Cystic and Cavitary Lung Diseases: Focal and Diffuse

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Cysts and cavities are commonly encountered abnormalities on chest radiography and chest computed tomography. Occasionally, the underlying nature of the lesions can be readily apparent as in bullae associated with emphysema. Other times, cystic and cavitary lung lesions can be a diagnostic challenge. In such circumstances, distinguishing cysts (wall thickness ≤ 4 mm) from cavities (wall thickness > 4 mm or a surrounding infiltrate or mass) and focal or multifocal disease from diffuse involvement facilitates the diagnostic process. Other radiological characteristics, including size, inner wall contour, nature of contents, and location, when correlated with the clinical context and tempo of the disease process provide the most helpful diagnostic clues. Focal or multifocal cystic lesions include blebs, bullae, pneumatoceles, congenital cystic lesions, traumatic lesions, and several infectious processes, including coccidioidomycosis, Pneumocystis carinii pneumonia, and hydatid disease. Malignant lesions including metastatic lesions may rarely present as cystic lesions. Focal or multifocal cavitary lesions include neoplasms such as bronchogenic carcinomas and lymphomas, many types of infections or abscesses, immunologic disorders such as Wegener granulomatosis and rheumatoid nodule, pulmonary infarct, septic embolism, progressive massive fibrosis with pneumoconiosis, lymphocytic interstitial pneumonia, localized bronchiectasis, and some congenital lesions. Diffuse involvement with cystic or cavitary lesions may be seen in pulmonary lymphangioleiomyomatosis, pulmonary Langerhans cell histiocytosis, honeycomb lung associated with advanced fibrosis, diffuse bronchiectasis, and, rarely, metastatic disease. High-resolution computed tomography of the chest frequently helps define morphologic features that may serve as important clues regarding the nature of cystic and cavitary lesions in the lung.


AIDS = acquired immunodeficiency syndrome; CCAM = congenital cystic adenomatoid malformation; HRCT = high-resolution computed tomography; LAM = lymphangioleiomyomatosis; PLCH = pulmonary Langerhans cell histiocytosis

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Cysts and cavities are commonly encountered lesions in the lung on chest radiography and chest computed tomography. The differential diagnosis of such lesions is broad because many different processes of acquired or congenital origin can cause these abnormalities. Cysts and cavities are seen as foci of decreased lung density with definable walls. In contrast, emphysematous airspaces usually lack such perceptible walls (bullae and blebs are exceptions). This distinction, i.e., presence or absence of a wall around a radiolucent area, can be accurately depicted by high-resolution computed tomography (HRCT) if it is not apparent on chest radiography. High-resolution CT examines 1-mm slices (collimation) by using a high spatial frequency reconstruction algorithm and depicts lung parenchymal details better than conventional CT.

The terms cyst, cystic airspace, and cavity have overlapping meanings and are sometimes used interchangeably. This is unfortunate because the terms cyst and cavity convey very different meanings and ranges of diagnostic possibilities to clinicians. Also, these terms have different connotations to pathologists. In this review, the term cyst is used to mean a clearly defined air-containing space surrounded by a relatively thin (≤ 4 mm) wall. In contrast, the term cavity is used to refer to an air-containing lesion with a relatively thick (> 4 mm) wall or within an area of a surrounding infiltrate or mass. This distinction is useful because diagnostic considerations and approach differ for these 2 categories, although some overlap exists. In particular, cystic lesions (as defined herein) in the lungs are rarely malignant. However, malignancy is commonly the first diagnosis to consider for a cavitary lesion, particularly in a middle-aged or older adult with a history of cigarette smoking. Clinicians generally pursue a definitive diagnosis in cases of cavitary lung lesions since the diagnostic possibilities are more worrisome compared with cystic lesions in which a benign nature may often be assumed based on the clinicoradiological context. Another important distinction is whether involvement is focal or multifocal vs diffuse (involving all lobes of both lungs). Diffuse cystic or cavitary changes are seen in a limited number of disorders, such as pulmonary lymphangioleiomyomatosis (LAM) and pulmonary Langerhans cell histiocytosis (PLCH).
Other radiological and clinical parameters that may provide helpful clues in the diagnostic evaluation of a patient with cystic or cavitary lung disease, especially when the disease is focal, are the measured thickness of the cavity wall, the character of its inner lining (irregular or smooth), the nature of its contents, and location. Woodring et al studied the diagnostic implications of cavity wall thickness in 65 cases of solitary cavities of the lung and found that all lesions in which the thickest part of the cavity wall was 1 mm were benign; of cavities in which the greatest wall thickness was 4 mm or less, 92% were benign; lesions 5 to 15 mm were equally divided between benignity and malignancy; and when the cavity wall was greater than 15 mm in thickness, 95% of lesions were malignant. Inner contour of the cavity is usually nodular or irregular in cancer, shaggy in acute lung abscess, and smooth in other cavitary lesions. Some cystic or cavitary lesions may be filled with fluid or solid contents. For example, a bronchogenic cyst may be filled with fluid and appear as a mass lesion on chest radiography. The presence of an air-fluid level does not correlate well with benignity or malignancy. Solid contents within a cavity may be seen in infectious processes, such as invasive aspergillosis, and in necrotic cancer. The location of focal lesions may be of help in limiting the differential diagnosis, e.g., propensity of tuberculosis to affect the upper lobes of the lung. Computed tomography can show the size, shape, and precise position of cysts and cavities when these details are not apparent on chest radiography.

