Open lung biopsy

Processing, evaluation, and diagnosis[1]

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The methods of processing and evaluating open lung biopsies are described. The diagnostic importance of frozen sections, light microscopy, immunohistochemistry, and electron microscopy is discussed.

Index term: Lung, biopsy

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Lung tissue for diagnostic purposes can be obtained by transbronchial endoscopic biopsy, transthoracic needle biopsy, and open lung biopsy, as well as segmental pulmonary resection, lobectomy, and pneumonectomy. Open lung biopsy provides a relatively large amount of tissue and is generally regarded as the most reliable biopsy method for diffuse pulmonary diseases as well as localized peripheral lung diseases. Open lung biopsy is often undertaken in emergent situations in patients with respiratory failure, especially in the immunocompromised state. Open biopsy is undertaken if diagnostic procedures, such as bronchoscopic biopsy and cytology, transthoracic needle biopsy and aspiration for cytology, pleural biopsy and cytology, mediastinoscopic biopsy, scalene node biopsy, and biopsies from extrathoracic sites, are not diagnostic. The open lung biopsy should provide enough tissue for light microscopy, immunohistochemistry, electron microscopy, and other special diagnostic procedures, including microbial cultures. At the Cleveland Clinic, we prefer to receive open lung biopsies fresh rather than in fixative so that frozen sections may be performed for diagnosis and determination of adequacy of the biopsy (*Table 1*).

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Table 1. Processing of open lung biopsy

Frozen section
Light microscopy
Immunohistochemistry
Electron microscopy
Special analyses
Microbial cultures

Frozen-section diagnosis

A frozen section of lung tissue stained with hematoxylin and eosin performed at the time of biopsy may be diagnostic (*Fig. 1*). A frozen section may determine if the open biopsy is representative or adequate. A variety of special stains may be performed on frozen tissue, including special stains for fungi, bacteria, acid-fast bacilli, and *Pneumocystis carinii* (*Fig. 2*). Immunohistochemistry can also be performed on the frozen tissue at the time of biopsy. Most commonly, this is performed to detect deposition of immunoglobulin and complement in lung tissue. Frozen sections with appropriate special stains for microbial organisms are important in patients with respiratory failure, especially if immunocompromised.

Light microscopy

Once an open biopsy is received in the surgical pathology laboratory, it is important to section the specimen with a sharp knife to avoid artifactually induced atelectasis. The open biopsy may be perfused with fixative to avoid artifactual atelectasis after aliquots are taken for immunohistochemistry, electron microscopy, microbial cultures, and other special procedures. The majority of diagnoses of lung diseases, including neoplasms, infectious diseases, granulomatous diseases, and a variety of idiopathic diseases, are made using the routinely performed hematoxylin and eosin stain and special stains for collagen, elastic membranes, bacteria, fungi, and acid-fast bacilli.

Neoplasms

A variety of neoplasms may involve the lung and may be detected in open biopsies from peripheral lesions. The most common primary carcinoma of the lung detected in open (peripheral) biopsies is adenocarcinoma, with or without bronchoalveolar features (*Fig. 3*). Large-cell undifferentiated carcinoma is also common in the peripheral portion of the lung (*Fig. 4*). Less commonly, primary squamous-cell carcinomas (*Fig. 5*) and small-cell undifferentiated carcinomas occur in the periphery of the lung (*Fig. 6*). *Table 2* summarizes the histologic types of primary carcinomas of the lung.

Clear-cell and giant-cell carcinomas are considered variants of large-cell undifferentiated carcinoma. Adenocarcinomas may present as a peripheral nodule or more diffuse disease involving a lobe or lobes. It is often difficult to determine if an adenocarcinoma is primary or metastatic in the lung. Squamous-cell carcinomas usually arise in the proximal bronchi, but occasionally may arise in the periphery. It is usually difficult to determine if a squamous-cell carcinoma in the periphery of the lung is primary or metastatic. The differential diagnosis of large-cell undifferentiated carcinoma includes metastatic carcinoma from extrapulmonary sites, metastatic melanoma, "large-cell" lymphoma, as well as poorly differentiated adenocarcinoma and poorly differentiated squamous-cell carcinoma of the lung (*Table 3*).

Uncommonly, small-cell undifferentiated carcinomas may arise in the periphery of the lung. Some of the peripheral small-cell carcinomas have been termed "atypical carcinoid." The differential diagnosis of small-cell undifferentiated carcinoma includes metastatic small-cell malignant neoplasm from extrapulmonary sites (Ewing's sarcoma, neuroblastoma, Wilms's tumor), as well as such neoplasms as lymphoma, plasmacytoma, leukemia, carcinoid tumor, and adenoid cystic carcinoma (*Table 4*).

Carcinomas metastatic to the lung

The most common metastatic carcinomas to the lung encountered in open lung biopsies, segmental excisions, and lobectomies performed at the Cleveland Clinic are metastatic renal-cell carcinoma and metastatic adenocarcinoma of the colon. Metastatic renal-cell carcinomas often exhibit clear cytoplasm; however, most metastatic adenocarcinomas are difficult to separate from primary adenocarcinomas based on purely histologic appearance. Metastatic papillary carcinomas of the thyroid and ovary may also exhibit papillary structures; however, primary adenocarcinomas of the lung may also exhibit papillary structures.

On a purely histopathologic basis, it is usually not possible to separate primary from metastatic

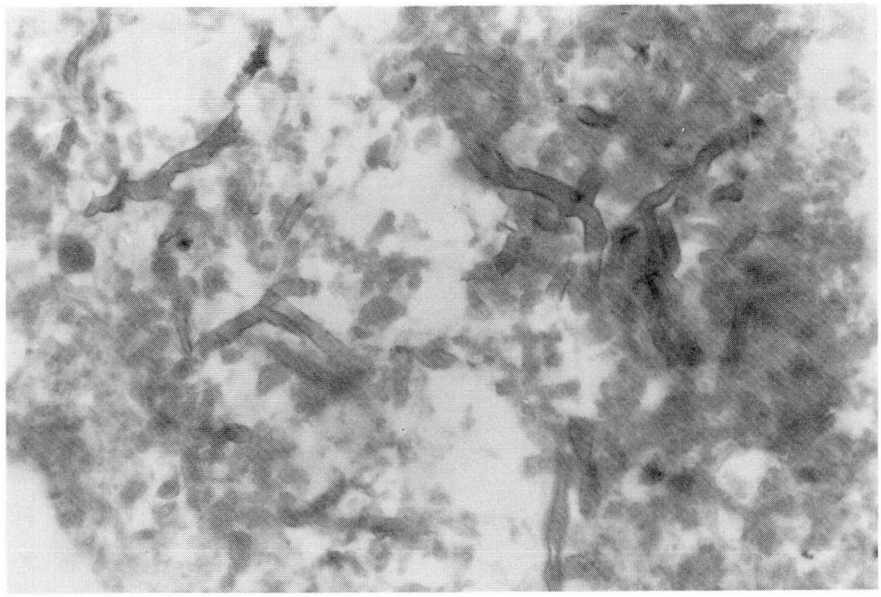


Fig. 1. Branching hyphae typical of *Aspergillus* species observed in a frozen section of a necrotic pulmonary mass (hematoxylin-eosin stain, ×420).

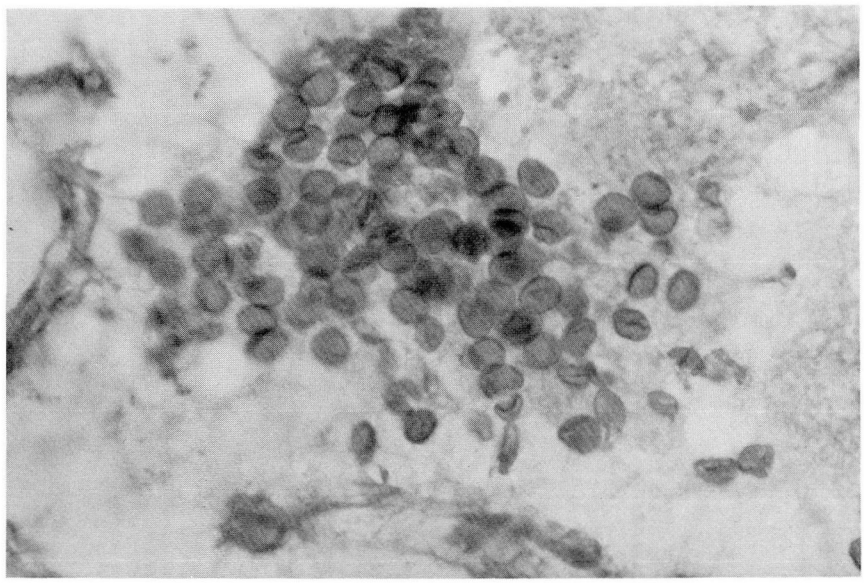


Fig. 2. Spherical structures typical of *Pneumocystis carinii* (toluidine blue stain, ×1,400).

squamous-cell carcinomas. The differential diagnosis of large-cell undifferentiated carcinomas and small-cell undifferentiated carcinomas has already been discussed.

Carcinoid tumors

Carcinoid tumors are usually centrally located and may occlude a bronchus. Occasionally, peripheral carcinoid tumors may be encountered in open biopsies. The peripheral carcinoids may be histologically identical to the central carcinoids (*Fig. 7*), but may exhibit certain atypical features, which may be similar to small-cell undifferentiated carcinoma.

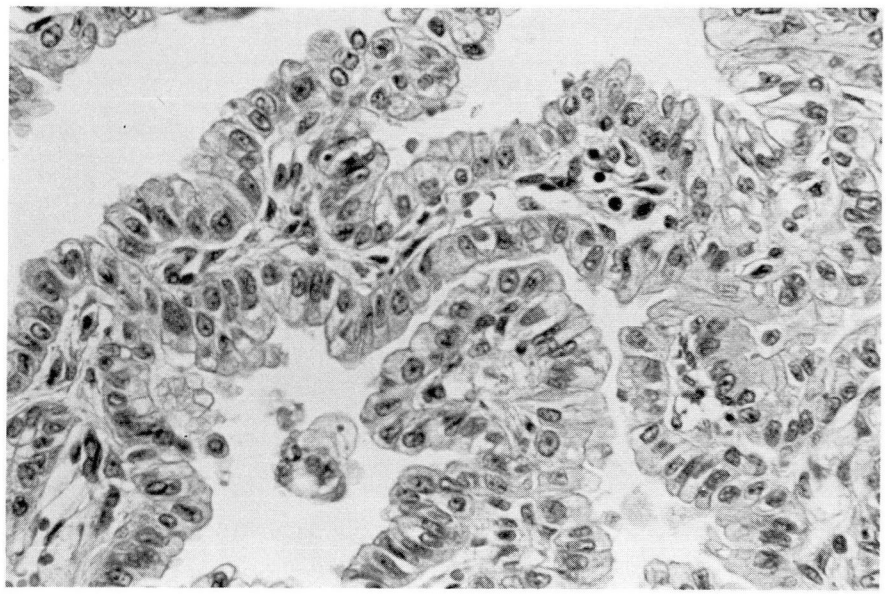


Fig. 3. Well-differentiated adenocarcinoma (bronchoalveolar type) (hematoxylin-eosin stain, ×560).

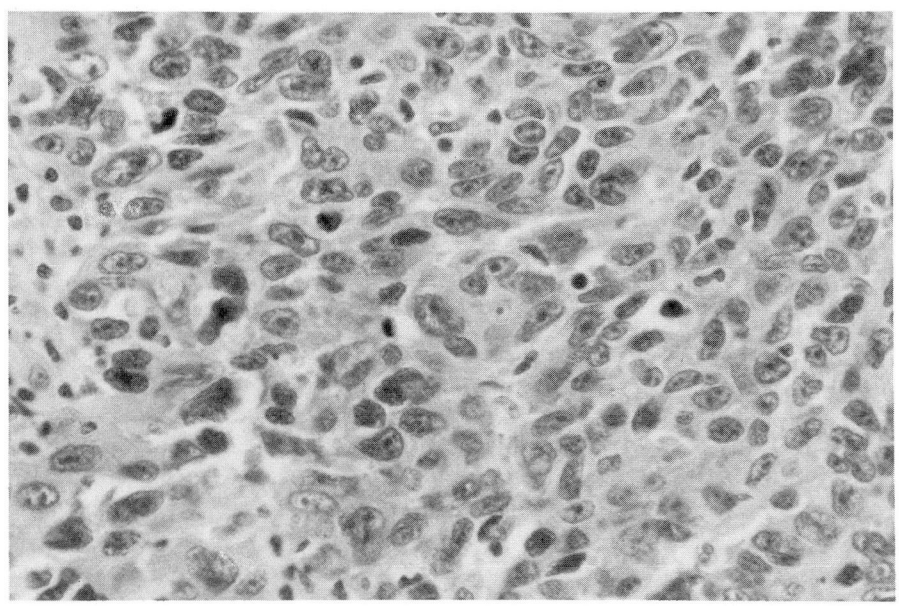


Fig. 4. Large-cell undifferentiated carcinoma, exhibiting abundant cytoplasm without keratinization or gland formation (hematoxylin-eosin stain, ×560).

