FRASER AND PARÉ

# DIAGNOSIS OF DISEASES OF THE CHEST

*An Integrated Study Based on the Abnormal Roentgenogram*

# DIAGNOSIS OF DISEASES OF THE CHEST

*An Integrated Study Based on the Abnormal Roentgenogram*

**VOLUME II**

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W. B. SAUNDERS COMPANY

Philadelphia London Toronto

W. B. Saunders Company: West Washington Square
Philadelphia, Pa. 19105

12 Dyott Street
London, WC1A 1DB

1835 Yonge Street
Toronto 7, Ontario

Diagnosis of Diseases of the Chest

 Press of W. B. Saunders Company. Library of Congress catalog card number 74-92132.

Print No. 2 3 4 5 6 7 8 9

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# NEOPLASTIC DISEASES OF THE LUNGS



## BENIGN NEOPLASMS

Primary neoplasms of the lung other than bronchogenic carcinoma are uncommon. The relative incidence may be gauged from the fact that, whereas bronchial adenomas constitute almost half of all "benign" neoplasms of the respiratory tract,[1705, 1707] they account for not more than 6 to 10 per cent of all primary lung neoplasms.[1705, 1706] In fact, Markel and associates,[1708] in a study covering 28 years, saw only 61 bronchial adenomas and approximately 3000 bronchogenic carcinomas, a ratio of roughly 1:50.

This section deals with all neoplasms, other than bronchogenic and bronchiolo-alveolar carcinoma, that originate from epithelial or mesenchymal tissues of the lung. It is emphasized that, although these neoplasms are called "benign" because usually they show benign histologic characteristics, many are potentially malignant. Their morphologic, roentgeno-

graphic, and clinical manifestations within the lung are highly variable and depend almost entirely upon the relationship of the neoplasm to an airway: if they occur in the periphery of the lung or are located near the hilum or within the medulla and are nonobstructive, they may cause no symptoms or signs and may be discovered only during screening roentgenography of the chest. If, however, they obstruct the lumen of a bronchus—the more common of the two modes of presentation—they cause atelectasis and obstructive pneumonitis, with bronchiectasis and abscess formation distal to the neoplasm; in these cases the clinical picture is more obvious, with cough, hemoptysis, wheezing, and repeated respiratory infections. Such differences in presentation bear little relation to the size of the neoplasm; a small endobronchial adenoma measuring no more than 4 to 5 mm in diameter may engender serious consequences in the area of lung distal to it, whereas a hamartoma measuring several centimeters in diameter in an area where it does not obstruct the bronchus may be silent.

## Bronchial Adenoma

Bronchial adenomas arise from the duct epithelium of the bronchial mucous glands.[1709] Although the term "adenoma" implies a benign epithelial lesion, bronchial adenomas are in reality neoplasms of low grade malignancy. Pathologically, they can be divided into two distinct groups—*carcinoid* and *salivary-gland types*. The salivary-gland type of bronchial adenoma can be subdivided into *cylindromas* (adenoid cystic carcinoma; adenocystic basal-cell carcinoma), *mucoepidermoid adenomas* and *pleomorphic adenomas* (mixed tumors).[1710, 1711] The carcinoid type comprises 85 to 95 per cent of bronchial adenomas;[1706, 1708, 1712–1715] the remainder consist of approximately two cylindromas to every one of the mucoepidermoid variety; pleomorphic adenomas are extremely rare. Bronchial adenoma is at least as common in females as in males,[1716] and most series indicate a higher incidence in the former.[1705, 1712, 1715, 1717] Ninety per cent of patients are less than 50 years of age, the mean age being the late 30's or early 40's.[1705, 1706, 1712, 1713, 1715–1717] Condon and Phillips[1713] found 19 cases reported in children under 12 years of age and 16 between the ages of 12 and 16 years.

### Pathologic Characteristics

Approximately 80 per cent of bronchial adenomas arise from the major bronchi and, therefore, are situated centrally.[1705, 1708, 1712, 1716, 1718] This central location favors bronchoscopic visualization, as was illustrated in one series in which the adenoma was identified bronchoscopically in 78 of 84 cases.[1716] The endobronchial group of neoplasms shows no predilection for a specific lobar distribution, although peripherally situated adenomas occur more often in the right upper lobe[1705] and in the right middle lobe and lingula.[1718]

Centrally placed adenomas usually are well-circumscribed masses in the submucosa of the larger bronchi. The overlying bronchial mucosa is usually intact unless secondary infection has resulted in ulceration. The degree of protrusion of the tumor into the bronchial lumen varies, from complete obstruction to an "iceberg" configuration in which much of the tumor extends into contiguous tissues and there is relatively little deformity of the bronchial lumen.

*Carcinoid adenomas* are composed of regular cuboidal cells, with fine granular cytoplasm and round or oval deeply-staining nuclei, usually arranged in sheets, strands, or islands. Mitotic figures are virtually absent. Unlike their occurrence in carcinoid tumors of the intestine, argentaffin granules are uncommon.[1708] In most cases the stroma of carcinoid neoplasms is highly vascular; its degeneration may result in hyalinization, calcification, and even ossification.[1728] A subvariety of carcinoid adenoma, known as the oncocytoid type, is composed of large cells with granular and strongly eosinophilic cytoplasm closely resembling oxyphil cells in the parathyroid glands. Also described is a spindle-cell variant which histologically may be confused with hemangiopericytoma or chemodectoma of the lung.

