Pulmonary Coccidioidomycosis: Pictorial Review of Chest Radiographic and CT Findings[1]

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

■ Describe the abnormalities associated with pulmonary coccidioidomycosis seen most commonly at imaging.

■ Identify the most important complications of coccidioidal infection.

■ Recognize the implications of host immune status on disease manifestations.

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TEACHING POINTS
See last page

Pulmonary coccidioidomycosis is a fungal disease endemic to the desert regions of the southwestern United States, Mexico, Central America, and South America. The incidence of reported disease increased substantially between 1998 and 2011, and the infection is encountered beyond the endemic areas because of a mobile society. The disease is caused by inhalation of spores of *Coccidioides* species. Individuals at high risk are those exposed to frequent soil aerosolization. The diagnosis is established by direct visualization of mature spherules by using special stains or cultures from biologic specimens. Serologic testing of anticoccidioidal antibodies is used for diagnosis and treatment monitoring. The infection is self-limited in 60% of cases. When the disease is symptomatic, the lung is the primary site of involvement. On the basis of clinical presentation and imaging abnormalities, pulmonary involvement is categorized into acute, disseminated, and chronic forms, each with a spectrum of imaging findings. In patients with acute disease, the most common findings are lobar or segmental consolidation, multifocal consolidation, and nodules. Adenopathy and pleural effusions are also seen, usually in association with parenchymal disease. Disseminated disease is rare and occurs in less than 1% of patients. Pulmonary findings are miliary nodules and confluent parenchymal opacities. Acute respiratory distress syndrome is an infrequent complication of disseminated disease. The acute findings resolve in most patients, with chronic changes developing in approximately 5% of patients. Manifestations of chronic disease include residual nodules, chronic cavities, persistent pneumonia with or without adenopathy, pleural effusion, and regressive changes. Unusual complications of chronic disease are mycetoma, abscess formation, and bronchopleural fistula. Patients in an immunocompromised state, those with diabetes mellitus, pregnant women, and those belonging to certain ethnic groups may show severe, progressive, or disseminated disease.

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Introduction

Coccidioidomycosis is a fungal infection caused by inhalation of spores from *Coccidioides* species, endemic to the southwestern United States and arid regions of Mexico, Central America, and South America (1). In the United States, endemic regions include southern Arizona, central and southern California, Nevada, southwestern New Mexico, western Texas, and Utah. Several areas are considered

"hyperendemic," including Phoenix and Tucson in Arizona and the southern San Joaquin Valley in California (2,3).

The incidence of reported coccidioidomycosis in Arizona and California has increased substantially in recent years (4). Many cases are also identified in nonendemic regions because of increased tourism to endemic areas and the high infectivity rate of the fungus (5). In addition, the more widespread use of immunosuppressive medication, the increase in organ transplantation, and the human immunodeficiency virus (HIV) epidemic have resulted in an increase in severe cases of infection.

Teaching Point

The lungs are the target organ in coccidioidomycosis and are involved in a wide spectrum of clinical and imaging manifestations that are categorized as acute, disseminated, or chronic disease. Acute coccidioidomycosis is responsible for up to 29% of cases of community-acquired pneumonia in endemic areas and is mostly self-limited (6). Disseminated or chronic disease occurs in a minority of cases and is associated with significant morbidity and mortality (7,8).

In this article, we discuss the causal organism, epidemiology, and diagnosis of coccidioidomycosis. We also describe the radiographic and computed tomographic (CT) manifestations of acute, disseminated, and chronic forms, with clinical implications and potential complications.

Mycologic Features

The *Coccidioides* genus encompasses two distinct species: *Coccidioides immitis* and *Coccidioides posadasii*. *Coccidioides immitis* causes most cases of disease in California and northern Mexico, whereas *C posadasii* is responsible for cases in Arizona, Utah, Texas, and Latin America. However, there is considerable geographic overlap in the distribution of the *Coccidioides* species, the clinical manifestations are similar, and laboratory personnel are not routinely able to distinguish between the two species (3,9).

Coccidioides immitis is a dimorphic fungus with a saprophytic (hyphal) phase that occurs in the soil and a parasitic form that occurs in the human host (10). The hyphal form proliferates during the rainy season and dies in the dry period, releasing highly infectious spores (anthroconidia) that become airborne because of wind, excavation, or farming. The risk of exposure is the highest in the dry period that follows a rainy season. After inhalation of anthroconidia into the small airways, the spores swell into spherules and reproduce through cleavage. The mature spherules rupture and release endospores, propagating the parasitic cycle and causing inflammation. When identified in tissues or fluid, the spherules that contain endospores are diagnostic of infection (11).