Two clinically important parameters in evaluating cystic and cavitary lesions are the tempo of the disease process and the clinical context. The diagnostic possibilities are strongly influenced by knowing whether a radiological lesion is acute or subacute vs chronic (>1 month in duration). This distinction is usually based on the duration and course of related symptoms and signs as well as comparison to previous imaging studies, when available. Acute and subacute processes that evolve over a relatively short period (days to a few weeks) generally suggest infectious or other progressive inflammatory disorders as well as disorders of cardiovascular (embolic) or traumatic causes. Chronic processes are more likely due to neoplastic diseases, long-standing inflammatory or fibrotic disorders, and congenital lesions. The clinical context is crucial and includes age, sex, smoking history, immunocompetency, underlying diseases, drug or other treatments, associated extrapulmonary symptoms and signs, environmental and occupational exposure, recent trauma, travel history, and relevant laboratory test results.

The clinical importance of cystic and cavitary lung diseases is related to their underlying nature. Active infectious processes and malignancies obviously need to be diagnosed promptly to minimize adverse outcomes. Other causes of cystic and cavitary lung disease with potentially devastating outcomes include pulmonary embolism and vasculitides such as Wegener granulomatosis. In addition, the presence of cysts and cavities in the lung predisposes to the occurrence of spontaneous pneumothorax.

### Table 1. Causes of Focal or Multifocal Cystic and Cavitary Lung Disease

<table>
<thead>
<tr>
<th>Cause</th>
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<tbody>
<tr>
<td>Cystic (wall thickness ≤4 mm)</td>
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<tr>
<td>Bullae</td>
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<tr>
<td>Blebs</td>
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<tr>
<td>Pneumatoceles</td>
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<tr>
<td>Congenital cystic lesions</td>
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<tr>
<td>Bronchogenic cyst</td>
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<tr>
<td>Congenital adenomatoid malformation</td>
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<tr>
<td>Infections</td>
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<tr>
<td>Coccidiodomycosis</td>
</tr>
<tr>
<td>Pneumocystis carinii</td>
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<tr>
<td>Hydatid disease</td>
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<tr>
<td>Traumatic cysts</td>
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<tr>
<td>Cavitary (wall thickness &gt;4 mm or surrounding infiltrate or mass)</td>
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<tr>
<td>Neoplastic</td>
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<tr>
<td>Bronchogenic carcinomas</td>
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<tr>
<td>Metastases</td>
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<td>Lymphomas</td>
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<tr>
<td>Infections</td>
</tr>
<tr>
<td>Bacteria</td>
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<tr>
<td>Staphylococcus aureus, gram-negative bacteria, pneumococcus, mycobacteria, melioidosis, anaerobes, actinomyces, nocardiosis</td>
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<tr>
<td>Fungi</td>
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<tr>
<td>Histoplasmosis, coccidiodomycosis, blastomycosis, aspergillosis, mucormycosis, cryptococcosis, P carinii, sporotrichosis</td>
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<tr>
<td>Parasites</td>
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<tr>
<td>Hydatid disease</td>
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<tr>
<td>Wegener granulomatosis</td>
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<tr>
<td>Rheumatoid nodule</td>
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<tr>
<td>Thromboembolism or septic embolism</td>
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<tr>
<td>Progressive massive fibrosis (pneumoconiosis)</td>
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<td>Bronchiectasis, localized</td>
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<td>Congenital lesions</td>
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<tr>
<td>Sequestration</td>
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<tr>
<td>Congenital adenomatoid malformation</td>
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### FOCAL OR MULTIFOCAL CYSTIC LUNG LESIONS

