fibrosis, deposition of asbestos bodies (golden-brown beaded rods consisting of asbestos fibers coated by ferroproteinaceous material); honeycombing lung in final stage |
| Asbestosis                                  |                              | Recurrent pleural fibrinous effusions, pleural fibrosis and pleural plaques (“sugar coating”), focal atelectasis secondary to pleural fibrosis |
| Pleural plaques and rounded atelectasis     |                              | Malignant mesothelioma (increased risk of bronchogenic carcinoma) |
| Neoplasms                                    |                              |                                                                                  |
| Berylliosis                                  |                              | Acute and recurrent pneumonitis, systemic sarcoidlike and fibrosing granulomas |
| Talcosis                                     | Talcosis                     | Foreign-body granulomas with birefringent talcum deposits; micronodular and diffuse interstitial fibrosis |

*Caplan’s syndrome occurs in patients with rheumatoid arthritis and some form of nodular silicosis. Deposition of microparticulate iron causes siderotic macrophage response with secondary focal or diffuse interstitial fibrosis.*
Fig. 3.20 Chest radiograph of a patient with stage IV interstitial lung sarcoidosis and very low lung volumes.

Fig. 3.21 Chest radiograph from a patient with miliary sarcoidosis.

Fig. 3.22 (a, b) Posteroanterior and lateral chest radiographs showing the classic 1-2-3 sign of sarcoidosis: right paratracheal adenopathy = 1, right hilar adenopathy = 2, and left hilar adenopathy = 3.
Fig. 3.23  (a–c) Axial CT scans demonstrating mediastinal and bilateral hilar lymphadenopathy
Fig. 3.24 Enlarged section of a lateral chest radiograph from a patient with miliary silicosis (simple silicosis). Note the diffuse fine granular opacities.

Fig. 3.25 Chest radiograph of a patient with progressive massive fibrosis or conglomerate masses in complicated silicosis. Progressive massive fibrosis in patients with complicated silicosis represents the coalescence of individual silica granulomas (the miliary nodules in simple silicosis), which are slowly retracted toward the hila, leaving emphysema in their wake.
Pathologic features of pulmonary infections are quite variable, depending on the etiologic organism and its toxicity, replication, and persistence, as well as on the quality and intensity of host defense mechanisms. Bacterial pneumonias (bronchogenic or hematogenous) commonly are suppurative, abscessing, necrotizing, or hemorrhagic. Viral pneumonias (through immune T-cell stimulation) are preferentially lymphocytic and, in severe cases, are necrotizing and hemorrhagic (e.g., classic influenza). Fungal infections in the lung stimulate macrophages and frequently cause granulomas (also an immune T-cell reaction); depending on their toxicity, they may cause additional necroses and vascular invasion with thromboses. Parasitic infestations and mycobacterial infections also stimulate phagocytosis and may cause granulomas. Only acute pneumonias without significant tissue necrosis can show complete resolution and healing. Longer-lasting or chronic pneumonitides will resolve incompletely with residual scarring. Chronic, persistent infections consequently also present a risk of the development of chronic restrictive lung diseases.
Fig. 3.26 Bronchopneumonia (a) with pseudolobular spread (b, c) and occasional abscess formation (d). Microscopy shows the typical bronchial inflammatory infiltrate spilling over into the adjacent alveolar complexes (e). This is the typical picture of an aerogenic (bronchial) bacterial infection causing acute bronchitis, peribronchitis, and alveolar neutrophilic inflammation. The extent of further spread (nodular, pseudolobular, segmental, lobular) depends on the defense potential of the patient, and the microscopic manifestation of the inflammatory exudate (with necrosis or hemorrhage) depends on the toxicity of the bacterial colonies (producing exotoxins or endotoxins)
Fig. 3.26 (continued)
Fig. 3.27 Variants of bacterial pneumonia include necrotizing pneumonia (a, b; here with *Pseudomonas* or *Nocardia* infection) and hemorrhagic pneumonia (c, d, here with *Klebsiella* infection)
Another variant of bacterial pneumonia is presented in this patient with leukemia and severe pancytopenia showing a combination of hemorrhagic and fibrinous pneumonia caused by mixed infection with staphylococci and *Klebsiella* species. (a) The cut surface of the lung shows a severe segmental, hemorrhagic pneumonia in the upper lobe (e.g., by *Klebsiella* species) and a pale, fibrinous pneumonia in the middle and lower lobe, preferentially by staphylococci. (b, c) Respective microscopic views. In (c) Weigert’s stain is used to demonstrate the blue fibrin network.
Fig. 3.29 Chest radiograph of bronchopneumonia, caused by pneumococci in this patient. The image shows focal consolidation of much of the left upper lobe, which obscures the left heart border, indicating the replacement of air with consolidation in the lingual lobe.

Fig. 3.30 Lobar pneumonia, a bacterial pneumonia (commonly pneumococcal), which affects an entire lobe with a uniform inflammatory infiltrate and progresses in stages: stage I, hyperemia; stage II, red-gray hepatization (fibrinous alveolar exudate); stage III, yellow hepatization (neutrophilic infiltrate); and stage IV, lysis of exudate and recovery. Shown here is the red-gray hepatization (uniform hyperemia with early fibrinous coagulation).
Fig. 3.31 Chronic organizing pneumonia ("carnification"). The inflammatory exudate in a bacterial or fungal pneumonia is not resolved but is replaced by organization tissue progressing to fibrosis. (a) The lung impresses grossly by its similarity to "fresh meat" (carnification). (b) Microscopy shows the complete obliteration of air spaces by granulation tissue progressing to fibrosis (scarring). Such lesions indicate a significant defense deficiency of the patient (e.g., inherited or acquired immune deficiency).