Salivary gland-type neoplasms

Mucoepidermoid adenocarcinoma, adenoid cystic carcinoma, and acinic-cell carcinomas occasionally involve the tracheobronchial tree or may be metastatic to the lung from primary sites in the major or minor salivary glands.

Lymphoid neoplasms and infiltrates

See **Immunohistochemistry**

Mesothelium

See **Immunohistochemistry**

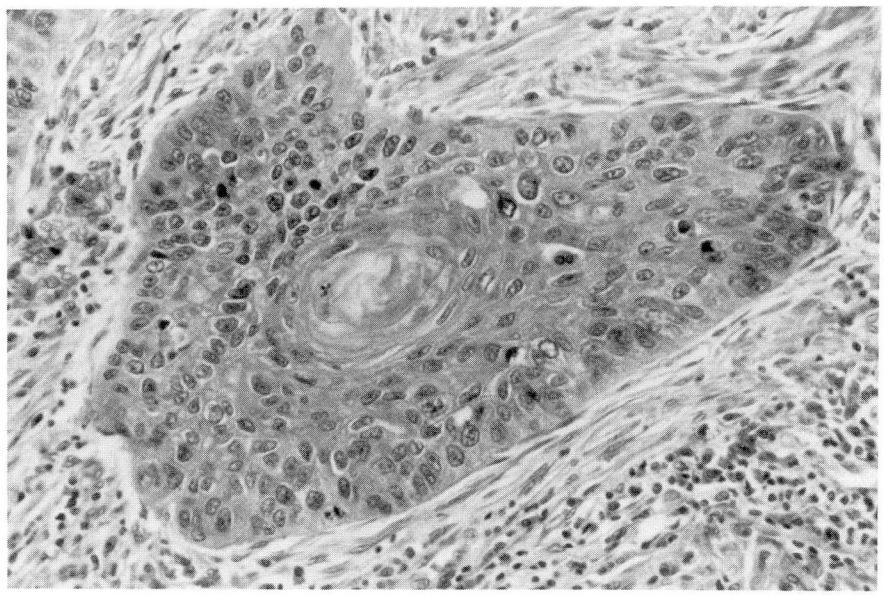


Fig. 5. Keratin pearl formation in a squamous-cell carcinoma (hematoxylin-eosin stain, ×260).

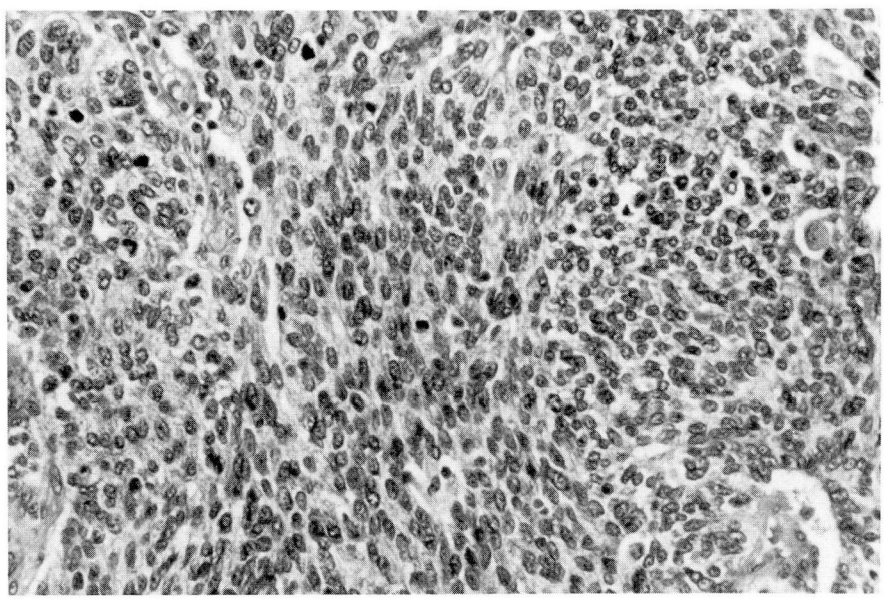


Fig. 6. Small-cell carcinoma, exhibiting no keratinization or gland formation. These cells exhibit only a small amount of cytoplasm. Some cells exhibit "spindle" and some cells exhibit "round-cell" features (hematoxylin-eosin stain, × 260).

Mesenchymal tumors

The most commonly observed mesenchymal tumor at the Cleveland Clinic is the hamartoma characterized by lobules of benign cartilage, sometimes associated with glandular epithelium. Lymphangioleiomyomatosis may be diagnosed at open lung biopsy and is characterized by diffuse proliferation of smooth muscle and associated

Table 2. Primary carcinomas of the lung

Adenocarcinoma
Large-cell undifferentiated carcinoma
Squamous-cell carcinoma
Small-cell undifferentiated carcinoma

Table 3. Differential diagnosis of large-cell undifferentiated carcinoma of the lung

Metastatic carcinoma (extrapulmonary site)
Metastatic melanoma (rarely primary in lung)
Lymphoma
Poorly differentiated adenocarcinoma
Poorly differentiated squamous-cell carcinoma

Table 4. Differential diagnosis of small-cell carcinoma of the lung

Metastatic small-cell neoplasms
Ewing's sarcoma
Neuroblastoma
Wilms's tumor
Lymphoma
Plasmacytoma
Leukemia
Carcinoid tumor (typical and atypical)
Adenoid cystic carcinoma (primary and metastatic)

lymphatic vessels (*Fig. 8*). Primary sarcomas of the lung are rare. More commonly, open lung biopsy is used to document metastatic sarcomas from bone and soft tissue (osteosarcoma, chondrosarcoma, and malignant fibrous histiocytoma). Metastatic renal-cell carcinomas may exhibit sarcomatous features, characterized by pleomorphic spindle cells. Spindle-cell carcinoma and melanoma should also be considered in the differential diagnosis.

Histiocytosis X/eosinophilic granuloma

This lesion may be focal or diffuse and is characterized by a mixture of benign histiocytes and eosinophils in varying proportions (*Fig. 9*). It is commonly overlooked or misdiagnosed as desquamative interstitial pneumonitis, obstructive pneumonia, or Hodgkin's disease.

Infectious disease

The histologic pattern and features often suggest the presence of infection and may be characteristic of certain types of infections; however, in immunocompromised hosts, these histologic features may be altered. It is, therefore, important to perform a variety of special stains for microorganisms as well as to obtain microbial cultures in such cases. Immunohistochemistry and electron microscopy also contribute to the diagnosis of certain infections. Certain bacterial infections involving the lung may be difficult to diagnose using cultures obtained from such sources as sputum, bronchoscopic washings, and pleural fluids. These include *Legionella* pneumonia (*Fig. 10*), nocardiosis, actinomycosis, and typical and atypical tuberculous infections. Open biopsy may lead to the diagnosis of infections secondary to fungi (*Figs. 11* and *12*) and viruses (*Fig. 13*), as well as *Pneumocystis carinii* (*Fig. 2*).

Granulomatous disease involving the lung

Necrotizing and non-necrotizing granulomata may involve the lung parenchyma in a variety of disease processes, including tuberculosis (*Fig. 14*), fungal diseases, sarcoidosis, extrinsic allergic alveolitis, Wegener's granulomatosis, and exogenous lipoid pneumonia (*Fig. 15*). Rheumatoid nodules are characteristic, but may be mistaken for granulomata. The pattern of granulomatous inflammation may suggest a specific diagnosis; however, a variety of diseases, some of known etiology, may produce similar histologic patterns, and special stains for microorganisms, microbial cultures, and elemental analysis are indicated (*Table 5*).

Distribution of pathologic processes in the lung

The distribution and components of the pathologic process are often diagnostic or suggestive of the diagnosis, indicating the necessity for special studies. The distribution may be interstitial-septal, intra-alveolar, bronchial-bronchiolar, vascular, or a combination of these sites (*Table 6*).

Pulmonary diseases characterized by interstitial abnormalities

Table 7 lists examples of interstitial diseases.

Fibrosing interstitial pneumonitis, characterized by diffuse interstitial fibrosis and inflammation of varying degrees, may be idiopathic (*Fig. 16*) or may be observed in asbestosis and certain systemic diseases (progressive systemic sclerosis and rheumatoid arthritis). Radiation and

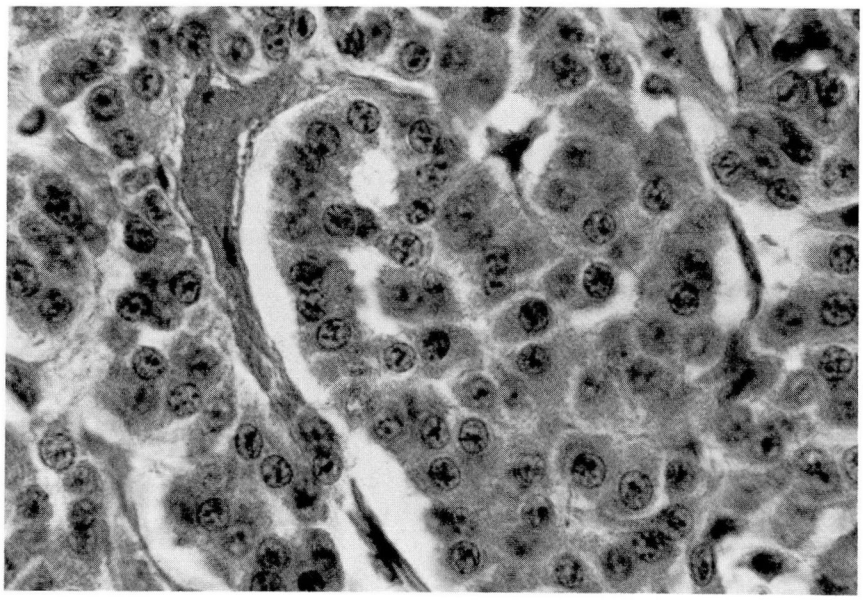


Fig. 7. Carcinoid tumor of the lung, exhibiting delicate strands of fibrous tissue separating groups of cells with uniform oval nuclei and moderately abundant granular cytoplasm (hematoxylin-eosin stain, ×1,000).

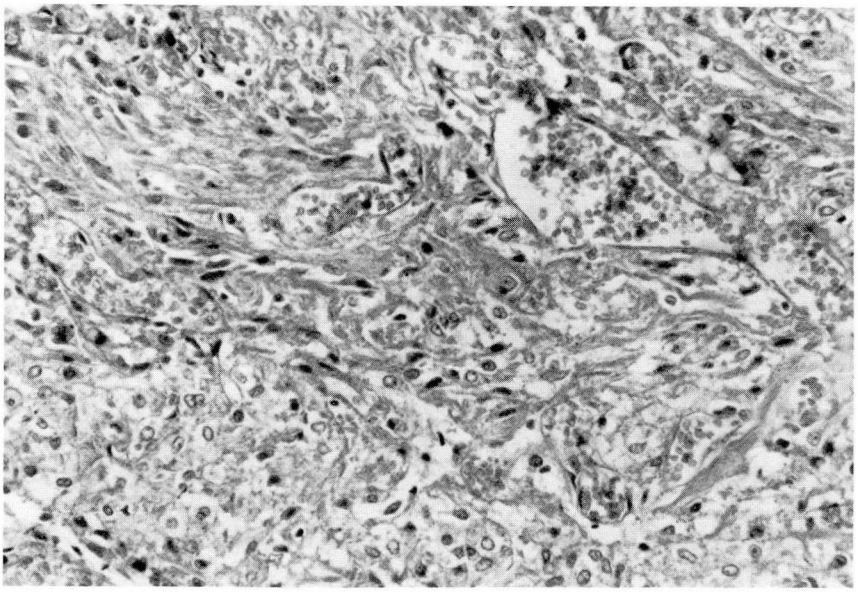


Fig. 8. Lympangioleiomyomatosis of the lung, characterized by proliferation of smooth muscle and delicate vessels (hematoxylin-eosin stain, ×420).

certain drugs (especially chemotherapeutic agents) may produce patterns similar to fibrosing interstitial pneumonitis, but may exhibit atypical alveolar lining cells which may be mistaken for malignant cells. Pneumonias characterized by interstitial lymphocytes and plasma cells without fibrosis may be seen in a variety of conditions and may be secondary to viral infections. Eosinophilic pneumonia may be a diffuse interstitial process (*Fig. 17*), but may involve alveolar spaces. Diffuse interstitial infiltrates of lymphocytes and plasma cells characterize lymphocytic interstitial

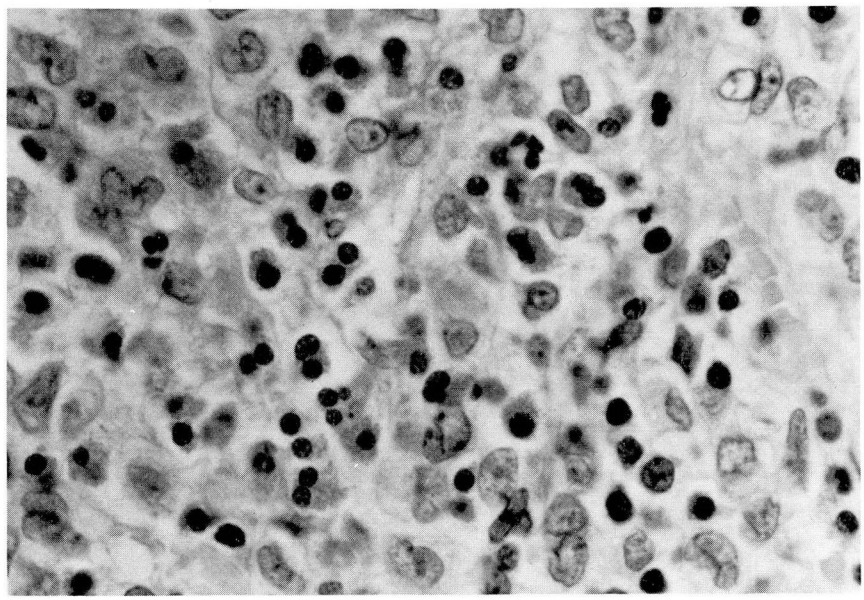


Fig. 9. Histiocytosis X/eosinophilic granuloma involving the lung, characterized by an infiltrate of benign histiocytes and eosinophils (hematoxylin-eosin stain, ×560).

pneumonitis (*Fig. 18*). Amyloidosis is often overlooked and may be predominantly interstitial, but may be concentrated in pulmonary vessels and may form mass lesions. Carcinomatosis may appear interstitial as extensive lymphatic permeation by carcinoma (usually adenocarcinoma) and may be secondary to a primary or metastatic carcinoma.