Epidemiologic Features

Coccidioidomycosis is considered a re-emerging infectious disease (1). In Arizona, California, Nevada, New Mexico, and Utah, coccidioidomycosis is a disease reportable to the Centers for Disease Control and Prevention. In these states, the incidence of reported infection increased substantially between 1998 and 2011, from 5.3 to 42.6 per 100,000 people (4). The reported incidence is probably underestimated because of the nonspecific symptoms and underdiagnosis of the disease. The reasons for this increase include an influx of susceptible individuals into the endemic regions, an increase in such activities as construction and agriculture, changes in climate, an increase in immunocompromised populations, and improved surveillance and physician awareness (4,12).

Most cases of coccidioidomycosis are caused by inhalation of the airborne anthroconidia in a high-risk region. The organism is not transmissible from person to person. Individuals at particularly high risk are those exposed to frequent soil aerosolization, including agricultural and construction workers, archaeologists and excavators, and military personnel who train in desert regions (3).

Most cases of coccidioidomycosis occur in adulthood, with recent studies showing a shift in disease incidence to older age groups (4,10). In California, the incidence is highest among the 40- to 59-year-old age group, whereas in Arizona and other endemic states, the incidence is highest among persons older than 60 years of age. This trend may be caused by relocation of susceptible individuals, who retire to endemic areas and acquire the infection within the first year of moving. During the 1998–2011 period, 65% of infections in California occurred in men, whereas in Arizona the incidence has shifted toward a female preponderance beginning in 2009 (4).

Risk Factors for Complications and Disease Severity

Teaching Point

Suppression of cellular immunity is a major risk factor for increased disease severity and dissemination. The most substantial risk factors are HIV infection, immunosuppressive medications, and high-dose glucocorticoid administration (8,13,14). For HIV-infected individuals, the risk increases substantially in patients with a CD4 lymphocyte count less than 0.25×10^9/L or a diagnosis of AIDS (13). Hematologic malignancies, pregnancy, diabetes, cardiopulmonary disease, old age, smoking, and male sex are additional risk factors (1,8,15–19). No racial or ethnic predilection for primary infection with *Coccidioides* species has been observed. However, persons of Filipino, African-American, and Pacific Islander ethnicity have

risk for disseminated disease that is up to 175, 14, and two times that of white persons, respectively (1,8,18,20,21). The racial predilection for dissemination may be caused by differences in the major histocompatibility complex genes, which play a role in cell-mediated immune response (18).

Diagnosis

Coccidioidomycosis is diagnosed by means of direct visualization of mature spherules with special-stain microscopy or isolation of *Coccidioides* species from biologic specimens at culture, such as sputum, bronchoalveolar lavage fluid, smear from cutaneous lesions, or tissue biopsy samples. *Coccidioides* species can be identified directly in fresh respiratory secretions by using potassium hydroxide, Calcofluor white (Santa Cruz Biotech, Santa Cruz, Calif), or Papanicolaou stains (22). Staining of fixed tissue with methenamine–silver nitrate (Grocott-Gomori) or periodic acid–Schiff stain can be performed to identify the typical doubly refractile spherule wall (23). Identification of the fungus at culture is possible within 3 weeks and is done most commonly in hospitalized patients.

Serologic testing is used for diagnosis and treatment monitoring. Anticoccidioidal antibodies develop in most patients, although the ability to detect them may lag behind the onset of illness by weeks or months, especially in immunocompromised hosts (8). Enzyme-linked immunoassays for immunoglobulin M and immunoglobulin G antibodies are the most sensitive screening test and should be performed first when available. Immunodiffusion tests for immunoglobulin M or complement-fixing immunoglobulin G antibody are highly specific and are used to confirm infection (11,22). In most patients, the anticoccidioidal antibodies decrease to undetectable levels after the infection resolves. The presence of antibodies indicates recent or persistent infection. A quantitative immunoglobulin G antibodies titer measured by means of complement fixation or immunodiffusion is used for monitoring response to treatment (11,22).

Bronchoscopy is a useful diagnostic procedure if sputum evaluation or serologic testing is not diagnostic (15). Bronchoscopy with bronchoalveolar lavage or transbronchial lung biopsy is helpful in patients with parenchymal consolidation, cavitary lesions, and endobronchial disease (24–26). Bronchoscopy has a low diagnostic yield in a solitary pulmonary nodule secondary to coccidioidomycosis.