Fig. 3.32 (a, b) CT scans of organizing pneumonia in a patient with dermatomyositis. When the etiology of organizing pneumonia is unknown, the same lesions are called cryptogenic organizing pneumonia (COP). COP represents an abnormal reparative response of the lungs and may be associated with pulmonary infections, aspiration, bronchial obstruction, drug reactions, collagen vascular diseases, or toxic fume inhalation. Organizing pneumonia has a good prognosis, and most patients respond to steroids.
Fig. 3.33 Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. The course of the disease and its spread to other organs are most obviously determined by two parameters: the toxicity of the bacterium (cord factor) and the extent of the body’s defense against it. Accordingly, TB is classified into various stages, as shown in Table 3.3. The figures in this section show typical examples of pulmonary TB. Acute exudative tuberculosis (a) shows various small foci in the lung with prevalent caseous necrosis (b) and rapid aerogenic and lymphatic progression. More commonly, acinar-nodular tuberculosis (c) with caseating granulomas (d) indicates a better local resistance and slower bronchial and lymphatic spread. Mycobacteria are shown by acid-fast Ziehl–Neelsen stain (e) or by auramine–rhodamine fluorescence (f).
### Table 3.3 Forms and features of pulmonary tuberculosis

| Stage                                      | Immune reactivity | Clinicopathologic features                                                                 |
|--------------------------------------------|-------------------|-------------------------------------------------------------------------------------------|
| **Stage I (primary)**                      |                   |                                                                                           |
| Initial infection                          | No immunity       | Clinically inapparent, nonspecific alveolitis                                             |
|                                            | Developing immunity| Ghon’s primary infection: isolated granulomatous reaction, most commonly in right upper lobe|
| Primary lymphatic spread                   | Developing immunity| Lymphatic spread of infection to regional lymph nodes with respective granulomas: Ranke’s primary complex |
| **Stage II (early postprimary generalization)** |                   |                                                                                           |
| Lymphatic spread                           | Good              | Isolated subpleural caseous granuloma, upper segments of right upper lobe                   |
| Bronchogenic spread                        | Intermediate      | Acinar-nodular pulmonary TB with progressive caseous granulomas                            |
|                                            | Poor              | Progressive caseous pneumonia without prominent granulomatous reaction                     |
| Hematogenous spread                        | Intermediate      | Systemic hematogenous caseous granulomas of different sizes (i.e., different ages)         |
| **Stage II (late postprimary generalization)** |                   |                                                                                           |
| Hematogenous spread                        | Nonimmune reactive| Miliary TB with systemic granulomas of uniform size (and age)                              |
| Hematogenous spread (also in early postprimary spread) | A-reactive | Miliary systemic necroses, tuberculosis acutissima, typhobacillosis Landouzy                |
| **Stage III**                              |                   |                                                                                           |
| Isolated organ TB                          | High              | Limited spread in isolated organs: cavernous pulmonary or renal TB, isolated tuberculomas (granulomas) in brain, spine, and other organs |
| Late generalization                        | High low          | Local or systemic spread of isolated organ TB (lymphatic, bronchogenic, or hematogenous)   |

*Several newer classification schemes for the stages of tuberculosis (TB) are available. The classic scheme is presented here in order to consider the three main factors determining the course and outcome of the disease: the toxicity of the mycobacterium, the reactivity of the infected, and the time after initial infection. The degree of immune reactivity (not resistance to disease) may be monitored by tuberculin skin testing; the toxicity of tubercle bacteria is partly determined by the “cord factor.”*
Cavernous tuberculosis with a large cavity drained by a bronchus (a). Microscopy shows the wall of a cavern with necrotic debris and giant cell reaction, suggesting ongoing infection (b). Cavernous TB represents stage III (localized organ involvement) and indicates a slower progression with good local defense. However, the granulomatous response itself destroys larger parts of tissues, and changes in host defense may cause late hematogenous generalization of the disease. In addition, chronic infection and inflammatory reaction in such foci may finally lead to amyloidosis.
Fig. 3.35 Miliary (hematogenous, systemic) tuberculosis with multiple small and well-delimited granulomas in lungs and other tissues (a), as shown by microscopy (b). Characteristically, all granulomas are of the same size (i.e., the same age), indicating that they developed within a short time window. This typically happens in late primary TB with nearly normal immune sensitivity, when mycobacteria disseminate hematogenously. Bacteria seed to various organs without major inflammatory response (typhobacillosis), resensitizing the host’s body. Once sufficient immune reactivity has been regained, multiple granulomas of the same age will develop at sites of mycobacterial colonies. This mechanism significantly distinguishes miliary TB from the more common hematogenous TB with a still-active primary site. In this case, tuberculous granulomas develop immediately as bacteria settle in various tissues, so the granulomas are of different sizes and ages. Miliary TB may even develop in patients not known to have had TB (with a clinically occult focus and “normal” immune sensitivity).

Fig. 3.36 (a, b) Axial CT scans of a right upper lobe cavitary tuberculosis. Shown for comparison is a large lesion in the same lung, representing a tuberculous cavity superinfected with Aspergillus species (a). Note the irregular shadows within the large cavity of this aspergilloma.
Fig. 3.37  Posteroanterior chest radiograph of a miliary tuberculosis. The radiologic differential diagnosis of miliary lung disease as shown here includes atypical mycobacterial disease, fungal diseases (histoplasmosis, coccidioidomycosis), *Pneumocystis carinii* pneumonia, sarcoidosis, silicosis, and coal workers’ pneumoconiosis, as well as miliary metastases from renal or thyroid cancers
Viral Pneumonitis