*Cylindromas* occur in the trachea and major bronchi;[1705, 1709, 1711, 1712] they usually recur after removal and are more malignant and locally invasive than the car-

cinoid type.[1705, 1709] Cylindromas originate from mixed serous and mucous glands. Like similar neoplasms which arise in the upper respiratory passages and salivary glands, they are composed of small pleomorphic and stellate cells with darkly staining nuclei; most of the cells are arranged in trabeculae or interlacing cylinders or tubes. The stroma surrounding the epithelial cells frequently undergoes myxomatous changes, with formation of pseudocartilaginous tissue resembling that of "mixed tumors"; true mixed tumors may be found occasionally. Mitotic figures are more numerous than in the carcinoid type.

*Mucoepidermoid tumors* are composed of a series of anastomosing cellular columns and masses separated by fine sheets of delicate connective tissue. The cells are cylindrical and pseudostratified. As the name indicates, distinct areas of squamous cells may be found together with mucus-secreting columnar cells.

Although the majority of bronchial adenomas have well-defined capsules, a small percentage show local invasion. The incidence of metastases varies in reported series from nil, even with long-term follow-up[1708, 1719, 1720] to 10 per cent with metastatic spread to regional lymph nodes or remote areas.[1709, 1712, 1714–1718, 1721, 1722] It is not known why metastases to bone, which occur rarely, usually are osteoblastic.[1722]

### Roentgenographic Manifestations

These depend largely upon the location of the adenoma. Since 80 per cent of these lesions are centrally placed in the major or segmental bronchi, bronchial obstruction is the most common morphologic and roentgenographic finding. Although it is conceivable that partial bronchial obstruction results in peripheral air-trapping, due to a check-valve effect, we have rarely seen this. In most cases obstruction is complete, with peripheral atelectasis and some degree of obstructive pneumonitis. Thus, the characteristic roentgenographic pattern is one of homogeneous increase in density confined precisely to a lobe or to one or more segments, usually with considerable loss of volume (Figure 8-1). Although massive collapse is fairly common,[1705, 1709] it should be remembered that collateral air-drift may prevent atelectasis, even with total obstruction of a major bronchus. We have seen one patient whose left lower-lobe bronchus was completely obstructed by a carcinoid adenoma and in whom the roentgenographic density of that lobe was actually reduced, presumably indicating reduction in perfusion in response to decreased ventilation (Figure 8-2). Segmental atelectasis and pneumonitis may show exacerbations and remissions from time to time, presumably as a result of intermittent relief of the obstruction. However, the recurrent infections that occur distal to the neoplasm inevitably result in bronchiectasis and lung abscesses (Figure 8-3).[1723]

If unassociated with bronchial obstruction, centrally placed adenomas appear roentgenographically as sharply circumscribed, somewhat lobulated, soft-tissue masses which may be separate from the hilar complex and thus discrete, or they may be contiguous with the hilum or mediastinum and thus produce hilar enlargement or mediastinal widening.[1717] Some central lesions which have given rise to peripheral atelectasis and pneumonitis may be identified as a discrete mass.[1712]

Bronchial adenomas which arise peripherally (roughly 20 per cent) are unassociated with bronchial obstruction and have the roentgenographic appearance of "coin" lesions (Figure 8-4). They are usually homogeneous in density, sharply circumscribed, round or oval,[1718] and in many cases slightly lobulated.[1706] They average about 4 cm in diameter in a range of 1 to 10 cm[1708, 1718] and occur most often in the right upper and middle lobes and in the lingula.[1705, 1718] Calcification and ossification are rare.[1724, 1728]

Tomography may be helpful in determining the morphologic characteristics of these neoplasms, particularly when the tumor is centrally situated and when deformity of a contiguous bronchial air column is anticipated (Figures 8-2 and 8-3). In the majority of cases bronchography outlines the tumor mass (Figures 8-1 and 8-4). Osteoblastic metastases, which may be revealed by roentgenographic bone survey, develop in but few patients, usually those with the carcinoid syndrome.[1722, 1725–1727]