Pulmonary diseases characterized by alveolar abnormalities

Table 8 lists examples of diseases in which the pathologic findings are concentrated in the alveolar lumina.

Pulmonary alveolar proteinosis is usually idiopathic, but may be secondary to chemotherapy. It is characterized by granular eosinophilic alveolar material, which is periodic acid-Schiff positive and diastase-resistant (*Fig. 19*). Desquamative interstitial pneumonitis is a diffuse process characterized by intra-alveolar macrophages, usually with minimal interstitial fibrosis and minimal interstitial inflammation (*Fig. 20*). Alveolar macrophages are also prominent in obstructive ("golden") pneumonia. Intra-alveolar hemorrhage, often associated with hemosiderin-laden macrophages, may be secondary to a variety of pulmonary diseases, as well as the less common idiopathic pulmonary hemosiderosis and Goodpasture's syndrome (antiglomerular basement membrane disease). Hyaline membranes lining alveoli are characteristic of "diffuse alveolar damage" observed in the acute respiratory distress syndrome. Foamy alveolar exudates are characteristic of *Pneumocystis carinii* pneumonia, but the exudate may not have a foamy appearance. Bacterial pneumonias are characterized by alveolar neutrophils and fibrin. A similar pattern may be observed in fungal, viral, and mycobacterial pneumonias.

Diseases of bronchioles

Chronic bronchitis and asthma are common diseases which predominantly involve the airways; however, these are not usually encountered in open biopsy specimens. *Table 9* lists certain diseases that involve the airways which may be seen in open lung biopsy specimens.

Bronchiolitis/bronchiolitis obliterans may occur in certain infections, especially viral infections, or be a part of any destructive pulmonary disease (*Fig. 21*). Extrinsic allergic alveolitis may affect alveoli as well as bronchioles (*Fig. 22*). Bronchiocentric granulomatosis is characterized by colonization of airways by *Aspergillus* species

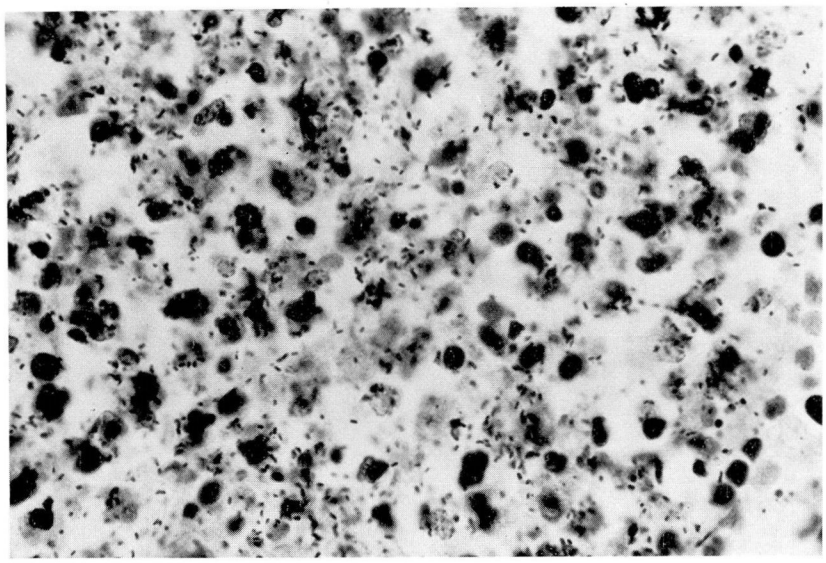


Fig. 10. *Legionella* pneumonia. The special stain demonstrates typical coccobacilli which did not stain with the routine gram stain. Nuclei of neutrophils are also stained (Dieterle silver stain, ×1,400).

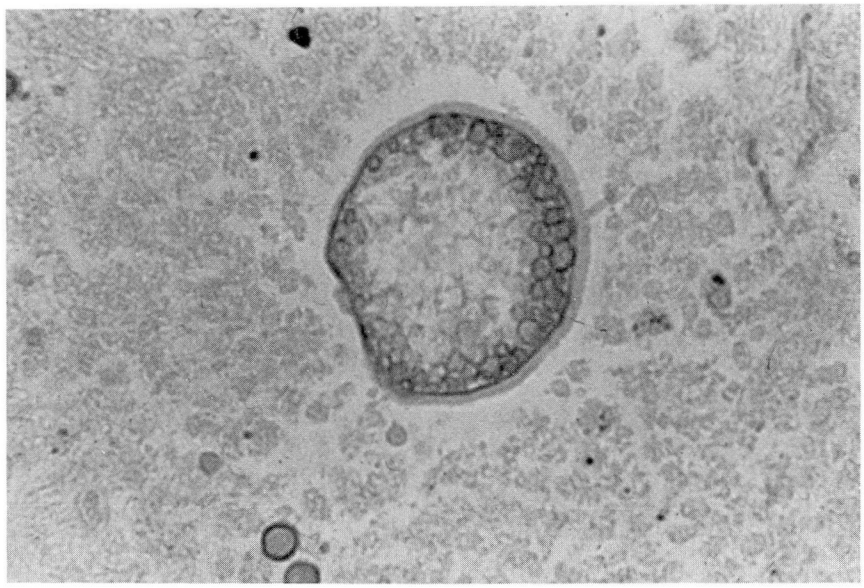


Fig 11. Lung containing a spherule with endospores typical of *Coccidioides immitis* (Gridley's stain, ×560).

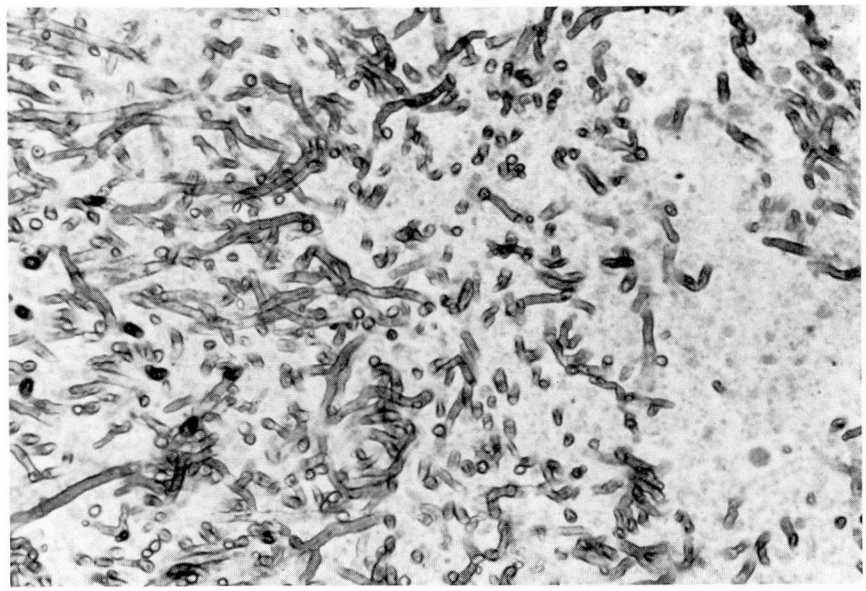


Fig. 12. Lung containing uniformly narrow, acute-branching hyphae typical of *Aspergillus* species. Occasional septa are present (Gomori's methenamine silver stain, ×350).

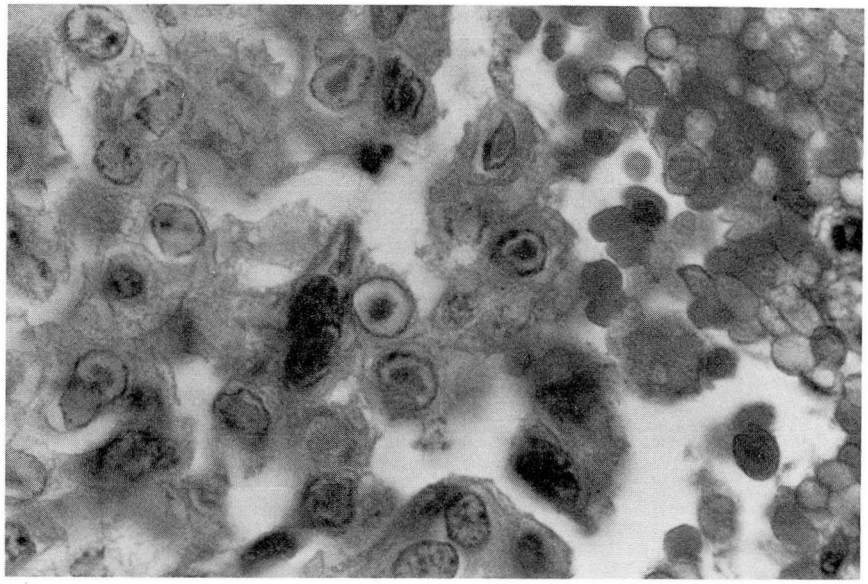


Fig. 13. Herpes simplex viral pneumonia, demonstrating prominent nuclear inclusions separated from the nuclear membrane by a clear halo (hematoxylin-eosin stain, ×1,400).

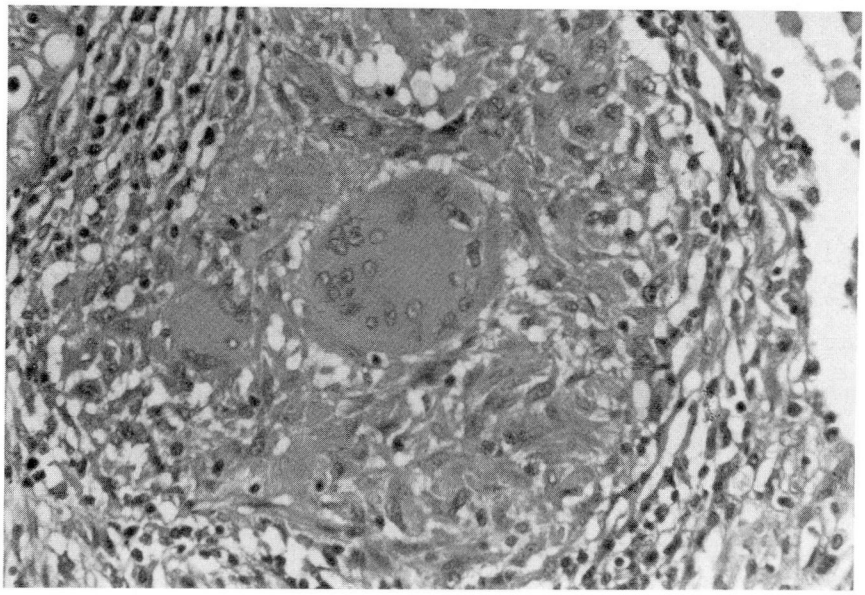


Fig. 14. A non-necrotizing granuloma in a case of atypical tuberculosis secondary to *Mycobacterium kansasii*, documented by lung-tissue culture (heamtoxylin-eosin stain, ×350).