Fig. 3.38 Acute viral pneumonitis is characterized by a variable combination of interstitial mononuclear, inflammatory infiltrates and diffuse alveolar damage. Depending on the “toxicity” of the virus, bronchiolitis obliterans, hemorrhages, or capillary endothelial damage with thrombosis may be superimposed. Shown in this chest radiograph are diffuse interstitial infiltrates (a). The gross feature of the lungs in most viral pneumonitides is a voluminous lung with a reddish, wet cut surface and increased consistency (b). The type of viral infection must be identified by microscopy and molecular or viral techniques. Microscopic examples show measles-virus pneumonitis (c) with Warthin–Finkeldey cells (d) or owl-eye cells in cytomegalovirus infection (e).
Fig. 3.39 Influenza virus infection is characterized by severe hemorrhagic pneumonitis. These examples show an acute influenza pneumonitis in a child (a) and severe hemorrhagic pneumonitis (b) and tracheobronchitis (c) in influenza virus infection of a young adult patient. Microscopy shows extensive tissue destruction and hemorrhage (d). The term pneumonitis is used to stress that the disease characteristic-ally affects all parts of the lung: air spaces, interstitial septae, and vasculature.
Fig. 3.39 (continued)
Fungal Pneumonia

Fig. 3.40  Fungal pneumonia shows quite variable features depending on the persistence and toxicity of the fungus and the type and extent of the body’s reaction to it. Fungal pneumonia frequently shows a combination of acute (exudative) and chronic (granulomatous) reactions. Examples here are an *Aspergillus* abscess in the lung on a typical radiograph (a), gross appearance of the same lesion on the cut surface of the lung (b), and microscopy with fungal organisms in periodic acid–Schiff (PAS) stain (c). Localized colonization by *Aspergillus* species (e.g., in the lungs or paranasal sinuses) may lead to immune sensitization in the patient and cause allergic aspergillosis. The radiograph (d) shows a typical pneumonic flare-up in allergic aspergillosis.
Fig. 3.41 Severe fungal pneumonia with dual infection. Note the slightly lobulated, firm, fleshy lung with focal abscesses surrounded by hyperemia and hemorrhage (a). The abscesses are colonized by *Candida tropicalis* organisms (b), and the diffuse pneumonia is caused by cryptococcal infection (c). The patient suffered from AIDS. Fungal infectious diseases of internal organs are always highly suspicious for underlying immune deficiency, including secondary forms that accompany malignant neoplasms.
Fig. 3.42  Lung of a newborn child with inherited immune deficiency and fungal abscess. Isolated fungi were of *Candida* species

Fig. 3.43  Axial CT image of the mid-lung zone of a patient with AIDS and disseminated miliary cryptococcosis

Fig. 3.44  Axial CT image of the lung apices showing a cavity filled with *Aspergillus* organisms (a mycetoma or, more specifically, an aspergilloma). The patient had a history of cavitary TB, and the left upper lobe cavity is a residuum from that TB
Fig. 3.45 Mucormycosis of the lung. Large necrotizing granuloma in the lung (a) with characteristic invasion of blood vessels by fungal organisms (b) causing pulmonary infarcts. Microscopy shows irregularly shaped fungal rods in necrotic debris (c). *Mucor* organisms are known to invade and destroy pulmonary tissues without recognizing any barrier, as seen by their vascular invasion.
Protozoal Infections

Fig. 3.46 *Pneumocystis carinii* pneumonia in a patient with AIDS. Radiography shows cloudy and streaky pulmonary infiltrates (a). The lungs are voluminous, pale, and of a slightly “rubbery” consistency (b). Microscopy shows a mild interstitial lymphocytic infiltrate and a marked foamy alveolar exudate containing many organisms (c). Organisms are stained with PAS (d) or methenamine silver stain (e). *Pneumocystis* organisms can also be shown clinically by immunofluorescence staining in bronchoalveolar lavage (f). Note that parasitic infestations of the lungs usually cause granulomatous reactions or abscesses and need to be distinguished from other lung diseases previously discussed, such as sarcoidosis, TB, abscessing pneumonia, and fungal infections.
Fig. 3.46 (continued)

Fig. 3.47 Posteroanterior chest radiograph of a patient with AIDS and *Pneumocystis carinii* pneumonia, showing diffuse interstitial and perihilar opacities as well as air space opacities.
Fig. 3.48 (a–d) Axial CT images from the patient in Fig. 3.47. Ground-glass opacities are seen, occasionally with upper lobe pneumatoceles, particularly in patients treated with aerosolized pentamidine
**Immunologic Diseases of the Lung**

Some lung diseases already mentioned—asthma (COPD) and acute hypersensitivity pneumonitis (an RPD)—have an immunologic pathogenesis. Similarly, for several forms of IPF (fibrosing alveolitis), autoimmune mechanisms are considered to be contributory in their pathogenesis or course. In addition, collagen vascular diseases such as systemic lupus erythematosus (SLE), primary systemic sclerosis (scleroderma), and rheumatoid arthritis frequently involve the lungs. Patients with rheumatoid arthritis may show features of silicosis (Caplan’s syndrome), and several forms of systemic vasculitides also affect the lungs, including Goodpasture’s syndrome, Wegener’s pneumogenic granulomatosis, and Churg–Strauss disease. Although gross features of these disorders are usually nonspecific, the figures show a few examples as a reminder for the differential diagnosis. All are thought to have an autoimmune pathogenesis, although the etiology remains obscure. Many of these diseases have genetic traits. (See also the figures on asthma and IPF under Sect. “Chronic Obstructive Pulmonary Diseases.”)