### Clinical Manifestations

Peripherally situated neoplasms typically occasion no symptoms. In the

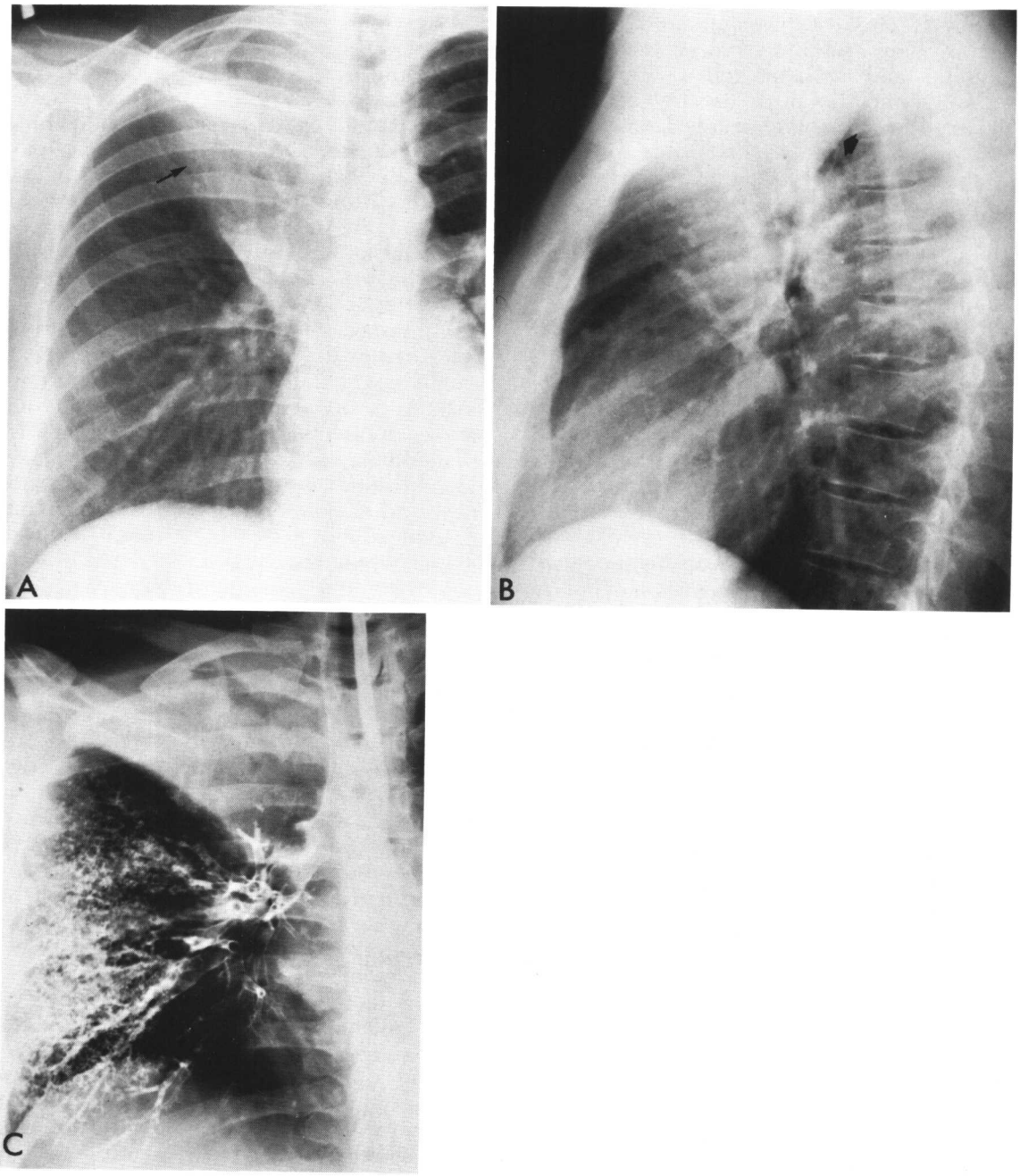


*Figure 8–1.* **Bronchial Adenoma (Carcinoid Type).** Views of the right hemithorax from posteroanterior (*A*) and lateral (*B*) roentgenograms demonstrate a roughly triangular shadow of homogeneous density occupying the superomedial portion of the right lung; the inferolateral border of the shadow is formed by the upward displaced minor fissure (*arrow* in *A*) and the posterior border by the anteriorly displaced major fissure (*arrow* in *B*). This shadow represents combined consolidation and atelectasis of the right upper lobe due to an endobronchial obstructing lesion (obstructive pneumonitis). A right bronchogram (*C*) reveals a smooth, rounded mass protruding into the right main-stem bronchus at the point of origin of the upper lobe bronchus; such an intraluminal filling defect is characteristic of bronchial adenoma. The lobe was resected; pathologic proof.