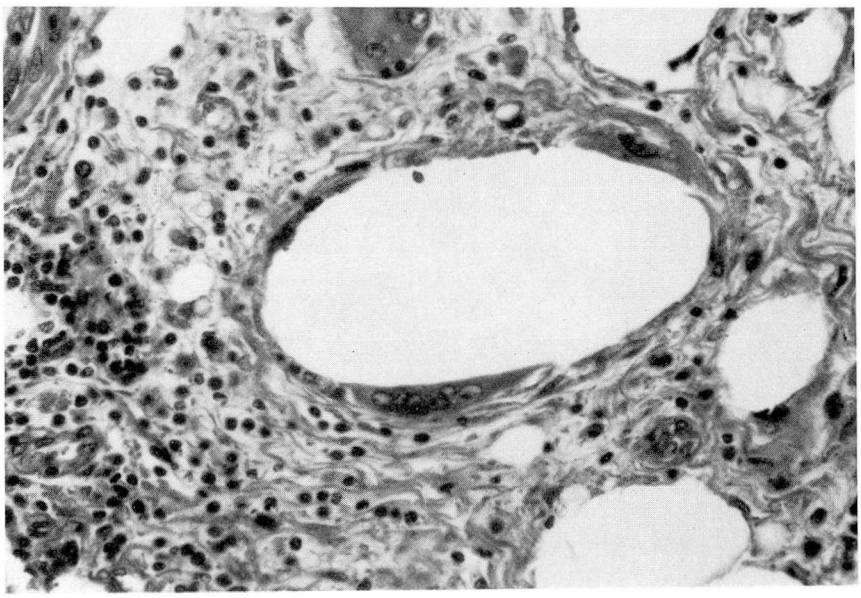


Fig. 15. Lipid globules with associated giant-cell reaction in a case of exogenous lipoid pneumonia (hematoxylin-eosin stain, ×350).

and by necrotizing granulomatous inflammation of bronchi and bronchioles.

Vascular diseases involving the lung

Table 10 lists certain diseases involving vessels which may be encountered in open biopsies.

A variety of emboli may be identified in pulmonary arterial branches (thromboemboli, foreign material, neoplasm). Wegener's granulomatosis is the most common type of vasculitis involving the lung and is characterized by necrotizing granulomatous inflammation involving pulmonary parenchyma and vessels (*Fig. 23*). Amyloidosis may involve predominantly pulmonary vessels, rather than interstitium. The changes of pulmonary hypertension (medial thickening, intimal hyperplasia, and complex capillary lesions) are characteristic, but may be variably distributed (*Fig. 24*). Special stains outlining the elastica in pulmonary vessels are helpful in diagnosing Wegener's granulomatosis as well as pulmonary hypertension. Arteriovenous malformations involving the lung are uncommonly encountered in open lung biopsies at the Cleveland Clinic and usually present no diagnostic difficulty.

Immunohistochemistry

Immunohistochemistry is crucial in the diagnosis and characterization of lymphoid neoplasms and infiltrates, as well as in separating lymphoid neoplasms from undifferentiated neoplasms such as carcinoma and melanoma (see the paper by Tubbs in this issue, pp 473–482).

Table 11 lists the various types of pulmonary lymphoid neoplasms and infiltrates.

B-cell lymphomas are characterized by monoclonal B-cell infiltrates, exhibiting either kappa immunoglobulin light chain staining or lambda immunoglobulin light chain staining, but not both (*Figs. 25* and *26*). Pseudolymphoma is a mass lesion characterized by a mixture of small lymphocytes and plasma cells, lymphoid follicles, and polyclonal B-cell infiltrates exhibiting kappa and lambda immunoglobulin light chains, as well as T cells (*Figs. 27–29*). Immunohistochemistry is especially helpful in differentiating pseudolymphoma from B-cell lymphoma in infiltrates composed predominantly of small lymphocytes. As for all lymphomas, frozen tissue is essential for adequate characterization of lymphocyte differentiation antigens and kappa and lambda immunoglobulin light chain evaluation. If frozen tissue is not available for evaluation, paraffin-embedded tissue may be evaluated for certain lymphocyte/leukocyte antigens (LN1, LN2, and common leukocyte antigen). If a cytologically malignant neoplasm exhibits these antigens and is morphologically compatible with a lymphoma, the diagnosis of lymphoma is confirmed (*Figs. 30* and *31*). Such neoplasms should also be studied for carcinoembryonic antigen and keratin antigens to exclude carcinomas. The S-100 antigen should be sought to exclude melanoma.

Lymphomatoid granulomatosis is characterized by a polymorphous atypical angiocentric infiltrate which may have features of lymphoma at presentation and/or follow-up (*Fig. 32*). In two cases histologically characteristic of lymphomatoid granulomatosis, only T cell antigens were observed in the lymphocytic infiltrates (*Fig. 33*).

Lymphocytic interstitial pneumonitis is char-

Table 5. Granulomatous diseases involving the lung

Tuberculosis (typical and atypical)
Fungal diseases
Sarcoidosis
Berylliosis
Extrinsic allergic alveolitis
Wegener's granulomatosis
Lipoid pneumonia (exogenous)
Rheumatoid nodule

Table 6. Distribution of pathologic processes in the lung

Interstitial-septal
Intra-alveolar
Bronchial-bronchiolar
Vascular
Combination of sites

Table 7. Interstitial lung diseases

Fibrosing interstitial pneumonitis
Interstitial pneumonitis
Eosinophilic pneumonia
Lymphocytic interstitial pneumonitis
Amyloidosis
Carcinomatosis (lymphangiitic)

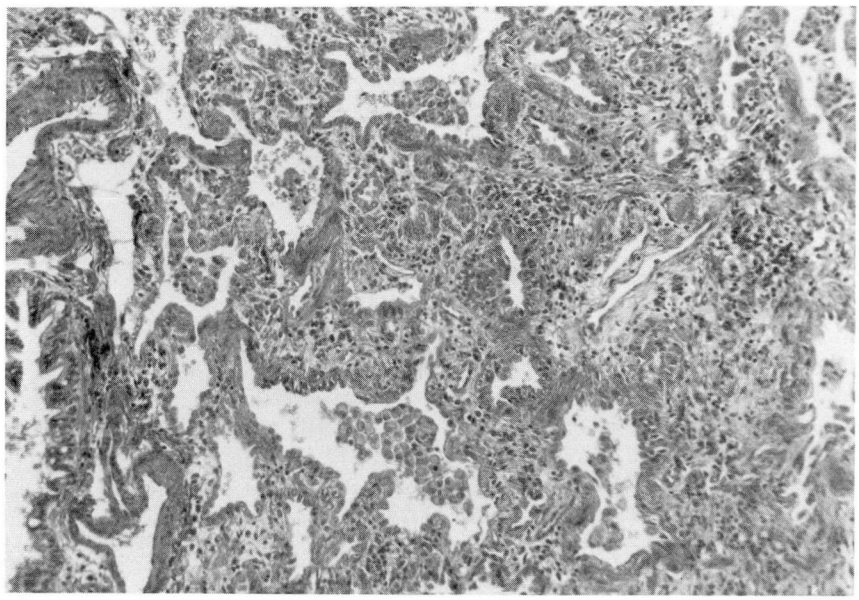


Fig. 16. Fibrosing interstitial pneumonitis characterized by widened alveolar septa containing mononuclear cells and an increased amount of collagen. Macrophages are present in some alveolar spaces (hematoxylin-eosin stain, ×140).

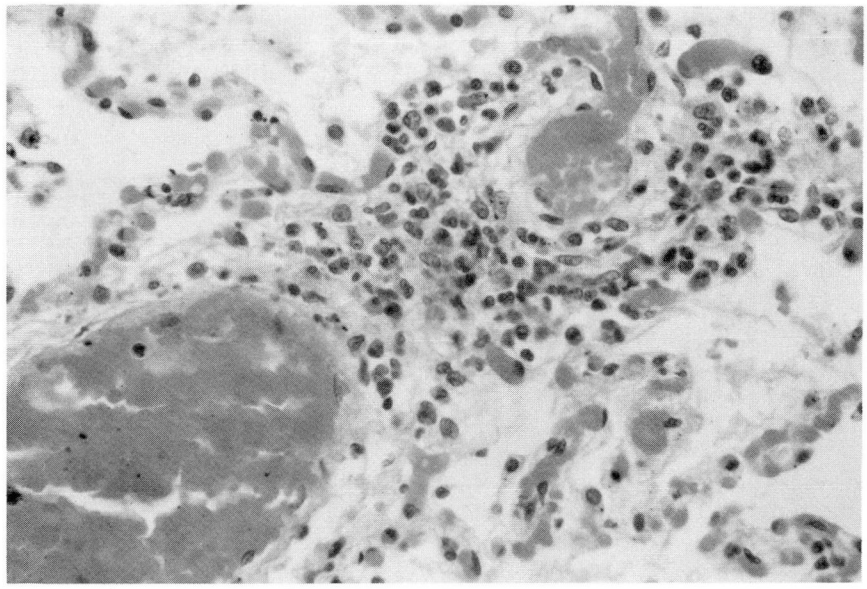


Fig. 17. Diffuse eosinophilic pneumonia characterized by perivascular and interstitial eosinophils (hematoxylin-eosin stain, ×560).

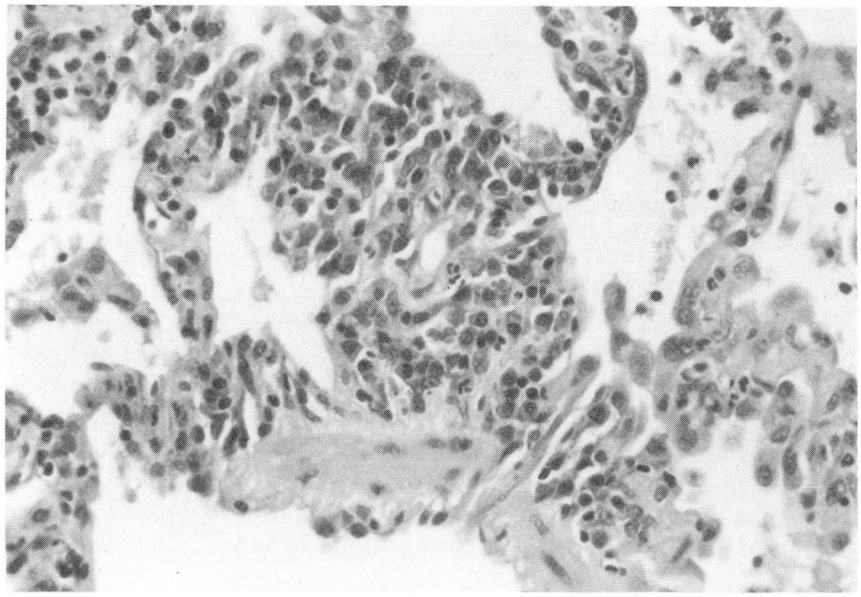


Fig. 18. Interstitial lymphocytes and plasma cells in a case of lymphocytic interstitial pneumonitis (hematoxylin-eosin stain, ×560).

acterized by a diffuse interstitial infiltrate of small lymphocytes and plasma cells (*Fig. 18*). Its relationship to pseudolymphoma/lymphoma is problematic since few cases have been studied for lymphocyte markers and immunoglobulin light chains.

Hodgkin's disease may involve the lung at presentation or as a recurrence. Typical Reed-Sternberg cells may be difficult to identify. The presence of prominent histiocytes and eosinophils may lead to confusion with eosinophilic granuloma/histiocytosis X (*Fig. 34*).

Immunohistochemistry is important in the diagnosis of undifferentiated malignant neoplasms, in which the differential diagnosis may include lymphoma, carcinoma (primary and metastatic), and melanoma. Carcinomas characteristically exhibit carcinoembryonic antigen and keratin antigens, but reactivity may be variable and not uniform, especially if the carcinoma is poorly differentiated. For the purpose of follow-up of patients with small-cell undifferentiated carcinoma of the lung, the carcinoembryonic antigen may be sought in the primary lung neoplasm (see the paper by Tubbs in this issue, pp 473–482) and serum antigen levels monitored. Metastatic adenocarcinomas may sometimes be diagnosed when positive for certain antigens (prostatic acid phosphatase, prostatic antigen). The S-100 protein is usually positive in metastatic melanomas. Ectopic hormone production may be demonstrated in some neoplasms (*Fig. 35*).

Malignant mesothelioma

Malignant mesotheliomas usually exhibit epithelioid, glandular, and/or papillary features which are difficult to separate from adenocarcinoma metastatic to the pleura. Typically, the neoplastic cells in the epithelioid type of malignant mesothelioma are negative for carcinoembryonic antigen and positive for low-molecular-weight keratin antigens. Many carcinomas are positive for both the carcinoembryonic antigen and keratin antibodies; however, some carcinomas are carcinoembryonic antigen negative. The role of immunohistochemistry in the differential diagnosis of pleural neoplasms should be considered developmental; routine light microscopic, histochemical, and electron microscopic evaluation remain essential in the evaluation of pleural neoplasms, as well as clinical, occupational, and radiographic data (see the paper by Tubbs in this issue, pp 473–482). Asbestos bodies should be sought in pulmonary parenchyma.

Table 8. Pulmonary diseases with intra-alveolar distribution

Pulmonary alveolar proteinosis
Desquamative interstitial pneumonitis
Hemorrhage
Alveolar microlithiasis
Hyaline membrane disease (diffuse alveolar damage)
Pneumocystis carinii pneumonia
Bronchopneumonia (bacterial, fungal, viral)

Immune deposits

Immunohistochemistry detects immunoglobulin and complement deposits in such diseases as lupus pneumonitis (*Fig. 36*) and Goodpasture's syndrome (anti-glomerular basement membrane disease, glomerulonephritis with pulmonary hemorrhage) (*Fig. 37*).