Cystic airspaces that present as focal or multifocal lesions usually represent bullae, blebs, pneumatoceles, infectious cysts, and congenital cystic lesions (Table 1). A bulla is generally defined as a sharply demarcated air-containing space of 1 cm or more in diameter within the lung that possesses a smooth wall that is less than 1 mm in thickness. Bullae usually result from coalescence of emphysematous spaces or from a Ball-valve type of airway obstruction. A bleb is a localized collection of air in the immediate subpleural lung or within the pleura and is usually less than 1 cm in diameter. Blebs are usually located in the apex of the lung and have been attributed to congenital
abnormalities, greater distending pressure at the apex of the lung, or obstructive airway diseases. A pneumatocele is a cystic airspace within the lung that characteristically increases in size over a period of days to weeks (probably due to Ball-valve air trapping) but resolves eventually. Pneumatoceles are typically associated with infection, particularly staphylococcal pneumonia, and occur more commonly in children.\textsuperscript{13,9}

Infectious causes of pulmonary cysts include coccidioidomycosis, \textit{Pneumocystis carinii} pneumonia, and hydatid disease. Most of the other necrotizing infections of the lung tend to cause cavitary lesions (thick walled) rather than cysts. Coccidioidomycosis is an endemic disease found mainly in semiarid regions of the southwestern United States, northern Mexico, and Central and South America.\textsuperscript{10,11} Cavitation is a major characteristic of chronic pulmonary coccidioidomycosis, and the wall of the focal lesion is often thin. A thin-walled cyst also can represent residue from a resolved primary infection (Figure 1).\textsuperscript{10} Cysts associated with \textit{P carinii} pneumonia are seen mainly in patients with underlying acquired immunodeficiency syndrome (AIDS).\textsuperscript{12-15} Most of these cysts are located in the upper lobes, are multiple, and measure 1 to 5 cm in diameter.\textsuperscript{14,15} Hydatid cysts are caused by the tapeworms \textit{Echinococcus granulosus} and \textit{Echinococcus multilocularis}. The disease is endemic in sheep-raising areas of the Mediterranean basin, Australia, and South America, but some cases have been acquired in North America.\textsuperscript{16-18} Cysts of hydatid disease in the lung are more commonly multiple than single, with walls ranging in thickness from 2 mm to 1 cm.\textsuperscript{16-19}

Congenital cystic lung lesions are rare; however, they can cause morbidity in children and young adults. Congenital cystic lesions include bronchogenic cysts, pulmonary sequestrations, and congenital cystadenomatoid malformations (CCAMs).\textsuperscript{20-23} Bronchogenic cysts arise from abnormal budding of the tracheobronchial tree during airway development. Although bronchogenic cysts are more often present in the mediastinum, approximately one third are located in the lung parenchyma, usually within the lower lobes (Figure 2).\textsuperscript{22} These cysts may contain air, fluid, or both. Clinical manifestations are related to various mass effects or secondary infection of the cyst. Pulmonary sequestration is defined as a lung tissue mass that receives its blood supply from an anomalous systemic artery and does not communicate with the bronchial tree via an anatomically normal bronchus.\textsuperscript{22} Intralobar sequestration refers to a sequestration contained within the visceral pleura of another lobe, while extralobar sequestration is contained in a pleural envelope separate from that of the normal lung.\textsuperscript{22} Sequestration usually presents as an incidental finding on chest radiography or with recurrent pneumonias and is commonly located in the posterior basal segment of the lung. Congenital cystic adenomatoid malformations present as cystic or solid lung masses restricted to part of one lung.\textsuperscript{22} Most CCAMs present with respiratory distress or compromise during infancy or with recurrent pneumonias in later years, including adulthood. Typically, chest radiography reveals multiple air-filled thin-walled cysts of varying sizes. Three types of CCAMs are recognized based on cyst size and number.\textsuperscript{22} Treatment of congenital cystic lesions usually consists of simple resection of the involved tissue or
lobectomy. Congenital lobar emphysema usually presents in young infants as massive hyperinflation of a pulmonary lobe rather than as a cystic lesion.\textsuperscript{22}