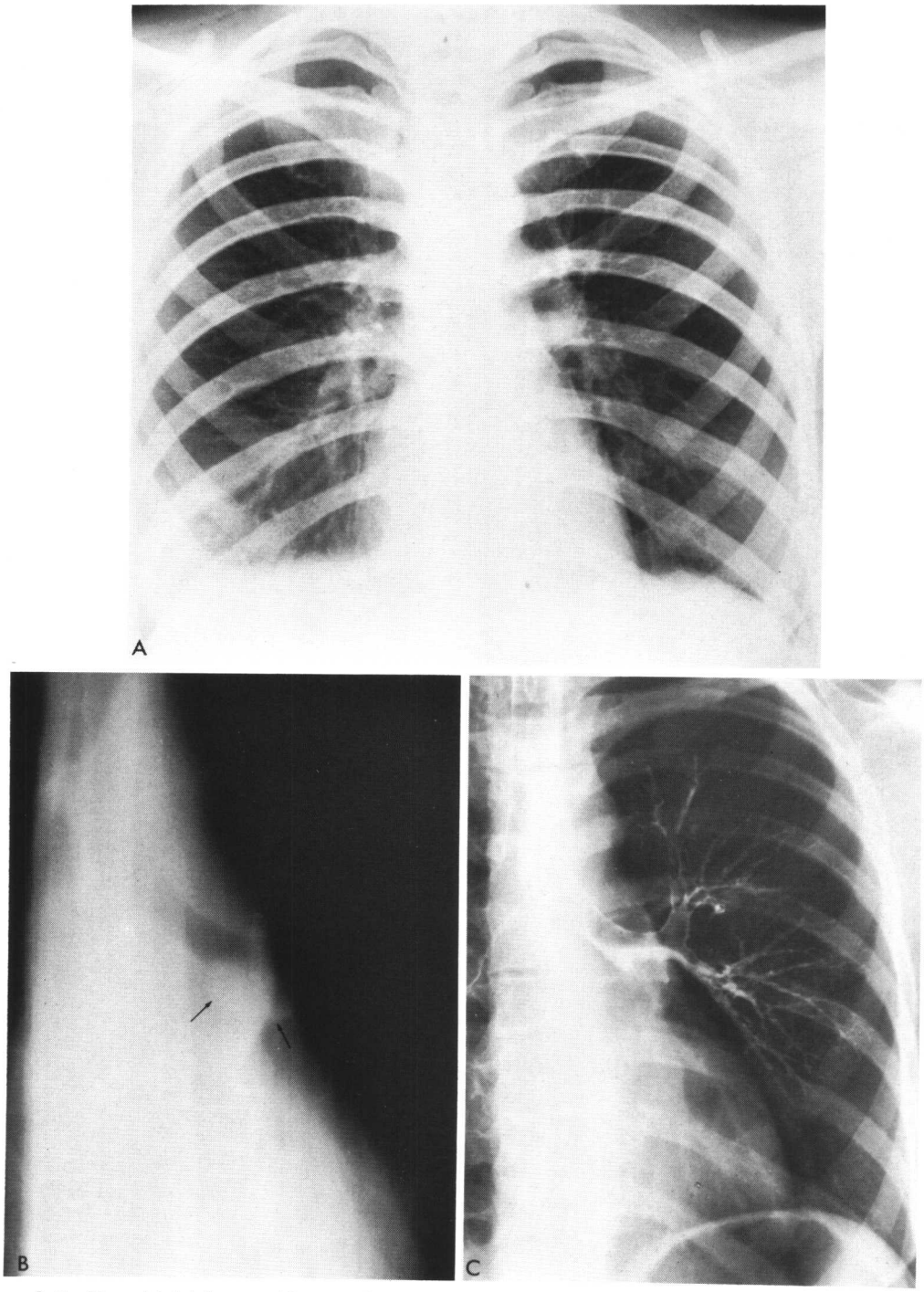


*Figure 8–2.* **Bronchial Adenoma (Carcinoid Type).** A posteroanterior roentgenogram (*A*) reveals asymmetrical density of the lower half of the two lungs, that on the left being more radiolucent than the right. The vascular markings to the left lower lobe are considerably less conspicuous than those of the right lower lobe. No other abnormalities are identified on this roentgenogram. An anteroposterior tomogram (*B*) reveals a smooth, well-defined soft tissue mass at the origin of the left lower-lobe bronchus (*arrows*); no air can be identified within this bronchus. A left bronchogram (*C*) demonstrates total obstruction of the lower-lobe bronchus at its origin by a somewhat irregular mass lying within its lumen. This 25-year-old woman complained of a nonproductive cough for six months prior to these roentgenographic studies; she had had two episodes of hemoptysis shortly before admission. The left lower lobe was resected; a bronchial adenoma of carcinoid type was found to be totally obstructing the left lower-lobe bronchus at its origin. The plain roentgenographic findings can be satisfactorily explained only on the basis of collateral air-drift from the normally ventilated left upper lobe across an incomplete chief fissure; the oligemia presumably was the result of arteriolar spasm secondary to alveolar hypoventilation.