**Fig. 3.49** Systemic lupus erythematosus. SLE belongs to the group of collagen vascular diseases, together with rheumatoid arthritis, progressive systemic sclerosis (scleroderma), polymyositis and dermatomyositis, mixed connective tissue disease, and Sjögren’s syndrome. Their clinical findings and pathology need to be distinguished from those of other idiopathic interstitial pneumonias, as previously discussed. Shown here is an example of SLE with grossly pale, fleshy lungs (a, b), pleural fibrosis, and diffusely increased firmness. Pulmonary disease commonly starts as acute alveolitis with edema and variable interstitial inflammation (e.g., nonspecific interstitial pneumonia [NSIP]) and may be complicated by focal hemorrhage. Later microscopy is variable, with pleural and focal interstitial fibrosis (c), occasional vasculitis, and frequent infections. End-stage changes usually consist of nonspecific fibrosis and sequelae of recurrent infections.
Lung in rheumatoid arthritis. The gross appearance shows patchy pleural fibrosis, increased firmness, and irregular emphysema (a). Microscopy shows chronic inflammation with lymphoid follicles, interstitial, peribronchial (“follicular bronchiolitis”), and pleural, with variable degrees of interstitial fibrosis. A specific form of rheumatoid arthritis occurring in association with silicosis is referred to as Caplan’s syndrome. The example shown here displays patchy and nodular fibrosis on the cut surface of the lung (b) and on microscopy (c). Rheumatoid nodules in the lung must be distinguished from Wegener’s granulomatosis (see Fig. 3.53).
Fig. 3.51 Systemic lupus erythematosus. The initial posteroanterior chest radiograph in this patient shows a normal-sized heart and clear lungs (a). Five months later, the cardiac silhouette is enlarged because of pericardial effusion (b), and parenchymal opacities are observed (c), which may represent hemorrhage or infections in patients with SLE.
Fig. 3.52 Caplan’s syndrome in a patient with rheumatoid arthritis also exposed to silica or coal dust. The image shows pulmonary nodules, preferentially in the upper lobes, which may cavitate. The differential for such pulmonary nodules (which cavitate) includes septic pulmonary emboli, lung metastases (usually from primary SCC), Wegener’s granulomatosis, or sarcoidosis (compare also Fig. 3.57). The most common chest manifestations in rheumatoid arthritis include pleural effusion, lower lobe subsegmental atelectasis, and basal interstitial lung disease, including the UIP pattern (see Table 3.1)
Fig. 3.53 Wegener’s granulomatosis. Wegener’s granulomatosis is a rare form of systemic vasculitis (see Table 1.1) affecting the upper respiratory tract, lungs, kidneys, and, rarely, any other organ. The etiology is unknown; it is thought to be a pneumogenic, autoimmune disorder characterized by the development of antineutrophil cytoplasmic antibodies. Pulmonary changes in Wegener’s granulomatosis feature necrotizing granulomas of various sizes (a, b) with possible cavitation. Necroses are punctate or geographic, with neutrophilic infiltration and nuclear dust, and occasionally bronchocentric or complicated by hemorrhage. Lymphoid cells, as well as giant cells and some eosinophils, occur (c, d). Wegener’s granulomatosis is generally fatal; immunosuppressive drugs may produce remissions, but recurrences are frequent.
Fig. 3.54 Primary systemic sclerosis (scleroderma) is a collagen vascular disease often affecting the lung. (a) Grossly, there are irregular, grayish densities of the parenchyma combined with signs of COPD (emphysema) and restrictive lung disease. (b–d) Microscopy shows a paucicellular interstitial infiltration with distinctive interstitial “collagenization,” leading to patchy and diffuse fibrosis (collagen fibers are blue, elastic fibers black). Focal emphysema, honeycombing, and pulmonary hypertension develop.
Fig. 3.55 Posteroanterior radiograph from a young woman with Wegener’s granulomatosis showing multiple cavitary nodules and a few noncavitated nodules. This patient also had sinusitis but no renal involvement.

Fig. 3.56 Posteroanterior radiograph from another patient with Wegener’s granulomatosis showing alveolar effects closely resembling the diffuse hemorrhages in Goodpasture’s syndrome (see Fig. 3.59)
Fig. 3.57 Primary systemic sclerosis (scleroderma). (a–e) Axial high-resolution CT images of the chest of a 40-year-old woman. These images depict the lung bases, the most involved parts of her disease. They demonstrate honeycombing, traction bronchiectasis, mild ground-glass opacities, and an air–fluid level in the esophagus (visible when the patient is prone). In this patient, the pattern is UIP because the ground-glass opacities are not the predominant abnormality. Patients with scleroderma also may present with a pattern of NSIP in which ground-glass opacities predominate.
Fig. 3.57 (continued)
Vascular Diseases of the Lung

Vascular lung diseases include primary or secondary changes of the structure of blood vessels. Most common are plexiform vessel disease (the end stage of pulmonary hypertension) and primary pulmonary glomangiosis (Masshoff and Röher disease [MRD]). Another group of vascular diseases in the lung occurs secondary to clotting disorders, with occlusion of intrapulmonary blood vessels by thromboembolism or local thrombosis (e.g., with the use of hormonal contraceptives). Structural vascular alterations, including extensive thromboses of small vessels, are commonly accompanied by severe pulmonary hypertension and cause cor pulmonale.

Thromboembolic and major thrombotic disorders may cause pulmonary hemorrhagic infarction (in cases of left ventricular heart failure) and ultimately also pulmonary hypertension. Acute massive thromboembolism of major pulmonary arteries will cause acute right heart failure and sudden death.

A related condition is “shock lung,” although it is caused by systemic circulatory failure rather than being a primary disease of the lung vasculature. Shock lung not infrequently determines the final outcome of the patient’s clinical course.

(See also the figures on Wegener’s granulomatosis under “Immunologic Diseases of the Lung.”)