Percutaneous transthoracic needle biopsy with image guidance is especially useful for diagnosis of a peripheral solitary pulmonary nodule or a cavity secondary to coccidioidomycosis (27,28). Most biopsies are currently performed with CT guidance, although they were performed previously with fluoroscopic control (29–31). The diagnosis is established by means of visualization of *Coccidioides* spherules with use of special stains. Culture of the biopsy specimen has a low sensitivity and is not recommended, and cytologic examination should be performed to rule out malignancy (29–31).

Pleural fluid culture has a low diagnostic yield, with isolation of *Coccidioides* species in less than one-third of patients (1,32,33). Pleural biopsy is useful in diagnosis of coccidioidal pleural effusion. Pleural biopsy specimens allow direct visualization of pathognomonic spherules, although the highest yield is obtained by means of culture of the biopsy specimen (34,35).

Surgical biopsy may be required if the diagnosis cannot be established by using serologic testing or through specimens obtained with a sputum-, bronchoscopy-, or CT-guided approach. Surgical biopsy is best suited for sampling lymph nodes or parenchymal lung disease (7,15,36).

Pulmonary Manifestations of Coccidioidal Infection

Sixty percent of coccidioidal exposures are clinically silent and impart lasting immunity, whereas infection that primarily affects the lung develops in 40% of patients (10,21). Clinical manifestations vary according to the degree of exposure to spores, immune status of the host, presence of comorbid diseases, and extent of infection (3).

On the basis of clinical and imaging findings, pulmonary coccidioidomycosis is categorized into acute, disseminated, and chronic forms.

Acute Disease

Acute symptomatic infection is also known as *primary coccidioidal infection*. After an incubation period of 7–21 days, patients present with symptoms that vary from mild influenza-like illness to acute pneumonia. The most common symptoms are cough, fever, headache, and chest pain, each occurring in more than 70% of patients (23). Helpful clinical symptoms are night sweats and prolonged fatigue, which may take months to resolve (2,37). Approximately 25% of white women and 4% of white men develop "valley fever," an allergic syndrome characterized by hypersensitive skin lesions, such as erythema multiforme or erythema nodosum, and polyserositis (10). Primary coccidioidal infection is typically a self-limited process of 3–6 weeks' duration, with complete recovery in 85%–95% of cases (21).
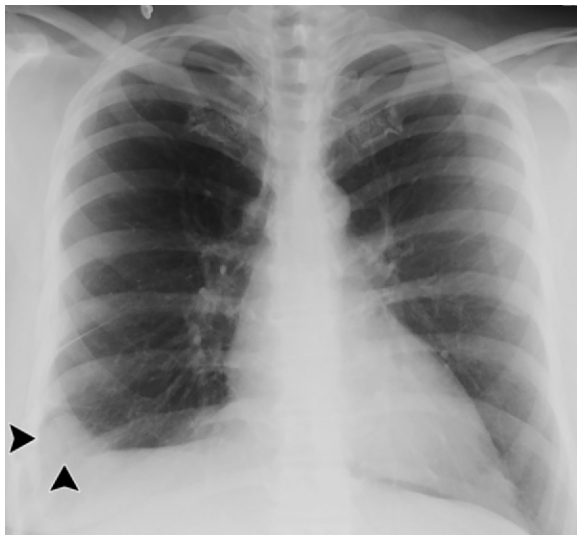
Imaging of Acute Pulmonary Coccidioidomycosis.—Thoracic manifestations of acute coccidioidomycosis include pulmonary parenchymal
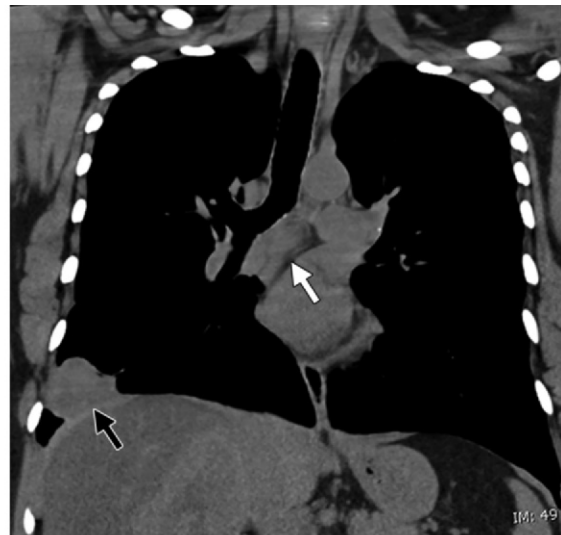
Teaching Point

Figure 1. Acute pulmonary coccidioidomycosis in a 26-year-old man. Frontal chest radiograph shows lingular consolidation.