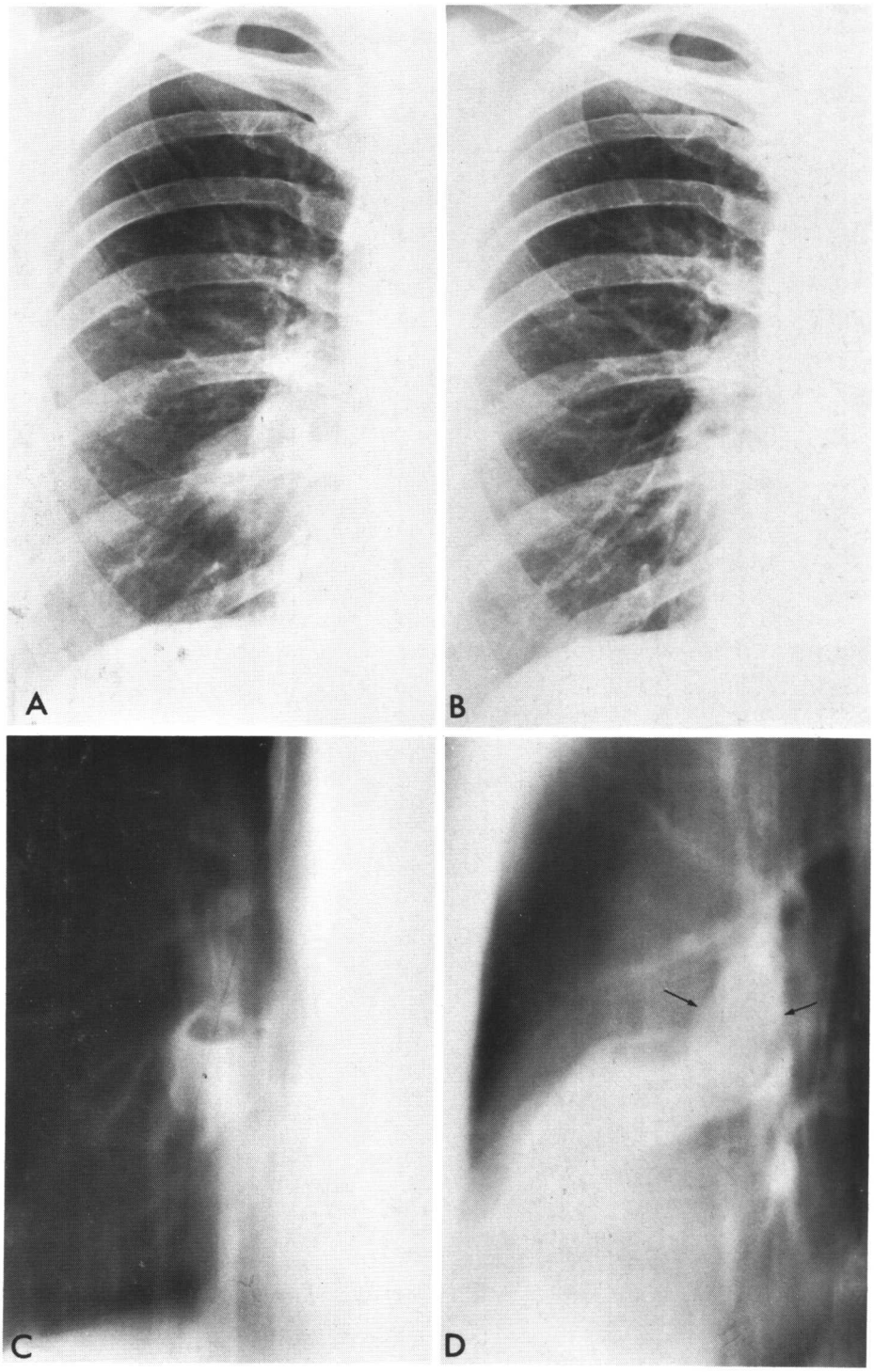


*Figure 8–3.* **Bronchial Adenoma (Carcinoid Type) Producing Obstructive Pneumonitis and Abscess Formation.** A view of the right hemithorax from a posteroanterior roentgenogram (*A*) reveals a triangular shadow of homogeneous density situated in the medial portion of the lung just below the hilum; the silhouette sign with the right border of the heart localizes the disease in the right middle lobe. Three months later (*B*), the shadow is smaller and somewhat less homogeneous; a small cystic space containing an air-fluid level can be identified in the upper portion of the shadow. At this time, anteroposterior (*C*) and lateral (*D*) tomograms reveal an elliptical shadow containing a small abscess in its upper portion. In lateral projection, there is a suggestion of a soft tissue mass just above the main shadow (*arrows*). The middle lobe was resected; proved bronchial adenoma of the right middle-lobe bronchus. The change that occurred in the three month interval resulted from partial relief of the bronchial obstruction, permitting air to enter an abscess in the obstructed lobe.