Fig. 3.58 (a) Acute thromboembolism in a pulmonary artery. (b) Angiogram showing an area of blocked pulmonary perfusion. The major sources of pulmonary emboli are thombosed lower extremity or pelvic veins, most often in persons who are obese, overweight, or immobilized. Acute, massive embolism of pulmonary arteries may cause immediate death. Surviving patients who also suffer from left heart failure will develop pulmonary infarcts (No infarcts will occur without left heart failure; see also Chap. 2)
Fig. 3.59  Goodpasture's syndrome. Goodpasture's syndrome is a systemic vasculitis (see Table 1.1) affecting small vessels in the lungs and kidneys after the development of anti-glomerular basement membrane antibodies. The etiology is unknown. Pathology is characterized by diffuse alveolar hemorrhages (a, b) with autoimmune capillaritis and occasional hyaline membranes. The disease is complicated by associated autoimmune glomerulitis (See also Fig. 3.62)

Fig. 3.60  Pulmonary hypertension. (a) In primary and secondary pulmonary hypertension, the lung is grossly enlarged, firm, and congested, with sclerotic pulmonary arteries. (b) In primary pulmonary hypertension (e.g., pulmonary glomangiosis [MRD], microscopy shows multiple arteriovenous shunts with prominent glomus structures in thin-walled vessels. (c) Secondary pulmonary hypertension (plexiform vessel disease) shows typical vascular changes, such as media hypertrophy and intimal fibrosis (not equally present in MRD) with secondary shunting
Fig. 3.61 Pulmonary embolus. (a–d) Four axial CT images of the chest with contrast, following the pulmonary embolus protocol, in a patient with acute saddle pulmonary embolus. The embolus straddles the bifurcation of the pulmonary trunk into the right and left pulmonary arteries and also extends into the lower lobe lobar and segmental pulmonary arteries. The embolus is the dark filling defect in the pulmonary artery, which is otherwise opacified (white) because of the iodinated contrast given intravenously for this study. Most often, the pulmonary embolus is nonocclusive.
Fig. 3.62 Posterior chest radiograph of a 17-year-old boy with proven Goodpasture’s syndrome who presented to the hospital with hemoptysis. He improved without treatment, but the disease recurred months later.

Fig. 3.63 Pulmonary arterial hypertension. A posteroanterior chest radiograph (a) and axial CT scan with intravenous contrast (b) show a markedly enlarged pulmonary trunk and right and left pulmonary arteries that taper abruptly in the periphery. On the CT image, the pulmonary trunk should measure approximately the same as the ascending aorta, which sits adjacent to it. In this case, the pulmonary trunk is easily 3.5 times larger than the ascending aorta. To make the diagnosis of pulmonary arterial hypertension (PAH), there must be enlargement of the pulmonary trunk and right and left pulmonary arteries with peripheral tapering of the vessels. If the pulmonary trunk and the right and left pulmonary arteries are enlarged but the peripheral vessels are not tapered but rather enlarge, then the image would be indicative of right-to-left shunt. Other clues on CT scans pointing to a diagnosis of PAH include evidence of right heart failure, such as contrast leaving the heart into the intrahepatic veins and inferior vena cava, indicating elevated right heart pressure, or convexity of the interventricular septum. Normally, the interventricular septum is straight or bowed toward the right ventricle during ventricular systole (interventricular septum is convex toward the lower pressure of the right ventricle). With PAH, the septum may be deviated toward the left ventricle, again a sign of elevated right heart pressure.
Shock lung. Shock is a microcirculatory and metabolic disturbance resulting in inadequate perfusion of vital organs (lungs, kidneys, heart, liver, adrenals, and others). It may be caused by various mechanisms: cardiogenic, hypovolemic, septic, traumatic, toxic, or allergic. Microvascular hypoxic or toxic damage to the endothelium initiates a cascade activation of cytokines (e.g., tumor necrosis factor, interleukin [IL]-1 and IL-6, platelet activation factor), which add to the local damage with hypoperfusion, stasis, and thrombosis. Shock is always a systemic reaction leading to multiple organ disease (i.e., multiple organ dysfunction syndrome). Various forms of acute and chronic inflammation develop, depending on the chronicity of the disturbance and the length of survival of the patient. Shock lung (compare ARDS and DAD) is characterized by diffuse, “cloudy” pulmonary infiltrate on radiography (a). Grossly, the lungs are pale (unless congested), voluminous, and of a “jellylike” consistency, with a humid cut surface (b). Microscopy shows a diffuse alveolar and interstitial edema with subsequent formation of hyaline membranes (c, d) and hyaline platelet aggregates (“shock bodies”) in capillaries and venules (e). As time progresses, interstitial inflammatory reactions occur with fibrosis (f).
Fig. 3.64 (continued)
Tumors of the Lungs and Pleura

Tumors of the lungs essentially comprise epithelial neoplasms (carcinomas), mesenchymal tumors (sarcomas), and metastases. All are classified according to the cell of origin (e.g., squamous cell carcinoma [SCC] of the bronchus, adenocarcinoma of the bronchial glands, or the alveolar pneumocytes). Sarcomas may include angiosarcomas, neurosarcomas, and lymphosarcomas. Other tumors include large cell or small cell carcinomas or tumors of specialized neuroendocrine cells in the lung, identified as carcinoids. Finally, the lungs are frequent targets for tumor metastases from cancers of the breast, pancreas, testes, bone, skin (e.g., malignant melanoma), and essentially from other sarcomas. Mesenchymal tumors of the pleura identified as mesothelioma can mimic epithelial adenoid structures.