Electron microscopy*

Electron microscopy is important in the differential diagnosis of "small-cell" and/or undifferentiated malignant neoplasms, in which the histologic differential diagnosis may include carcinoma, carcinoid tumor, lymphoma, and melanoma (*Figs. 38–41*). Electron microscopy is also important in the differential diagnosis of malignant pleural mesothelioma (*Fig. 42*) versus adenocarcinoma metastatic to the pleura.

Electron microscopy is often helpful in detecting infectious organisms (viruses, *Pneumocystis carinii*, bacteria, and fungi). It is especially helpful in detecting a variety of viruses, since routine light microscopic sections may fail to reveal typical viral inclusions (*Fig. 43*).

In cases of immune complex-type disease, such as lupus pneumonitis, electron microscopy may demonstrate dense deposits in alveolar-septal capillaries (*Fig. 44*).

Electron microscopy is also important in the study of the pneumoconioses and is discussed in this issue (see the paper by McMahon in this issue, pp 503–512). Asbestos bodies may be detected by electron microscopy. Energy-dispersive x-ray analysis is helpful in characterizing asbestos and other silicates.

For the evaluation of lower atomic-weight elements and some organic chemicals, fresh or frozen tissue is necessary for mass spectrometry.

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* Dr. James McMahon contributed most of the electron photomicrographs which illustrate this section.

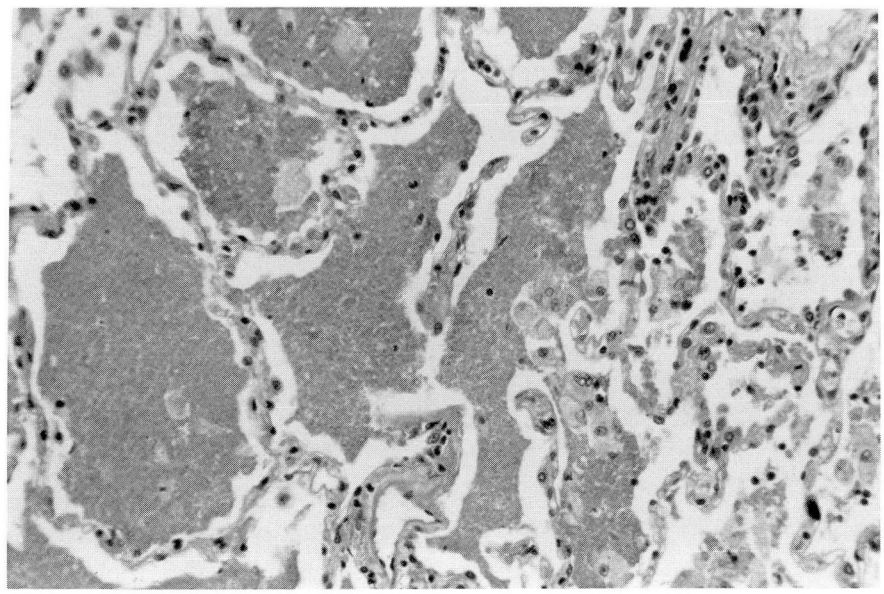


Fig. 19. Intra-alveolar granular material characteristic of pulmonary alveolar proteinosis (periodic acid Schiff stain, ×350).

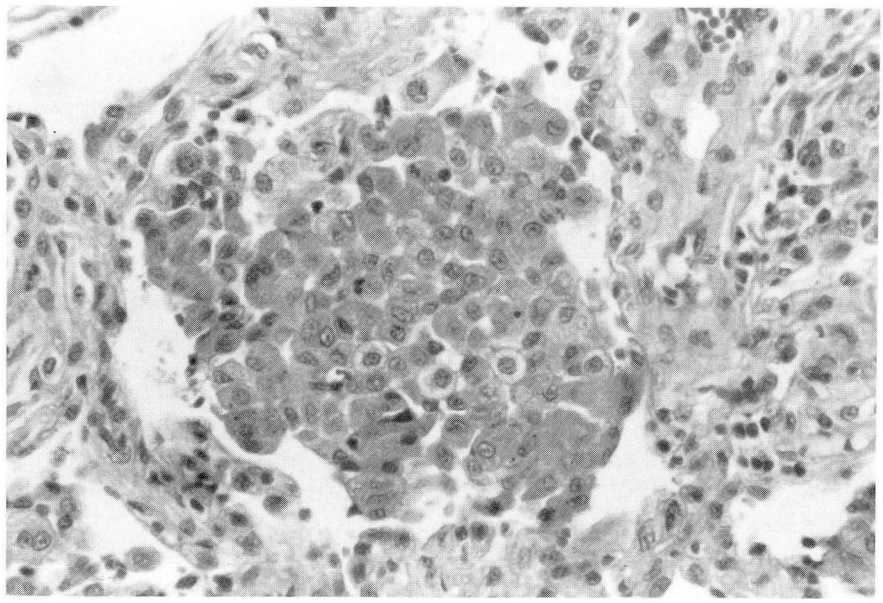


Fig. 20. Prominent alveolar macrophages in a case of desquamative interstitial pneumonitis (hematoxylin-eosin stain, ×560).

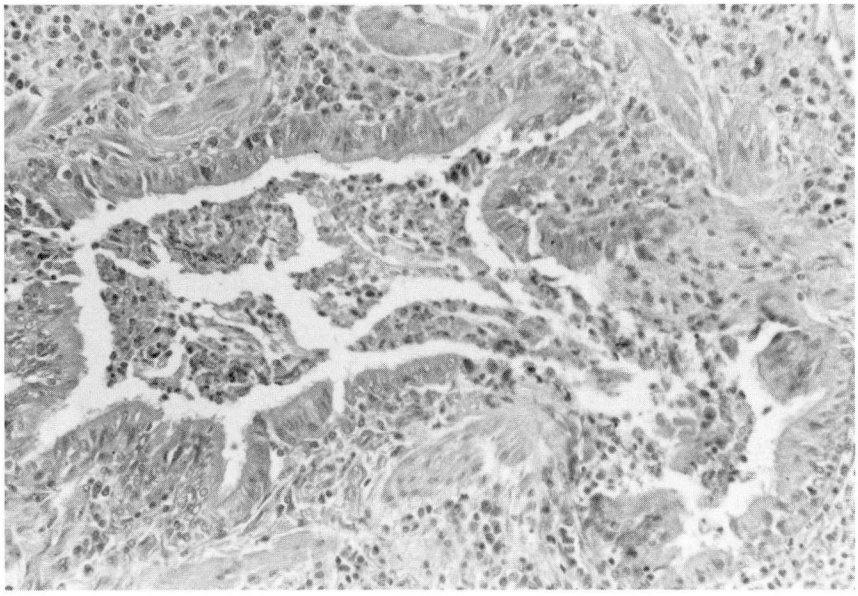


Fig. 21. Acute and chronic inflammation with focal epithelial necrosis in a case of bronchiolitis of unknown etiology (hematoxylin-eosin stain, ×140).

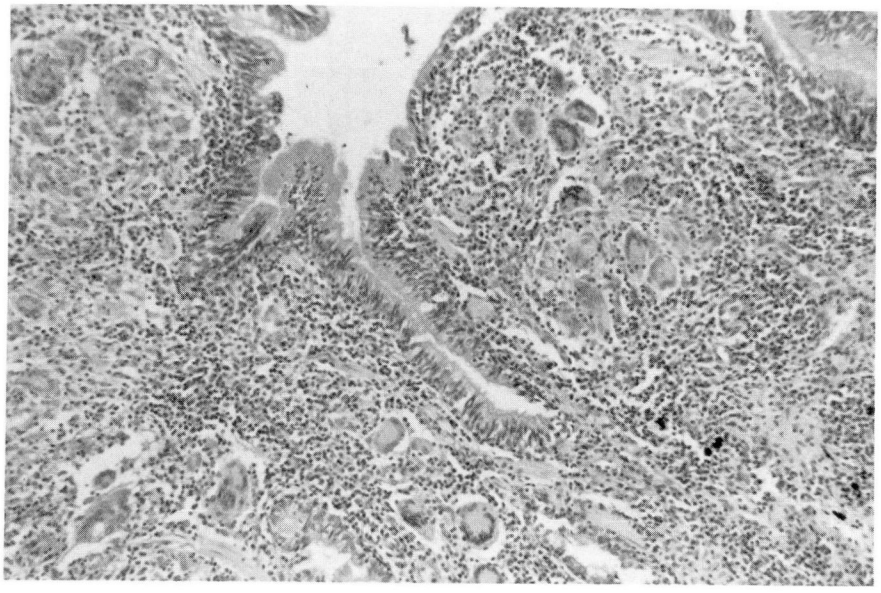


Fig. 22. Granulomatous inflammation of a bronchiole in a case of extrinsic allergic alveolitis (hematoxylin-eosin stain, ×140).

Table 9. Diseases involving peripheral airways

Bronchiolitis
Extrinsic allergic alveolitis
Bronchocentric granulomatosis

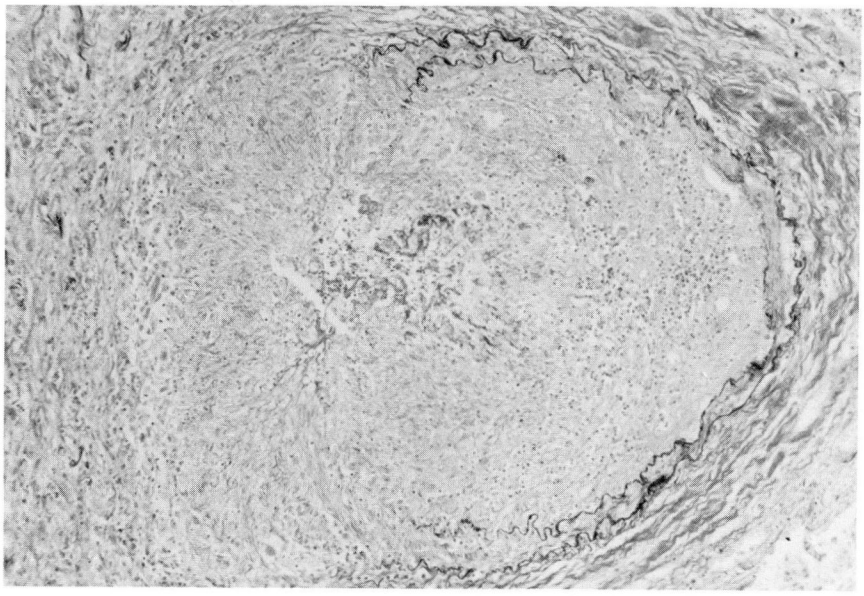


Fig. 23. Vascular destruction and inflammation in a case of Wegener's granulomatosis involving the lung. Elastic membranes of the vessel are obliterated (Van Gieson elastic stain, ×140).

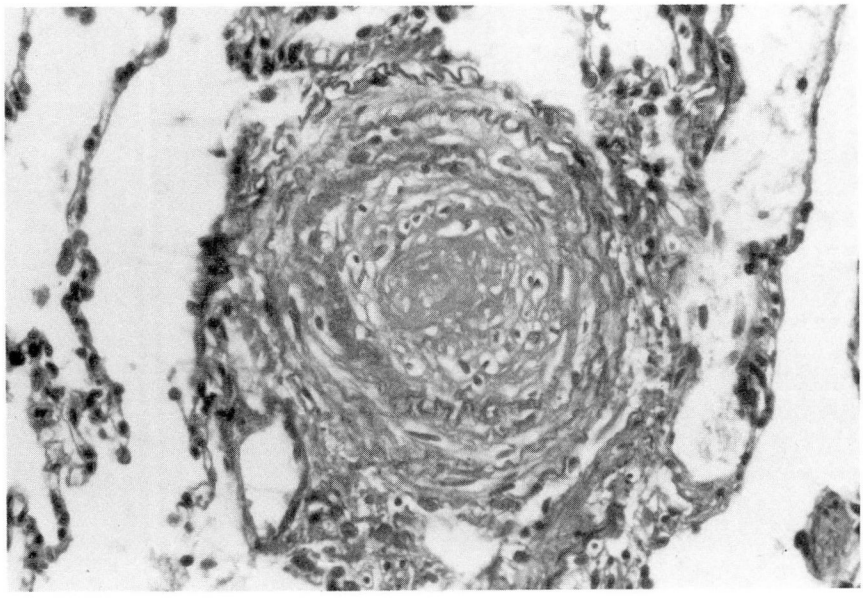


Fig. 24. Obliteration and total occlusion of a pulmonary blood vessel in primary pulmonary hypertension (Van Gieson elastic stain, ×1,400).