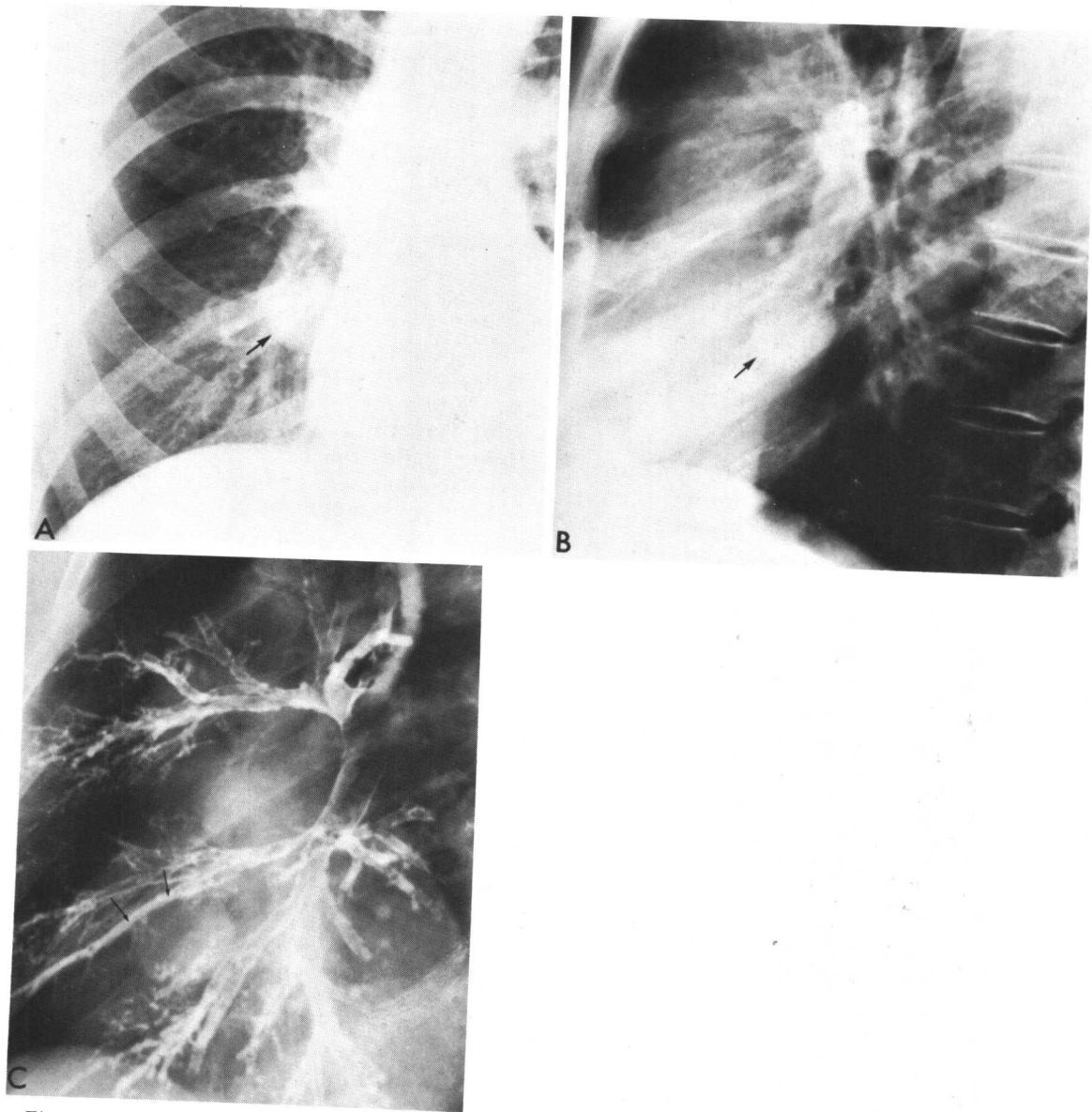


*Figure 8–4.* **Bronchial Adenoma (Carcinoid Type): Solitary Nodule.** Views of the lower half of the right hemithorax from posteroanterior (*A*) and lateral (*B*) roentgenograms of a 72-year-old asymptomatic man reveal a smooth, round, sharply-circumscribed nodule measuring 3 cm in diameter in the medial portion of the right middle lobe (*arrows*). The peripheral parenchyma is normal. An oblique view of the right bronchogram (*C*) demonstrates a minor degree of pressure deformity of the medial segmental bronchus of the right middle lobe (*arrows*).

majority of patients, however, the lesion is endobronchial and symptoms and signs result from atelectasis and pneumonitis secondary to bronchial obstruction. Symptoms include cough, expectoration, fever, wheezing, and chest pain. Hemoptysis occurs in at least 50 per cent of patients,[1705, 1706, 1708, 1712, 1713, 1717, 1719] an incidence that reflects the highly vascular nature of these neoplasms. Physical signs depend upon the degree of obstruction, the size of the bronchus obstructed, and the presence or absence of peripheral infection. Percussion may be impaired, and breath sounds may be decreased over a segment, a lobe, or an entire lung, and rales and even a friction rub may be heard when infection is present.

Massive atelectasis is reflected in the clinical signs of loss of volume, such as mediastinal shift.

Some carcinoid adenomas give rise to symptoms and signs of the *carcinoid syndrome*; however, this syndrome occurs more commonly in cases of argentaffin-cell neoplasms of the distal small bowel with hepatic metastases. Argentaffin granules are seldom seen in the cells of bronchial carcinoid adenomas. Sandler and associates' 1961 review of the literature cited 20 cases of functioning bronchial carcinoids,[1725] and since then a further 20 cases have been reported.[1726, 1727, 1731–1735] Most carcinoid neoplasms either produce no 5-hydroxytryptamine (serotonin)[1736] or secrete it in insufficient quantities to produce symptoms and signs.[1737]

Patients who exhibit the clinical picture of the carcinoid syndrome invariably have widespread metastatic disease, usually but not invariably involving the liver.[1731, 1732, 1734, 1738]