Fig. 3.65 Lung carcinoma. Carcinoma of the lung is among the most common causes of cancer death in the world. Its etiology includes chemical carcinogenesis (e.g., smoking, air pollution, occupational chemical exposure) and viral carcinogenesis (e.g., papillomavirus, adenovirus). For immediate clinical and therapeutic purposes, lung carcinoma is subdivided into small cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC). Pathohistologically, one distinguishes SCC from adenocarcinoma, SCLC, large cell undifferentiated carcinoma (LCUC), and salivary gland-type tumors. Some have endocrine activities, and others are overt neuroendocrine tumors. These gross pictures show an example of SCC of the bronchus (a), with paratracheal and mediastinal lymph node metastases (b). In SCC, the cut surface is friable, gray-white, and somewhat granular; larger tumors have central necrosis, leading to cavitation. Microscopy shows atypical invasive squamous epithelium with focal keratinization (c). Such tumors may be well differentiated, moderately differentiated, or poorly differentiated.
Fig. 3.66  Small cell lung carcinoma of the bronchus, belonging to the type of neuroendocrine carcinomas (grade III, small cell type) previously also called *oat-cell carcinoma*. These gray-tan, fleshy tumors occasionally resemble malignant lymphomas. (a) Shown here is an advanced tumor with speckled necrosis and extensive poststenotic (bronchostenotic) pneumonia (dirty discoloration of friable lung tissue). (b) Microscopy shows small, partly spindle-celled atypical cells growing in irregular, invasive clumps. Typical for this tumor are small foci of pyknotic tumor cells and necroses (not shown here).
Fig. 3.67 Large cell undifferentiated carcinoma appears to be derived from different epithelial sources and includes undifferentiated variants of adenocarcinoma, SCC, adenosquamous cell carcinoma, and “true” LCUC. Some have neuroendocrine features. Shown here are a typical radiograph (a) and gross photo (b) of LCUC of the lung with pleural spread. Microscopy shows a diffuse proliferation of polymorphic, large cells with suggestive adenoid features (c). Further subclassification requires detailed histochemical and molecular studies.
Fig. 3.68 Squamous cell carcinoma of the lung. These posteroanterior chest radiograph (a) and axial CT images of the chest with contrast (b–d) are from a patient with central SCC of the left lower lobe (LLL), producing collapse of the lobe. Part (d) shows the endobronchial component of the tumor.
Fig. 3.69 Small cell lung cancer. A posteroanterior radiograph (a) and three axial CT images with contrast (b–d) show an older woman with a central tumor confirmed by bronchoscopy as SCLC producing lower lobe collapse. The tumor narrows the left mainstem bronchus and invades the mediastinum. (Note that the patient has bilateral saline breast implants.). Bronchogenic tumors currently are classified histologically and for treatment purposes into two major categories: SCLC and NSCLC. These tumors are staged, and if staging indicates, the patient is eligible for curative surgery. SCLC is presumed to be metastatic at the time of diagnosis, and these patients have chemotherapy rather than surgery for their treatment.
Fig. 3.70 Alveolar cell carcinoma. Alveolar cell carcinoma (bronchioloalveolar carcinoma [BAC]) appears to be a special subtype of pulmonary adenocarcinoma. (a) Tumor growth in the lung (or lungs) grossly mimics pneumonia; it resembles a viral tumorous disease of sheep previously identified as “Jaagsiekte.” A viral etiology accordingly has been suggested. Shown here is a typical BAC of the lung, with a pneumonia-like growth pattern on the cut surface and a lymph node metastasis in the upper center. Two distinct subtypes, mucinous and nonmucinous variants, are identified by microscopy, but mixtures of both may occur. (b) A primarily nonmucinous type of BAC with a “tapestry” of atypical, proliferating alveolar cells in the affected parts of the lung.
Fig. 3.71 Adenocarcinoma of the lung. (a) Common adenocarcinoma of the lung is usually a peripherally located, well-circumscribed mass with early lymphatic spread to local lymph nodes. Lymphatic spread also may cause intrapulmonary “satellite” tumor nodules, sometimes raising the question of multiple primary tumors. Microscopy is usually classified as tubulopapillary, solid, or BAC (see Fig. 3.70). (b) Frequent adenocarcinoma with tubuloadenoid structures and various amounts of fibrous stroma.
Fig. 3.72 Neuroendocrine carcinoma of the lung. Neuroendocrine carcinoma of the lung is classified as submacroscopic pulmonary endocrine “lesions” (e.g., tumorlets), tumors with common neuroendocrine features (e.g., typical or atypical carcinoid, large cell neuroendocrine carcinoma, SCLC), NSCLC with neuroendocrine features (by immunostaining or electron microscopy), or uncommon primary tumors with neuroendocrine features (e.g., primitive neuroectodermal tumors). (a, b) Gross photographs of a common carcinoid, with its nodular, fleshy infiltrate of pink to tan, which may occur at multiple sites. (c) Immunohistochemistry shows tumor cells producing synaptophysin (brown cells).

Fig. 3.73 Axial chest CT image showing a possible peripheral adenocarcinoma in the right upper lobe.
Fig. 3.74 (a, b) Coronal and axial chest CT scans showing a very small, mixed solid and ground-glass nodule, which biopsy proved to be a BAC. In certain classifications, the term BAC has been replaced by the terms adenocarcinoma in situ, minimally invasive adenocarcinoma, and invasive mucinous adenocarcinoma (mucinous BAC). The inhomogeneity of classifications reflects the current lack in knowledge of the etiopathogenesis of adenocarcinoma and BAC.
Fig. 3.75 Carcinoid tumor in the lung. The gross photo (a) shows the bronchoscopic view of the intrabronchial part of the tumor. Most carcinoids are endobronchial, with a small percentage occurring more distally within the bronchus, appearing within the lung. A posteroanterior radiograph (b) and four axial chest CT images (c–f) show an endobronchial mass extending into the right lower lobe bronchus, with very smooth margins. The tumor was proven by biopsy in a young, non-smoking patient with hemoptysis.
Pulmonary sarcoma. Pulmonary sarcomas are uncommon lesions and sometimes need to be distinguished from “sarcomatoid” carcinomas (using immunohistochemistry and molecular techniques). Among the true primary sarcomas of the lung are preferentially vascular tumors (Kaposi’s sarcoma, hemangioendothelioma, hemangiopericytoma), malignant fibrous histiocytoma, fibrosarcoma, and more rarely, chondrosarcoma, rhabdomyosarcoma, and synoviosarcoma. All impress grossly as pink, fleshy nodules with or without hemorrhage and necrosis. Shown here is a hemangiopericytoma of the lung with nodules of well-circumscribed, fleshy tumors.
Fig. 3.77 Kaposi’s sarcoma. Kaposi’s sarcoma in the lung occurs preferentially in patients with immune deficiency syndrome, such as the AIDS patient in this case. (a) Note the sharply demarcated, reddish foci in gross lung. (b) Microscopy shows dense arrangements of polymorphic spindle cells and atypical small proliferating vessels, primarily capillary-like. (c) In situ hybridization shows viral DNA of human herpesvirus type 8 in atypical blood vessels.
Mesothelioma of the pleura is a slow-growing, malignant tumor developing most often in persons with previous sustained exposure to asbestos fibers. Patients suffer from recurrent pleuritic effusions with shortness of breath, and grossly, the lesion impresses as pleural plaque. (a) In the further course, however, the tumor develops into a large, sarcomatous lesion encasing the lungs. (b) Microscopy shows a mixture of fibroblasts in collagenous stroma and epithelial-like (mesothelial) cells with occasional formation of glandular structures (Van Gieson’s stain for connective tissue). The microscopic features are quite variable, with epithelioid, sarcomatous, or biphasic subtypes. Patients usually die of cardiorespiratory failure or pulmonary superinfection.
Fig. 3.79 Patients with AIDS and pulmonary Kaposi’s sarcoma. Posteroanterior radiographs (a, b) and CT chest images (c, d) show characteristic “flame-shaped” nodules, which are not well defined because of perinodular hemorrhage, hilar mediastinal adenopathy, and, occasionally, hemothorax. The nodules originate from a peribronchovascular region and do not cavitate (If they did, the cavity would immediately be filled with blood and would not be discernible)
Fig. 3.80  (a, b) Posteroanterior and lateral radiographs from a patient with calcified pleural plaques, including the pathognomonic calcified diaphragmatic pleural plaque indicative of asbestos-related pleural disease. Axial CT images (not shown) exhibited numerous noncalcified pleural masses, especially adjacent to the left heart border but also ventrally behind the anterior ribs. A biopsy proved the diagnosis of a malignant mesothelioma, sarcomatous type.