Focal or multifocal cystic lesions in the lung have also been seen with penetrating or closed chest trauma,\textsuperscript{24-27} lymphocytic interstitial pneumonia,\textsuperscript{28,29} Down syndrome,\textsuperscript{30,31} Ehlers-Danlos syndrome,\textsuperscript{32} follicular bronchiolitis,\textsuperscript{33} and rare cases of metastatic cancer (Figure 3).\textsuperscript{34-36} Some of the lung "cysts" related to closed chest trauma may be thick walled or are associated with dense infiltrate due to contusion or hemorrhage, particularly in the earlier stages.\textsuperscript{26,27} Lymphocytic interstitial pneumonia is a rare disorder characterized by diffuse interstitial infiltration of the lung with lymphocytic and plasma cell components.\textsuperscript{37} Lymphocytic interstitial pneumonia may occur on its own as an idiopathic disorder or in association with various underlying disorders, including human immunodeficiency virus infection, Sjögren syndrome, Hashimoto thyroiditis, chronic active thyroiditis, primary biliary cirrhosis, myasthenia gravis, and other disorders.\textsuperscript{37} Although areas of ground-glass attenuation and centrilobular nodules are the predominant findings on HRCT in lymphocytic interstitial pneumonia, thin-walled cystic spaces may also be seen in two thirds of patients.\textsuperscript{28} Other forms of focal pulmonary cysts may be seen in adults outside these clinical settings and are of obscure origin but are thought to be related to smoking.\textsuperscript{30}

**FOCAL OR MULTIFOCAL CAVITARY LUNG LESIONS**

The differential diagnosis of a cavitary lesion is broader than that of a cystic lesion and includes neoplasms (bronchogenic cancer, lymphoma, metastasis), many types of infectious processes and abscesses (bacteria, mycobacteria, fungi, parasites), pulmonary infarct, septic embolism, vasculitides, congenital anomalies (sequestration, congenital adenomatoid malformation), rheumatoid nodule, and progressive massive fibrosis occurring with pneumocooniosis. More often than not, cavitiation implies an active process.

Most isolated cavitary lung lesions are bronchogenic carcinomas (Figure 4). Cavitation occurs in approximately 10% to 15% of bronchogenic carcinomas, more commonly with squamous cell carcinomas than with other cell types.\textsuperscript{38} Occasionally, even disease metastatic to the lung may present with an isolated cavitary lesion.\textsuperscript{39} Some lymphomas may also cavitate.\textsuperscript{40} In contrast, cavitary lung disease in patients with AIDS is usually caused by infections, including bacteria (including nocardia), mycobacteria, \textit{P carinii} and other fungi, and cytomegalovirus.\textsuperscript{41} The clinical context is clearly of importance in prioritizing diagnostic possibilities.

Cavitation within the consolidated lung is seen in necrotizing pneumonia, most commonly caused by \textit{Staphylococcus aureus} (Figure 5), gram-negative bacteria, anaerobic bacteria, and tuberculosis.\textsuperscript{32} Cavitation seen with bacterial infections, particularly anaerobic bacteria, can evolve into a discrete abscess, a relatively round cavity with an irregular thick wall that may be associated with an air-