The symptoms and signs of the carcinoid syndrome consist of flushing, fever, nausea and vomiting, diarrhea, hypotension, wheezing, and respiratory distress.[1722, 1726, 1731, 1732, 1734, 1738, 1739] Heart murmurs seldom develop; when present they may be restricted to the left side of the heart, owing to endocardial damage from high concentrations of 5-hydroxytryptamine entering the pulmonary veins from the lungs[1726, 1740] (in contrast to the right-sided endocardial damage in abdominal carcinoids). Melmon and associates[1726] described what they believe to be distinctive clinical manifestations of bronchial carcinoid syndrome in contrast to the syndrome resulting from neoplasms of the small intestine: these consist of prolonged and severe flushing attacks, anxiety, tremulousness, temperature elevations, periorbital and facial edema, increased lacrimation and salivation, rhinorrhea, diaphoresis, explosive diarrhea, nausea and vomiting, hypotension, and oliguria. These authors stated also that osteoblastic bone metastases occur in many of the cases of this variant of the carcinoid syndrome. Sandler and associates[1725] believe that there is a relationship between neoplasms secreting 5-hydroxytryptophan (the precursor of 5-hydroxytryptamine) and the presence of gastric ulcers and of widespread metastases, especially to bone.

*Cushing's syndrome* has been described in association with bronchial adenoma.[1741] ACTH (adrenocorticotrophic hormone) has been found in assays of such tumors and clinical remission has followed excision of the adenoma. There has been one report of insulin secretion by a carcinoid adenoma of the bronchus with widespread metastases.[1742]

*Laboratory tests* are of little or no value in the diagnosis of bronchial adenoma. However, carcinoid syndrome may be diagnosed when large amounts of 5-hydroxyindole acetic acid (5-HIAA), the end-product of 5-hydroxytryptophan (5-HTP) and 5-hydroxytryptamine (serotonin; 5-HT), are found in the urine.[1731, 1732, 1734, 1738, 1739] *Pulmonary function values* are normal in cases of peripheral neoplasm; in the central variety, function values indicate obstructive or restrictive insufficiency, the amount of change depending upon the degree of obstruction and the size of the affected bronchus. In patients with bronchospasm due to serotonin (5-HT), pulmonary function-test findings are indicative of obstructive overinflation; the diffusing capacity is normal.

## Pulmonary Hamartoma

A hamartoma is a "tumor" composed of the tissues that normally constitute the organ in which it occurs, but the tissue elements are not organized. Despite the generally accepted concept that this tumor originates from an embryologic rest, it seldom becomes roentgenographically visible

until adulthood. In fact, the peak incidence is in the sixth decade[1744, 1748] (as with bronchogenic carcinoma[1745, 1746]) and only 6 per cent occur under the age of 30;[1744] thus they are best considered neoplasms rather than congenital malformations. Some cases have been reported in children, and of ten patients reported in one series three were less than ten years of age.[1747] They occur more often in males, the sex ratio being 2 to 3:1.[1744, 1748] In Bateson's review of 2958 solitary lung lesions,[608] 5.7 per cent were hamartomas, and in their report of 7,972 necropsies McDonald and associates[1753] recorded 20 hamartomas (0.25 per cent).

### Pathologic Characteristics

Unlike bronchial adenomas, the great majority of hamartomas lie in the peripheral parenchyma. Only about 10 per cent are endobronchial,[608, 1750, 1751] although even the peripheral tumors are considered pathologically to arise in the connective tissues of small bronchi.[1752] They tend to be well circumscribed and usually are slightly lobulated; contiguous lung parenchyma is compressed. Cartilage is almost invariably present and often is the predominant tissue; however, it bears no relationship to the cartilage lining the conducting airways. Various other tissues often are present, including epithelium (seldom ciliated), fibrous connective tissue, smooth muscle, adipose tissue and, sometimes, bone. These tissues are arranged in a haphazard fashion with complete lack of organization. Hamartomas are always benign.

### Roentgenographic Manifestations

Pulmonary hamartomas characteristically present as a "coin" lesion; the majority measure less than 4 cm in diameter[608, 1723, 1744, 1748] and show no lobar predominance.[608, 1745] They are nearly always well circumscribed and are more often lobulated than smooth, in a ratio of 2:1;[608] a smooth outline is of some value in differentiation from bronchogenic carcinoma, which almost invariably is lobulated.[608] Calcification probably is less common than was thought formerly: the usual reported incidence is 25 to 30 per cent,[608, 1748] although in one series[1745] this was apparent on the roentgenogram preoperatively in only two of 65 lesions removed surgically. The roentgenographic appearance of calcification may resemble popcorn, a finding which is almost diagnostic (*see* Figure 5-18, page 437). Rarely, hamartomas are multiple.[1754–1756] Serial roentgenographic examination may reveal slow and rarely rapid growth of these lesions,[668, 669, 1754, 1757] a fact which increases the difficulty in differentiation from bronchogenic carcinoma. Cavitation is extremely rare;[1723] one case was reported in which a hamartoma had a cystic appearance resembling that of mycetoma.[1759] Metyš[1748] has stressed peripheral radiolucencies seen on tomography as of diagnostic import. These cystic and radiolucent areas may be due to fat within the tumor. Bronchial obstruction leads to atelectasis, obstructive pneumonitis and progressive peripheral lung destruction in only a small percentage of cases.