Table 10. Vascular diseases involving the lung

Emboli
Vasculitis (Wegener's granulomatosis)
Amyloidosis
Primary and secondary pulmonary hypertension
Arteriovenous malformation

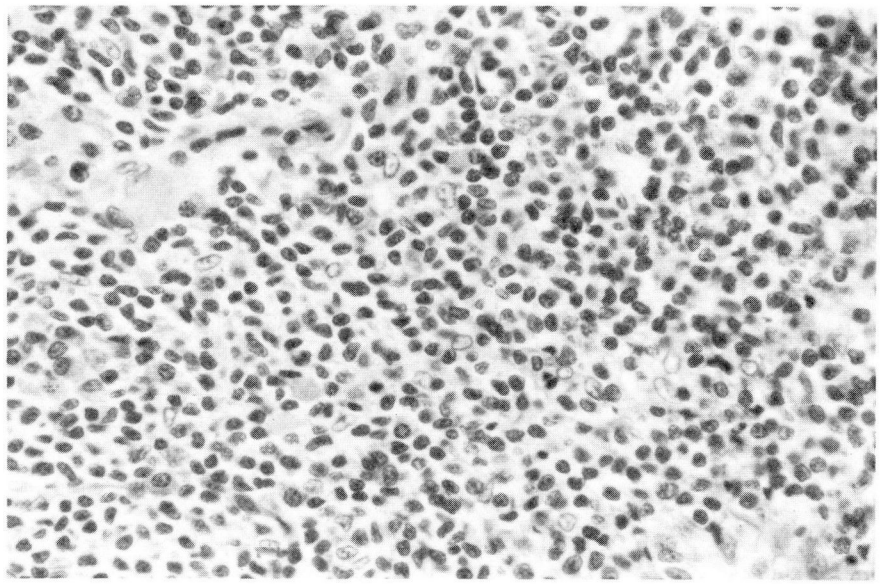


Fig. 25. B-cell lymphoma (small lymphocytic type), primary in the lung (hematoxylin-eosin stain, ×350). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

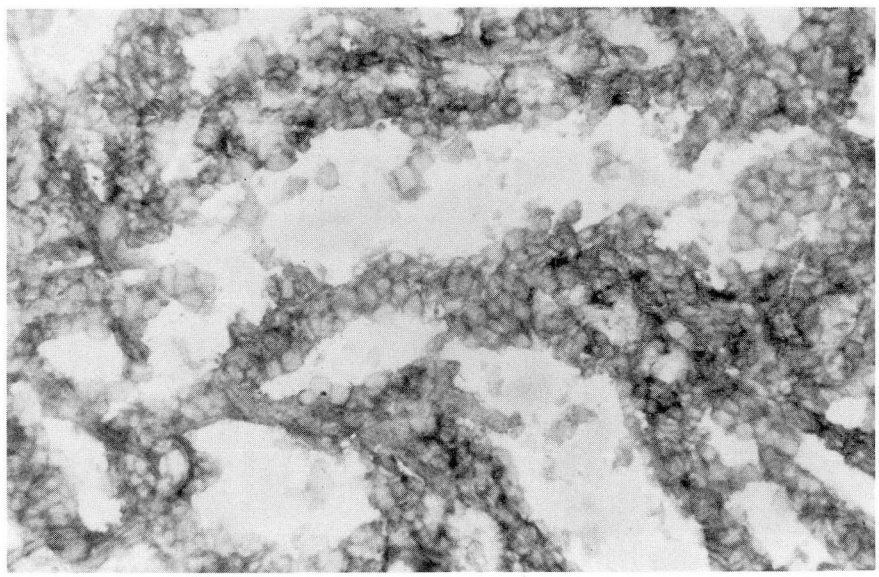


Fig. 26. B-cell lymphoma (small lymphocytic type), demonstrating surface lambda immunoglobulin light chain in the majority of cells from the same case as illustrated in **Fig. 25.** Immunoperoxidase was negative for kappa immunoglobulin light chain (immunoperoxidase, ×350). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

Table 11. Pulmonary lymphoid neoplasms and infiltrates

Lymphoma
Pseudolymphoma
Lymphomatoid granulomatosis
Lymphocytic interstitial pneumonitis
Hodgkin's disease

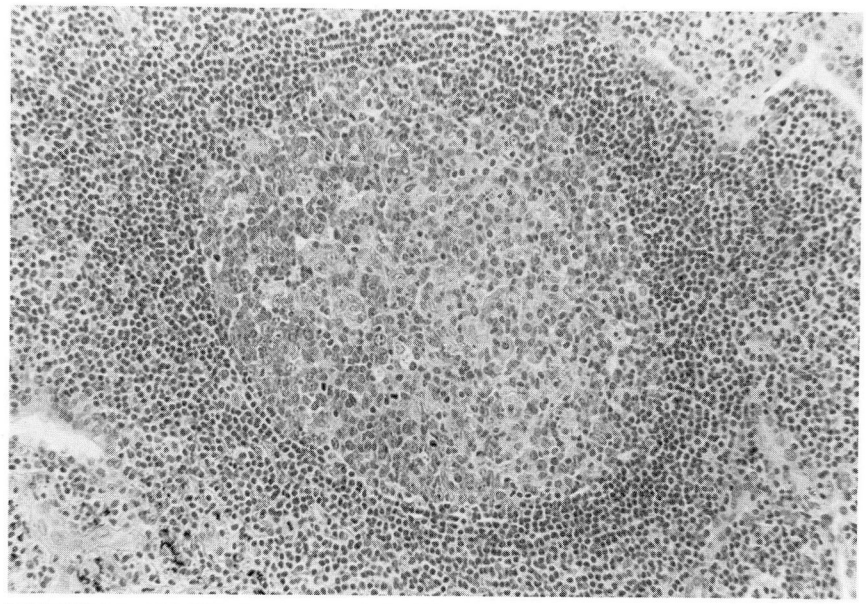


Fig. 27. Prominent germinal center surrounded by small lymphocytes in a case of pseudolymphoma of the lung (hematoxylin-eosin stain, ×180). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

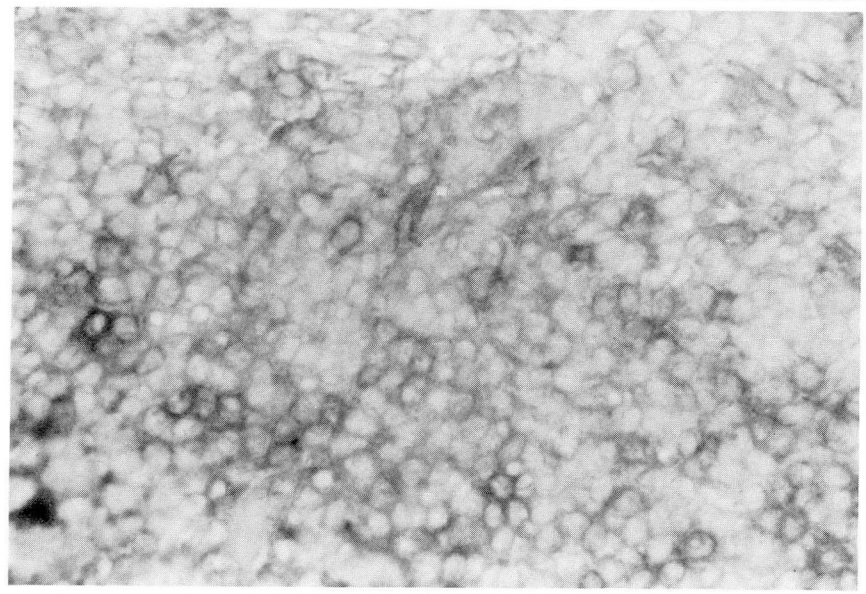


Fig. 28. Lambda immunoglobulin light chain demonstrated in some cells in a pseudolymphoma of the lung (immunoperoxidase, ×350). This case is the same as illustrated in **Fig. 27.** Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

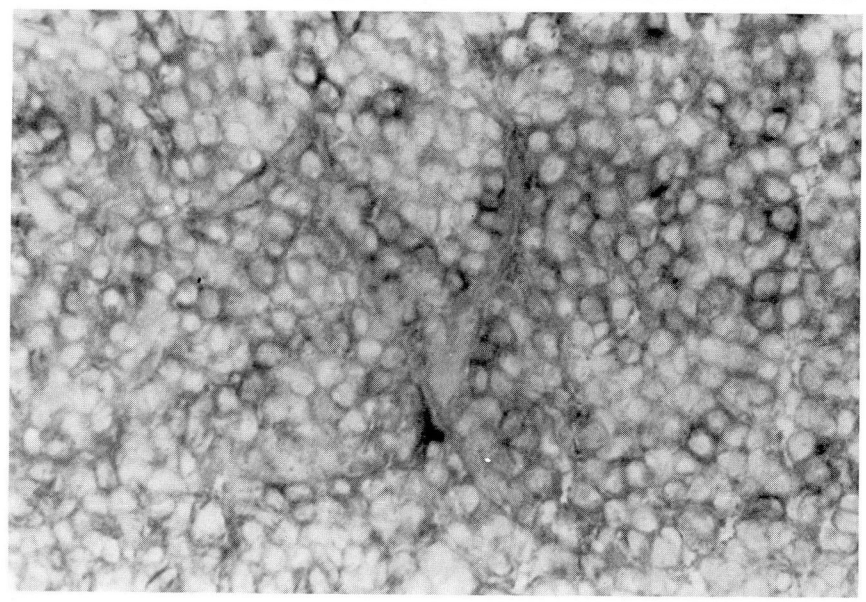


Fig. 29. Kappa immunoglobulin light chain demonstrated in some cells in a case of pseudolymphoma of the lung (immunoperoxidase, ×350). This is the same case as illustrated in **Figs. 27** and **28.** Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

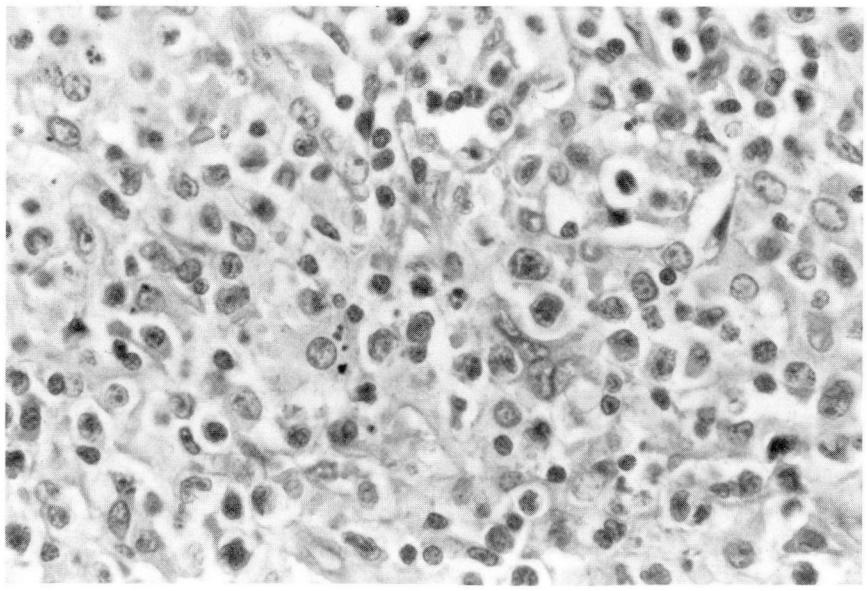


Fig. 30. Large-cell noncleaved lymphoma, primary in the lung (hematoxylin-eosin stain, ×560). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

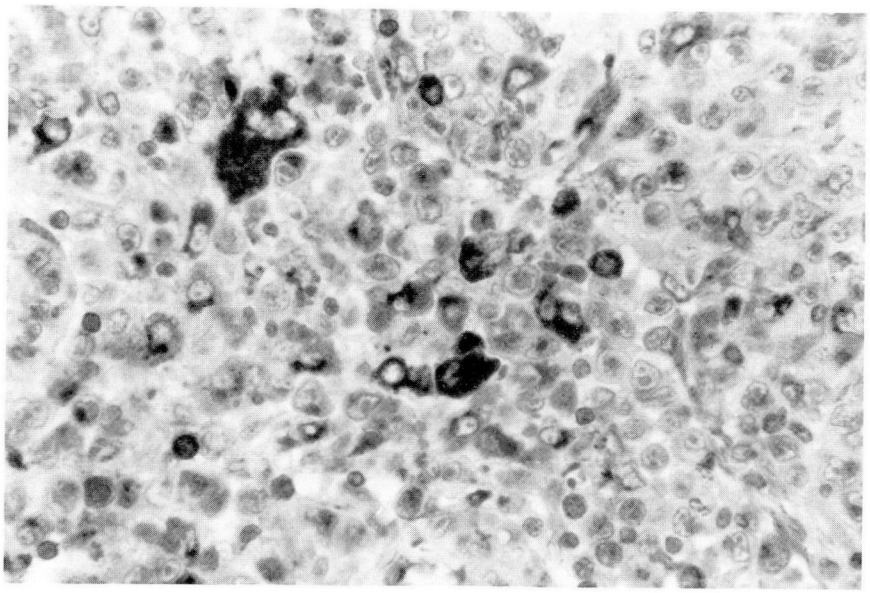


Fig. 31. Large-cell noncleaved lymphoma, primary in the lung, exhibiting cells positive for the LN2 antigen. Immunoperoxidase was performed on deparaffinized tissue (immunoperoxidase with hematoxylin counterstain, ×560). This is the same case as illustrated in **Fig. 30.** Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

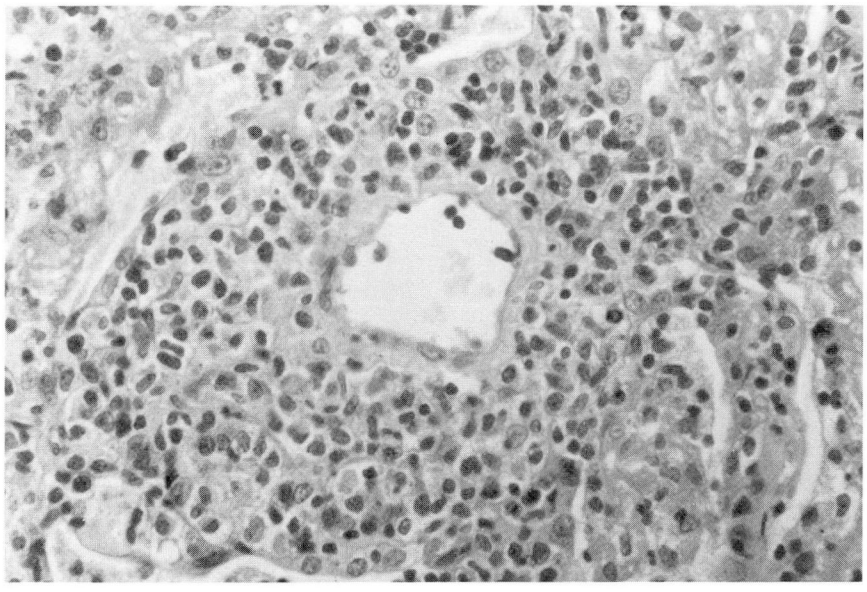


Fig. 32. Angiocentric infiltrate in a case of lymphomatoid granulomatosis involving the lung. The infiltrate is composed predominantly of lymphocytes (hematoxylin-eosin stain, ×350).