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure3.png}
\caption{Computed tomogram of colon cancer metastatic to the lung. Note irregular but relatively thin-walled cystic structure. This is an unusual manifestation of adenocarcinoma metastatic to the lung.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure4.png}
\caption{Computed tomogram of the chest shows a large cavitated squamous cell carcinoma. Note air-fluid level in mass and nodular irregular cavitary wall thickening consistent with malignancy; small right pleural effusion.}
\end{figure}
with chronic disease than with acute disease.\textsuperscript{10,11,45,46} Nocardiosis, sporotrichosis, and opportunistic fungal infections including aspergillosis and cryptococcosis can also cause cavitating pneumonias.\textsuperscript{47,48} Air crescent formation is a relatively common finding (typically a late manifestation) in invasive pulmonary aspergillosis (Figure 7) and can also be seen with aspergilloma (mycetoma).\textsuperscript{49} Chronic necrotizing pulmonary aspergillosis is another form of pulmonary disease caused by \textit{Aspergillus} species that is associated with cavitary infiltrates.\textsuperscript{50}

Actinomycosis usually manifests as an area of persistent consolidation or a mass, either of which may contain cavi
tation.\textsuperscript{51} It may invade the chest wall. Pulmonary actinomycosis may look similar to a bronchogenic carcinoma.\textsuperscript{51} Other unusual infections, such as paragonimiasis, melioidosis, and hydatid disease, should be considered in the differential diagnosis of a cavitary pulmonary process in a patient with an appropriate travel history or epidemiological background.

Noninfectious inflammatory processes associated with cavitary lung lesions include pulmonary vasculitides such as Wegener granulomatosis and rheumatoid nodules.\textsuperscript{52} Wegener granulomatosis may present as bilateral multiple masses with cavitiation (Figure 8) or, less commonly, as a single cavitary lung mass. Rheumatoid nodules in the lung are also more often multiple than singular and may cavitiate.

Pulmonary embolism causes infarction in less than 15\% of cases, and only about 5\% of infarctions cavitate.\textsuperscript{53} Cavitary pulmonary infarction has also been reported in immunocompromised patients. Pulmonary embolism is a treatable disease that must be considered in the differential diagnosis of cavitary lung disease in immunocompro-

Figure 5. Chest radiograph of patient with cavitating staphylococcal pneumonia. Note lower lobe consolidation with large cavity and air-fluid level.

Figure 6. High-resolution computed tomogram of patient with postprimary tuberculosis. Note multiple regions of cavitation with consolidation in the posterior aspects of the superior segments of both lower lobes.

Figure 7. Computed tomogram of immunocompromised patient with invasive aspergillosis. Note cavitated mass (2 x 3 cm) with air crescent sign.
mised patients. Septic emboli show multiple well-defined pulmonary nodules in various stages of cavitation (generally 1-3 cm in diameter) and subpleural wedge-shaped infiltrates.34

Progressive massive fibrosis in pneumoconiosis, such as silicosis and coal workers pneumoconiosis, is seen as irregularly shaped masses of fibrotic tissue in the upper lung zones. Cavitation can occur in these fibrotic masses due to ischemic necrosis or superimposed infection including tuberculosis.35

**DIFFUSE CYSTIC AND CAVITARY LUNG DISEASES**

*Diffuse* implies involvement of all lobes of both lungs. Although the disease necessarily is widespread, it need not affect all lung regions uniformly. The differential diagnosis of diffuse cystic or cavitary diseases is limited compared with that of focal or multifocal involvement. Diffuse cystic disease is classically associated with 2 uncommon lung diseases, LAM and PLCH (Table 2). In these 2 diseases, innumerable cystic spaces may not be individually identifiable on chest radiography because of the superimposition of the thin walls, which results in a delicate reticular pattern. However, HRCT provides precise delineation of cystic changes and their distribution.

Pulmonary LAM is a slowly progressive lung disorder that almost exclusively affects women of childbearing age.56-58 Histologically, it is characterized by a proliferation of atypical smooth muscle in the lung parenchyma associated with diffuse cystic changes. These cystic changes may be inapparent on chest radiography, which may look normal or reveal only hyperinflation and diffuse interstitial infiltrates. High-resolution CT shows numerous cystic changes that are uniformly scattered throughout the lung with normal intervening lung parenchyma and no sparing of any particular lung zones (Figure 9).59 Cysts are typically 2 mm to 2 cm in diameter and are thin walled. Irregularly shaped cysts are uncommon until late in the course of disease when there is coalescence of lesions into larger, more bizarre-shaped cystic airspaces. Clinical manifestations of LAM include progressive dyspnea, chest pain, cough, hemoptysis, recurrent pneumothoraces, chylothorax, and chylous ascites.56-58 Pulmonary LAM can be associated with renal angiomyolipomas and extrapulmonary lymphangioleiomyomas. Of note, 25% to 40% of women with tuberous sclerosis complex have LAM.60-62

Pulmonary Langerhans cell histiocytosis is a smoking-related interstitial lung disease that affects predominantly adults in their 20s and 30s who smoke.63,64 Chest radiography usually shows reticulonodular infiltrates with cystic changes that have upper and middle lung zone predominance with relative sparing of the costophrenic angles.