Fig. 3.81  Lymphoma. The lung (like the gastrointestinal tract, skin, and central nervous system) is a common site for the development of extranodal malignant lymphomas in adults. Many primary pulmonary lymphomas are of B-cell lineage and are derived from mucosa-associated lymphoid tissue. Others are large cell lymphomas (B-cell or anaplastic T-cell type), primary plasmacytomas, or, more rarely, angiocentric lymphomas and Castleman’s disease (see also Chap. 8).

(a) Gross photograph of a primary non-Hodgkin’s lymphoma of the lung with “pneumonia-like” interstitial infiltrates.  (b) Microscopy in this case shows diffuse and somewhat nodular (epibronchial) infiltrates of monomorphic lymphoid cells, identified as B-cell “marginal zone” lymphoma. This lesion needs to be distinguished from nontumorous lymphocytic interstitial pneumonia.
Fig. 3.82  Hodgkin’s disease. Primary Hodgkin’s disease of the lung is rare. In most patients, pulmonary Hodgkin’s disease represents a concomitant involvement of the organ together with mediastinal, suprACLAVICULAR, or cervical Hodgkin’s disease. (a) In the lung, nodular infiltrates of epibronchial lymph nodes with lymphangitic spread may mimic grossly certain types of bronchial carcinoma. (b) Microscopy reveals the diagnosis of Hodgkin’s disease with polymorphic lymphoid infiltrates, certain eosinophilia, and typical Reed–Sternberg or Hodgkin’s giant cells (See also Chap. 8)
Involvement of the lung by mycosis fungoides (primary lymphoma in the skin) may occur during the further course of the dermal disease (see Chap. 10). (a, b) Plaque-like pulmonary infiltrates may encase partly anthracotic, tumorous lymph nodes. (c) Microscopy reveals the characteristic atypical lymphoid cellular infiltrate with giant (Sézary) cells.
Fig. 3.84 Malignant non-Hodgkin’s lymphoma. A CT scanogram (a) and three axial chest CT images (b–d) demonstrate many nodules of various sizes with irregular, lobulated borders. Two bronchograms (b, c) show air coursing through the left lower lobe and indicate the soft texture of the nodule, which allows air-filled bronchi to remain open with air as the bronchus courses through the tumor. All images are from a middle-aged AIDS patient with primary pulmonary lymphoma. These tumors usually are not associated with mediastinal or hilar lymphadenopathy and may cavitate.
Fig. 3.85 A CT scanogram and four axial CT images of a 27-year-old woman with nodular sclerosing Hodgkin’s lymphoma. (a) The CT scanogram shows mediastinal widening due to lymphadenopathy. (b–e) The CT scans show multiple enlarged, anterior mediastinal lymph nodes consistent with lymphoma. The lungs are clear. The differential diagnosis for masses in the anterior mediastinum includes the “4 Ts”: thyroid, thymus, teratomas, and “terrible” lymph nodes (e.g., lymphoma, granulomatous disease, metastases, infection).
Miscellaneous Lung Diseases

Additional images in this chapter depict some entities not covered in the earlier paragraphs: lipid pneumonia (LP), alveolar proteinosis, pulmonary fluid overload syndrome (PFOS), pulmonary hypoplasia, and sequestration of the lung. LP may be either exogenous or endogenous. Most reported cases of exogenous LP have resulted from inhalation of mineral oil or petrolatum or occupational exposure to oil mist (steel industry, airline engine maintenance). Endogenous LP is rare; it is independent of exogenous lipid exposure, and its etiology is often unclear. It has been described as accompanying diseases of airway obstruction (“resorptive pneumonitis”) as well as in certain infections or parasitic infestations. The latter may cause overproduction of surfactant by type II pneumocytes, with accumulation of related substances in lipid-filled macrophages.