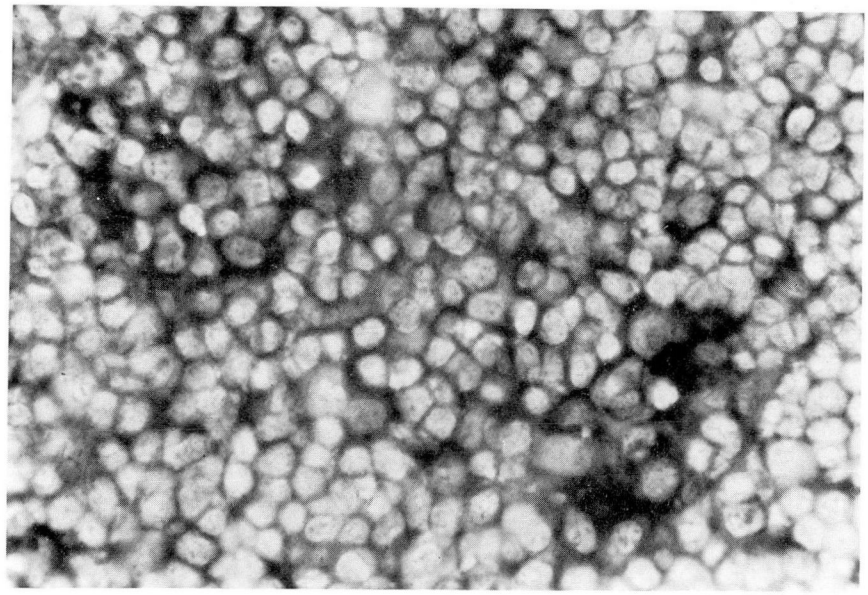


Fig. 33. T3 antigen demonstrated in the majority of cells composing the infiltrate in a case of lymphomatoid granulomatosis involving the lung (immunoperoxidase, ×560).

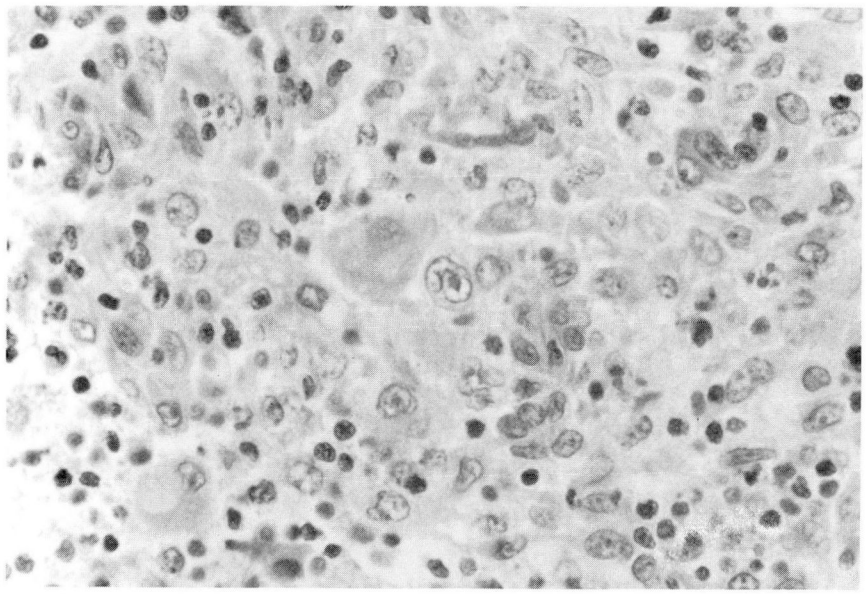


Fig. 34. Hodgkin's disease involving the lung. An atypical mononuclear cell characteristic of Hodgkin's disease is present in the center of the photomicrograph. Typical Reed-Sternberg cells were rare. Lymphocytes, histiocytes, and eosinophils are also present (hematoxylin-eosin stain, ×420).

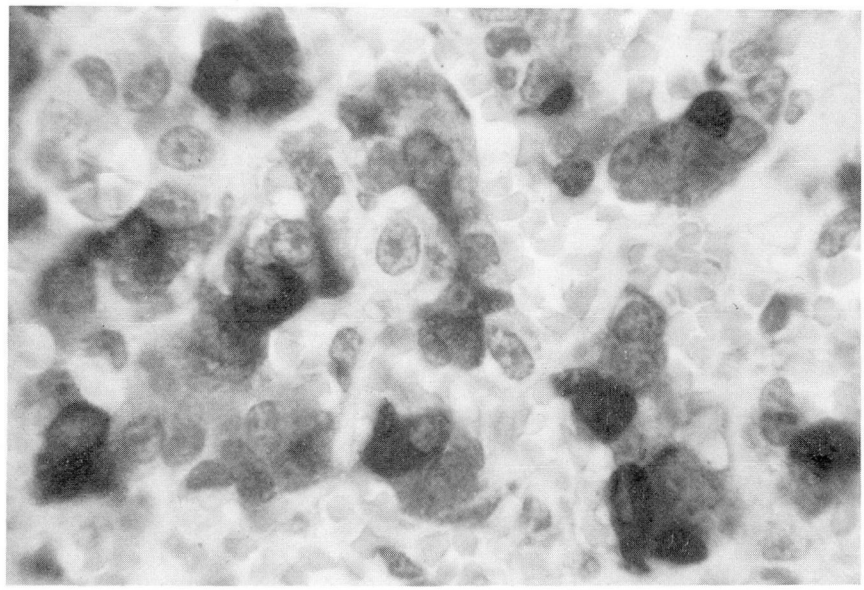


Fig. 35. Immunoperoxidase demonstrated cells containing adrenocorticotropic hormones in a carcinoid tumor of the lung (immunoperoxidase with hematoxylin counterstain, ×560). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

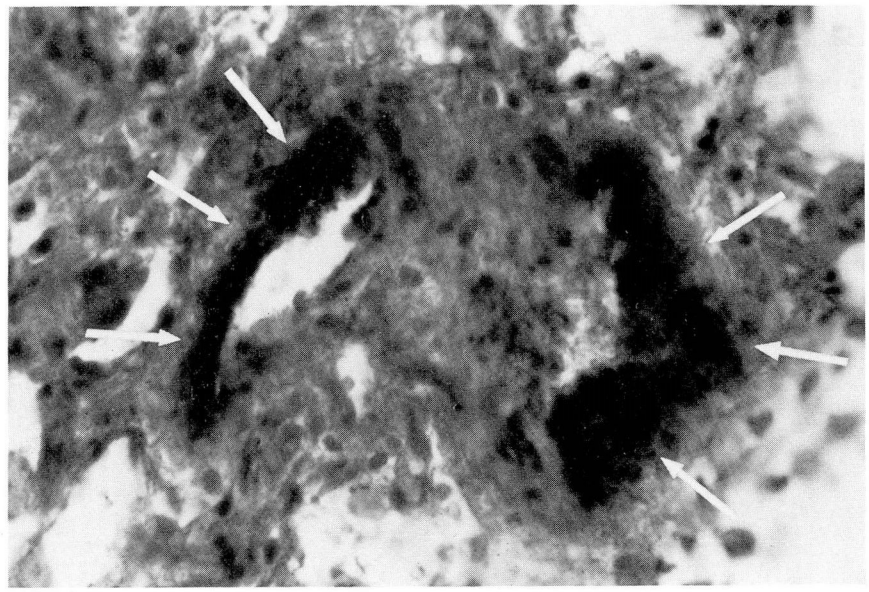


Fig. 36. Prominent deposits of C3 (third component of complement) in pulmonary vessels (arrows) in a case of lupus pneumonitis with extensive intra-alvelolar hemorrhage (immunoperoxidase with hematoxylin counterstain, ×560). Used by permission from Dr. Raymond Tubbs and the American Society of Clinical Pathologists.

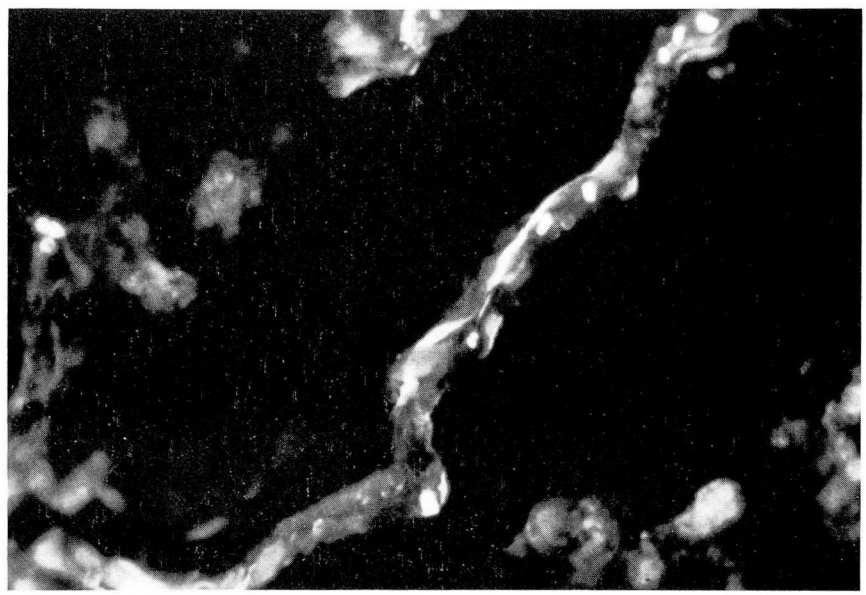


Fig. 37. Linear deposition of IgG demonstrated in a pulmonary alveolar wall in a case of Goodpasture's syndrome/anti-glomerular basement membrane disease (immunofluorescence, ×560). The patient also had linear deposition of IgG in glomerular basement membranes and crescentic glomerulonephritis.

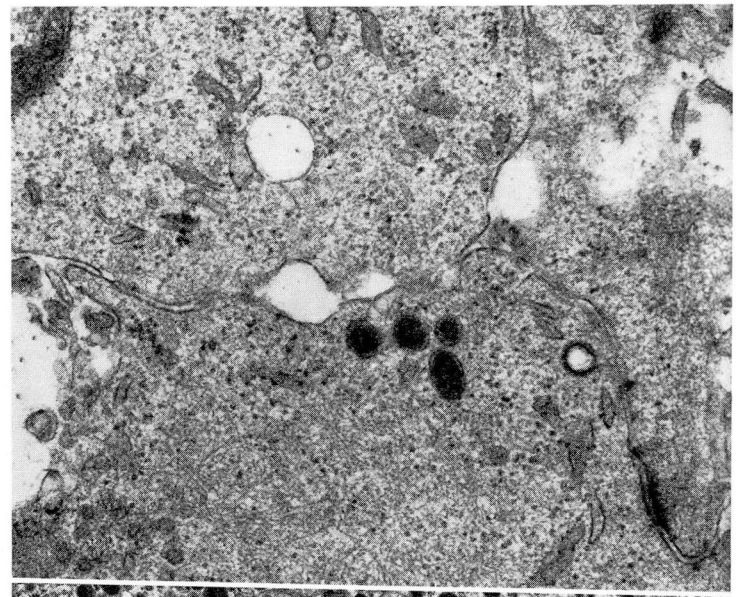


Fig. 38. Membrane-bound dense core granules in a case of small-cell carcinoma of the lung. These structures are found in small-cell undifferentiated carcinoma and carcinoid tumors of the lung (lead citrate and uranyl acetate stain, ×45,000).