### Clinical Manifestations

The peripheral location of hamartomas renders them unlikely to give rise to symptoms. Hemoptysis is rare.[1751] In the few cases in which the lesion obstructs a bronchus, the signs and symptoms are those of atelectasis or pneumonitis—fever, cough, expectoration, and chest pain;[1723, 1747, 1750–1752, 1760–1762] in such circumstances, bronchoscopy and biopsy may reveal the diagnosis.

In the absence of characteristic "popcorn" calcification, the differential diagnosis of peripheral hamartoma must be from bronchogenic carcinoma, and thoracotomy will be required for definitive diagnosis.

## PAPILLOMA

Papillomas are the most common laryngeal tumors in children, but seldom develop in adults. They may be single or multiple and, when the latter, sometimes extend down the tracheobronchial tree into the lungs and there obstruct the airways. Distal spread occurs in about 2 per cent of cases of juvenile laryngeal papillomatosis, usually limited to the trachea.[1763] Recent reviews of the literature revealed only seven well-documented cases in

which the lesions extended into the bronchi, bronchioles, alveolar ducts, and atria;[1763, 1764] five of the patients were known to have had laryngeal papillomas before they were five years old, and the average interval between development in the larynx and the detection of broncho-alveolar lesions was 12 years.[1764] Bronchial papillomas very rarely precede laryngeal or tracheal lesions or develop in their absence.[1723, 1764–1766]

*Pathologically,* papillomas contain a core of vascular connective tissue covered by stratified squamous epithelium and occasionally by a surface layer of ciliated respiratory columnar epithelium.[1763, 1767–1769] The lesions probably are viral in origin.[1763] Malignant change occurs in some.[1765, 1768]

*Roentgenologically,* the manifestations are somewhat variable. The papillomas characteristically obstruct airways, resulting in peripheral atelectasis and obstructive pneumonitis; cavitation and bronchiectasis are frequent.[1766–1768] Multiple papillomas deep in the smaller bronchi and alveolar ducts may be visualized as multiple nodular lesions, frequently associated with cavitation[1763] and often resembling advanced cystic bronchiectasis. The demonstration of defects in the air columns, by tomography of the lungs and of the trachea, is of diagnostic value.[1768]

*Clinically,* the diagnosis should be suspected in any patient with a history of recurrent papillomas of the larynx in whom cough, hemoptysis, asthma-like symptoms, recurrent pneumonia, and atelectasis develop.[1723, 1766, 1770, 1771] The diagnosis is virtually certain when roentgenography reveals multiple areas of segmental atelectasis or cavitation; and bronchoscopic and biopsy identification of the lesions is confirmatory.

## Leiomyoma

This neoplasm arises from the smooth muscle of the periphery of the lung or from the walls of the trachea or bronchi and is as often malignant (leiomyosarcoma) as it is benign.[1772] Both benign and malignant forms occur more often in females.[1772] The majority of patients are over 40 years of age when the lesion is first discovered,[1772, 1773] although some cases have been reported in children.[1772] Leiomyoma of the uterus may occur in association with pulmonary lesions;[1774] it has been noted that pulmonary metastases from leiomyosarcoma of the uterus may be mistaken histologically for benign leiomyomas.[961]

*Morphologically,* most of these tumors are encapsulated. The majority are situated in the lung periphery and some, especially leiomyosarcomas, are endobronchial or endotracheal in position. The peripheral type tends to be more fibrous in consistency and perhaps should be termed fibroleiomyoma. Hyaline degeneration and calcification may occur.

The *roentgenographic manifestations* relate to the peripheral location of the majority of lesions which present as solitary nodules or "coin" lesions of various sizes.[1723, 1772, 1773] Those that arise from the wall of a major or segmental bronchus may obstruct the lumen and give rise to atelectasis and obstructive pneumonitis. Defects in the air column of the trachea or large bronchi may be apparent when the lesions are not obstructive; tomography may be a valuable aid in such assessment.

*Clinically,* the peripheral lesions occasion no symptoms as a rule, although leiomyosarcoma commonly provokes hemoptysis.[1775] The atelectasis and obstructive pneumonitis caused by endobronchial lesions lead to cough, expectoration, dyspnea, and chest pain.[1723, 1772, 1776] The clinical picture may simulate asthma, and Sanders and Carnes[1776] emphasized the importance of suspecting the lesion in patients who have paroxysms of wheezing with change of body position, especially if they have a history of hemoptysis and have not responded to usual therapy for asthma.

## Fibroma

Fibrous-tissue neoplasms of the lung may be benign (fibroma)[1777] or malignant (fibrosarcoma).[1778, 1779] They may arise from the peripheral parenchyma or from the walls of the trachea or bronchi.[1779, 1780] As with other mesenchymal neoplasms of the lung, various combinations of tissues may be present, and it is difficult to establish a precise descriptive histologic terminology.[1781] Spindle cells predominate, with various amounts of collagen, myxomatous tissue, or calcification.

The *roentgenographic appearance* is not distinctive, peripheral fibromas presenting as "coin" lesions. Since neoplasms which