High-resolution CT most commonly reveals diffuse cystic changes with intervening architectural distortion that includes nodules and reticular densities (Figure 10). Cysts in PLCH are more irregular and complex than those in LAM, particularly in later stages of the disease. Most cysts are less than 10 mm in diameter, but larger cysts may be seen as the disease advances.59,63,64 These cysts have walls that are barely perceptible to a few millimeters in thickness. In a minority of patients with PLCH, bone lesions (eosinophilic granuloma) and diabetes insipidus are associated features.65

Diffuse cystic airspaces may be present with advanced fibrosis (honeycombing) in idiopathic pulmonary fibrosis, asbestosis, pulmonary fibrosis associated with connective tissue disorders, chronic hypersensitivity pneumonitis, and sarcoidosis. The cystic airspaces in honeycomb lung are

![Figure 8. Posteroanterior chest radiograph of patient with Wegener granulomatosis. Note bilateral lung nodules and masses with cavitation. The walls of the cavitated masses are greater than 4 mm.](image)

**Table 2. Causes of Diffuse Cystic and Cavitary Lung Disease**

| Pulmonary lymphangioleiomyomatosis |
| Pulmonary Langerhans cell histiocytosis |
| Honeycomb lung |
| Idiopathic pulmonary fibrosis |
| Connective tissue disease-related pulmonary fibrosis |
| Asbestosis |
| Chronic hypersensitivity pneumonitis |
| Advanced sarcoidosis |
| Bronchiectasis, diffuse |
| Metastatic disease (rare) |
usually 3 to 10 mm in diameter and have thicker fibrous walls (1-3 mm) compared with those in LAM. Honeycombing is usually accompanied by other findings of lung fibrosis, including traction bronchiectasis, irregular linear opacities, and architectural distortion. The distribution of these cysts seen on HRCT is often helpful in suggesting a diagnosis. Honeycombing in idiopathic pulmonary fibrosis and connective tissue disorder–related pulmonary fibrosis involves mainly the subpleural lung regions of the lower lung zones (Figure 11), whereas the cysts in sarcoidosis have a predominantly perihilar distribution with relative sparing of the lung bases.

Although bronchiectasis represents irreversibly dilated bronchi, it may manifest as diffuse cystic or cavitary changes on chest radiography and HRCT (Figure 12). In particular, allergic bronchopulmonary aspergillosis causes proximal bronchiectasis that is cystic or varicose in appearance. There may be air-fluid levels in these dilated cystic airways. With HRCT (cross-sectional views), bronchiectasis may present mainly as ring shadows. Distinguishing bronchiectasis from cystic lung diseases is usually easy because the continuity of bronchiectatic airways is appreciated on adjacent sections of HRCT. For the diagnosis of diffuse lung disease and bronchiectasis, HRCT is the key imaging technique.

Rarely, neoplastic processes may underlie diffuse cystic or cavitary lesions. This has been described with metastatic cancers, including adenocarcinomas, sarcomas, and other tumors (Figure 13).

CONCLUSIONS
Cystic and cavitary lung lesions can be caused by a diverse array of pathologic processes. In evaluating a patient with such lung lesions, it is helpful to distinguish cysts from cavities and to categorize focal or multifocal vs diffuse distribution. These characteristics correlated with the tempo of the disease process and the clinical context provide the basis for prioritizing the diagnostic possibilities that will guide the subsequent evaluation.
High-resolution CT of the chest is a valuable procedure in characterizing cystic and cavitary diseases. Morphology, location, distribution, and associated radiological findings provide important clues to the nature of the underlying disease.

REFERENCES