Pulmonary alveolar proteinosis (PAP) is a rare disease with excessive accumulation of granular phospholipoproteinaceous materials in air spaces. Patients suffer from progressive dyspnea and are treated with repeated bronchopulmonary lavage. The etiology is unknown; primary (idiopathic) forms have been described, as well as secondary PAP occurring after inhalation of substances such as silicates, beryllium, aluminum, and insecticides. PAP also occurs more frequently in patients with hematologic malignancies or in immunosuppressed persons.

Pulmonary fluid overload syndrome is a serious complication of hyperinfusion and poor electrolyte balance. The lungs show a massive alveolar and interstitial edema, with fibroplasia if the disorder persists over a prolonged period. PFOS may be further complicated by bronchospasm and acute respiratory distress syndrome, in which antibodies against plasma proteins and neutrophils initiate anaphylactic reactions.

Pulmonary hypoplasia and pulmonary sequestration are developmental disorders. Pulmonary hypoplasia is frequently related to urogenital malformations of the fetus, such as urethral aplasia (prune belly syndrome). Pulmonary sequestration consists of abnormal development of a lung segment (or lobule) that is separated from the normal lung (located either within or outside it). This segment usually receives its arterial blood supply directly from the aorta and its venous drainage via the inferior pulmonary vein or azygos or hemiazygos veins. Impaired bronchial drainage will cause changes previously described as cystic alveolar dysplasia.
Lipid pneumonia. Lipid or lipoid pneumonia results from enhanced accumulation of exogenous or endogenous lipids in terminal air spaces. Aspiration of foreign materials with a high lipid content will cause a foreign-body reaction (pneumonia) with lipid droplets, foam cells, and giant cells (classically Touton type). Exogenous lipid pneumonia occasionally has also been found after infusion of nutritive fluids with a high lipid content. Endogenous lipid pneumonia, a rare condition, arises from the slow degeneration of cells under low oxygen pressure (e.g., slow degeneration of macrophages and neutrophils with breakdown of lipid-containing cellular membranes [fat phanerosis]). Besides residual neutrophils and macrophages, pneumonic infiltrates show many foam cells without significant foreign-body giant cell reaction. These figures show different views of lipid pneumonia: gross photographs of unfixed tissue (a–c) and of fixed lung tissue (d). Parts (a, c) resemble endogenous lipid pneumonia as shown on microscopy (g), whereas parts (b, d) histologically resemble the exogenous type (e, f) with concomitant lymphoid nodular reaction.
Fig. 3.86  (continued)
Fig. 3.87 Pulmonary alveolar proteinosis. PAP (lipoproteinosis) is a rare disease of variable cause. It has been observed in certain patients with compromised immunity, including leukemia and cancer patients, occasionally in pulmonary infections, and also in persons exposed to occupational inorganic dusts, such as aluminum dust ("aluminosis"). The suggested pathogenesis is a deficiency of type II pneumocytes and alveolar macrophages, resulting in an increased deposition of lipids (surfactant) and exudative proteins with deficient resorption. Grossly, the lungs show a pneumonia-like, dry, fatty infiltrate (a). Microscopy shows a proteinaceous, granular exudate in alveoli, staining positive in PAS (b, c) and fat stain, including lipid-laden macrophages (d), and showing fatty-acid crystals in polarized light (e).
Fig. 3.88 Posteroanterior chest radiograph (a) and axial CT image (b) showing bilateral opacities in a patient with PAP. The CT scan shows the typical “crazy paving” pattern consisting of ground-glass opacities and thickening of the interlobular septae, as described for PAP. The differential diagnosis is more extensive, however, including certain types of pneumonia (such as Pneumocystis species), edema, or hemorrhage if acute. In chronic cases, considerations in addition to PAP include UIP, IPF, NSIP, hypersensitivity pneumonitis, COP, chronic eosinophilic pneumonia, and diffuse BAC.
Pulmonary fluid overload syndrome (PFOS) designates a fluid imbalance with grave clinical consequences. It is a rare disturbance resulting from clinical hyperinfusion in patients with limited fluid clearance (e.g., postoperative or postpartum patients with infusion of large volumes of fluid and limited renal excretion; usually the fluid and electrolyte balance are not closely monitored). Fluids accumulate in interstitial tissues (edema) and in the lungs to an extent that they cause life-threatening circulatory and respiratory deficiencies. The gross appearance at autopsy shows voluminous lungs of “water-pillow” consistency (a). Microscopy shows massive alveolar and interstitial fluid retention (b, c). The result is right heart failure and cardiogenic shock (see “shock bodies” in pulmonary capillaries [c]), or if the patient survives, secondary pneumonia (d).
Fig. 3.90  Congenital hypoplasia of the lungs. (a) Note the small lungs in the thorax cavity compared with the normal heart and liver. (b) The lungs are pale with increased uniformity of consistency. (c) Microscopy shows various degrees of an immature glandular pattern.

Fig. 3.91  Pulmonary sequestration. This figure shows a supplemental lung lobe or segment with abnormal vascular supply and possibly various degrees of developmental inhibition (See Fig. 3.92 for explanation).
Fig. 3.92 (a, b) Radiologic images of pulmonary sequestration. Anterior and lateral radiographs show an abnormal opacity behind the heart in the right lower lobe. (c–e) Three axial chest CT images with contrast demonstrate the low attenuation of the smoothly margined mass in the right lower lobe; this mass does not contain air and is fed by a large, anomalous vessel coming directly from the descending thoracic aorta. Sequestrations are an anomaly of the tracheobronchial branching with persistence of a separate, “sequestered” lung fragment, which retains its embryonic blood supply. There are two types of sequestration: intralobular and extralobular. Intralobular sequestration (as in this patient) is more common; the sequestered lobe fragment is enveloped in the lobe’s visceral pleura. It is part of the normal lobe. Two thirds of cases occur in the left lower lobe and one third in the right lower lobe, without other anomalies. Extralobular sequestration is rare and is more commonly seen in neonates and young children with respiratory distress. Ninety percent of cases of extralobular sequestration occur in the left lower lobe and have associated anomalies.
Reference

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