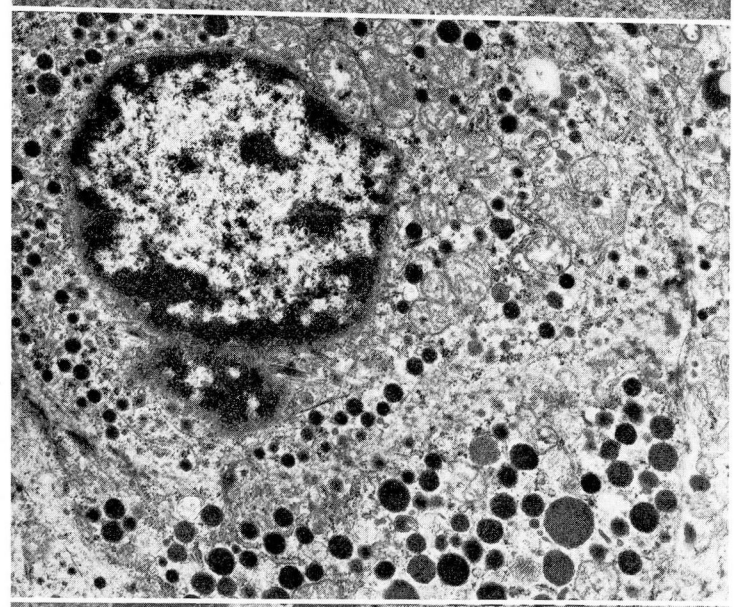


Fig. 39. Electron photomicrograph, demonstrating numerous membrane-bound dense core granules in a carcinoid tumor of the lung (lead citrate and uranyl acetate stain, ×11,000). This is the same case as illustrated in **Fig. 35.**

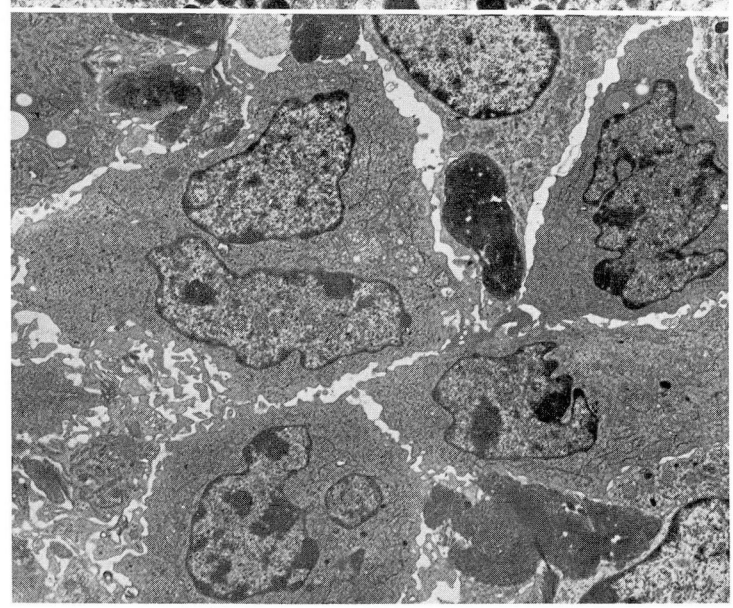


Fig. 40. Electron photomicrography of a large-cell lymphoma of the lung, demonstrating pseudopod-like cytoplasmic extensions, but no other differentiating feature (lead citrate and uranyl acetate stain, ×4,000). This is the same case as illustrated in **Fig. 30.**

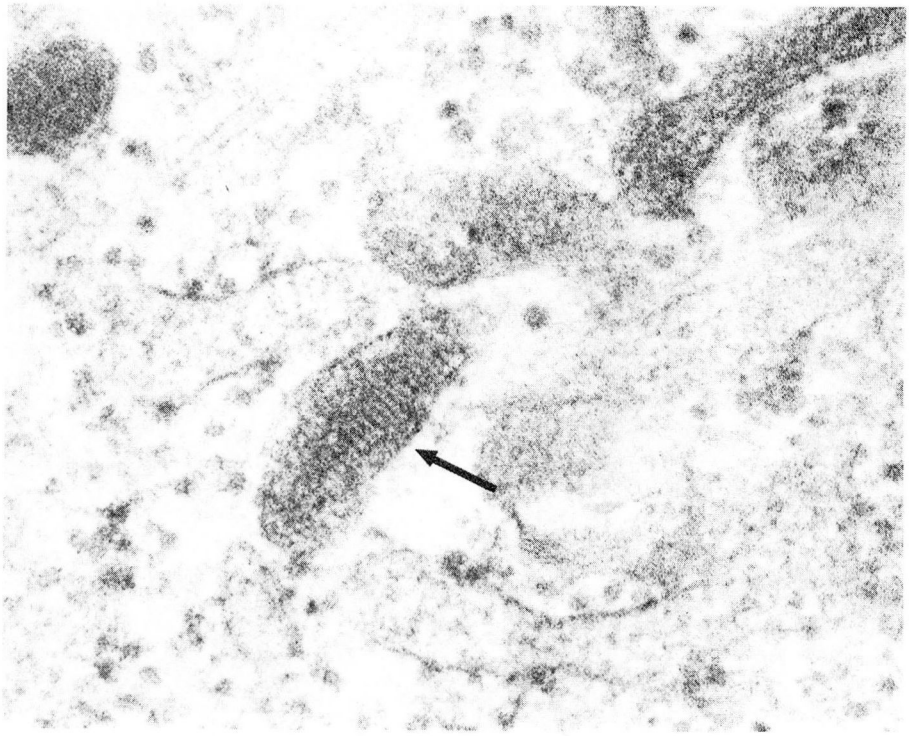


Fig. 41. Electron photomicrograph, demonstrating a premalanosome (arrow) in a metastatic melanoma involving the lung (lead citrate and uranyl acetate stain, ×133,000).

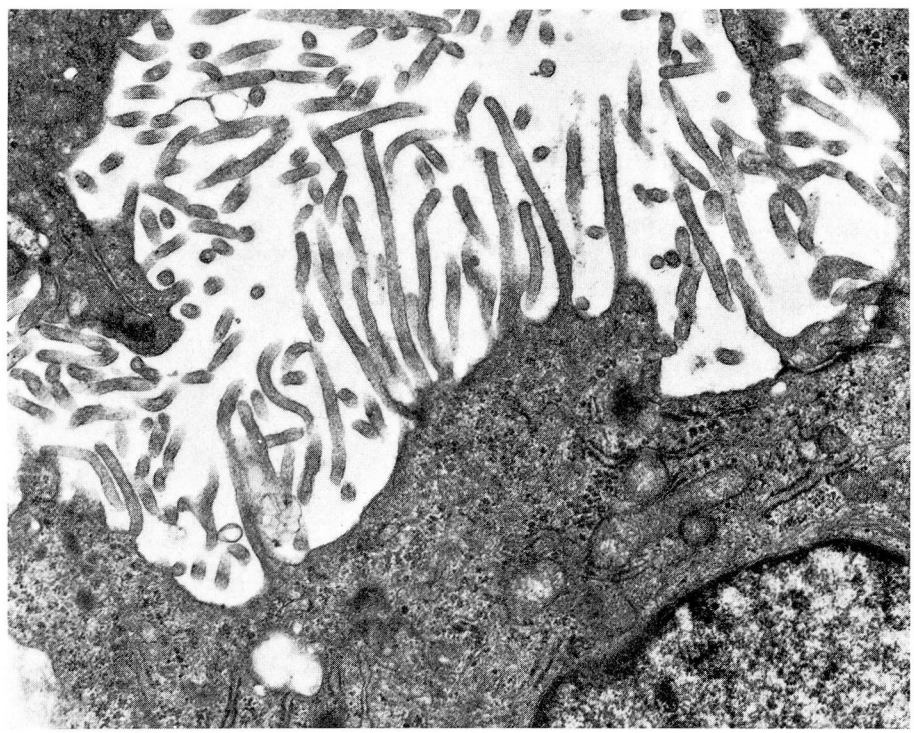


Fig. 42. Electron photomicrograph of a malignant epithelioid mesothelioma, involving the pleura. Long, delicate microvilli are demonstrated (lead citrate and uranyl acetate stain ×14,000).

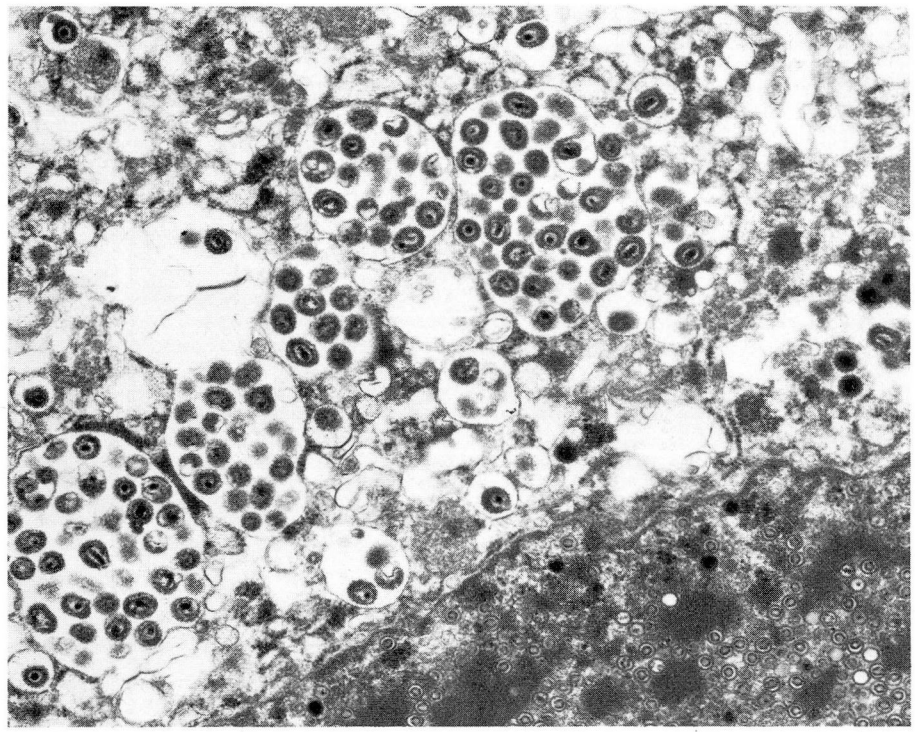


Fig. 43. Electron photomicrograph, demonstrating typical cytoplasmic and nuclear inclusions in a case of cytomegalic virus pneumonia (lead citrate and uranyl acetate stain, ×16,000).

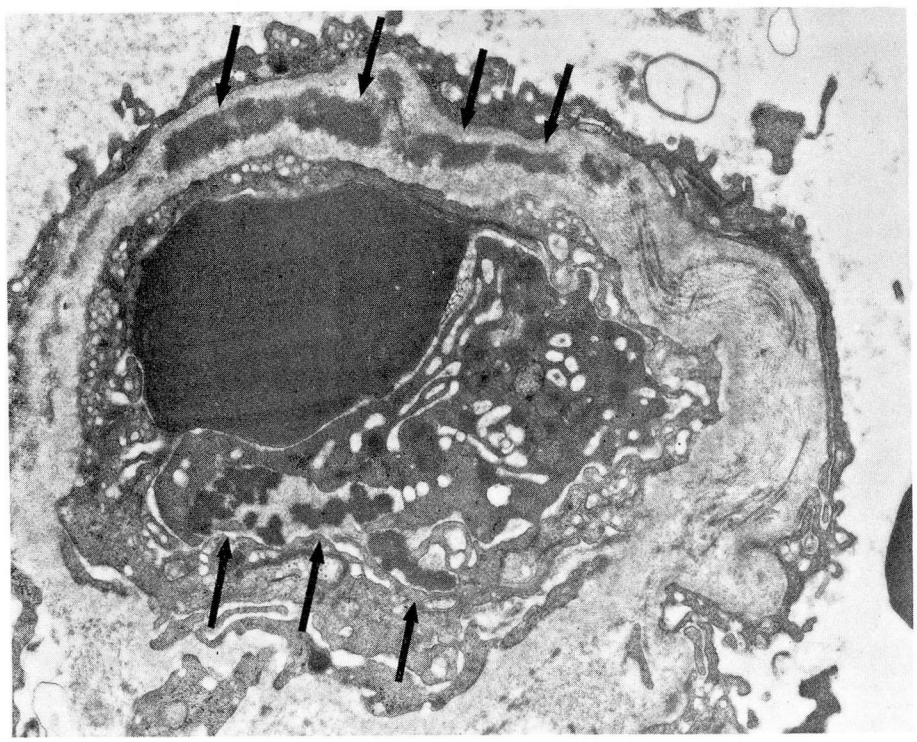


Fig. 44. Electron photomicrograph, demonstrating dense deposits in an alveolar-septal capillary wall in a case of lupus pneumonitis with pulmonary hemorrhage (lead citrate and uranyl acetate stain, ×31,200). This is the same case as illustrated in **Fig. 36.**

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