Figure 2. Acute pulmonary coccidioidomycosis in a 75-year-old man. Frontal chest radiograph shows bilateral multifocal consolidations.

a.   b.

Figure 3. Acute pulmonary coccidioidomycosis in a 53-year-old woman. Frontal chest radiograph **(a)** and coronal CT image **(b)** show a nodular opacity in the right lower lobe (arrowheads in **a**, black arrow in **b**) and subcarinal adenopathy (white arrow in **b**). Fine-needle aspiration of the nodule showed *Coccidioides* species.

abnormalities, intrathoracic adenopathy, and pleural effusion. Pulmonary parenchymal abnormalities occur in most symptomatic cases and consist of consolidation, nodules, cavities, and peribronchial thickening (10,21,38).

Parenchymal Abnormalities.—The most common lung abnormality is consolidation, occurring in 75% of cases and manifesting as solitary or multiple areas of segmental or lobar opacification (21). The distribution is mostly unilateral, with perihilar and basilar predominance, although consolidation may occur in any region of the lung (Fig 1) (1). The density of parenchymal opacification varies from a ground-glass appearance to dense homogeneous consolidation,

simulating bacterial pneumonia. Occasionally, an area of pulmonary consolidation undergoes excavation, resulting in a thin- or thick-walled cavity (21). These cavities have been described in 2%–8% of hospitalized patients with acute primary infection. They resolve spontaneously in most cases, although persistent chronic cavities have been identified.

Multifocal consolidation or diffuse lung opacities may also be seen (Fig 2) (21). A migratory pattern of parenchymal disease called *phantom infiltrates* has been described, in which parenchymal consolidation resolves at one site and reappears in a different location (23). Rapid progression to diffuse consolidation is seen occasionally (38). Bronchial involvement in the early stage of

Figure 4. Acute pulmonary coccidioidomycosis in a 62-year-old man. Axial CT image shows multiple nodules (arrows), with two nodules in the right middle lobe and one in the left lower lobe.
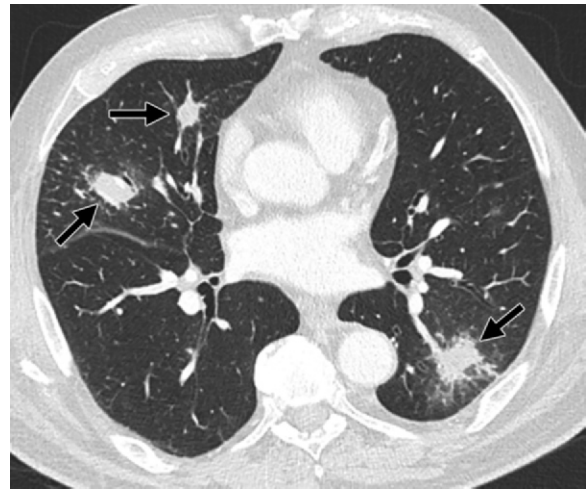
infection may result in peribronchial thickening, manifesting as linear opacities that radiate from the hilar region to the basilar region (10).

Another common parenchymal manifestation is nodular opacities, seen in as many as 20% of cases at chest radiography (1,10). Nodules can be similar in size or vary from 0.5 to 2.5 cm. They are often multiple and well circumscribed and are seen predominantly in the perihilar and lower lung zones, simulating metastatic disease. A solitary pulmonary nodule or mass indistinguishable from primary lung malignancy may also be demonstrated. One study showed that lung nodules were a common finding at CT and were frequently seen in association with consolidation, interlobular septal thickening, or lymphadenopathy (Fig 3). Most nodules seen at CT were multiple and bilateral, with ill-defined borders, and ranged between 0.5 cm and 3 cm in diameter (Fig 4). Cavitation occurred in most nodules, and a coalescent pattern was often noted (39).

Most acute parenchymal abnormalities seen at chest radiography resolve within 6 weeks (21,23). Dense consolidation resolves over several months, whereas pulmonary nodules or cavities may persist for months or years. Parenchymal opacities involving more than half of one lung or both lungs are an indication for antifungal treatment (3).

Intrathoracic Adenopathy.—Approximately 20% of patients demonstrate hilar or mediastinal adenopathy at chest radiography, in conjunction with ipsilateral parenchymal consolidation, nodules, or peribronchial thickening (Fig 5) (1,10). Bronchopulmonary and tracheobronchial lymph node enlargement may be the only radiographic finding in up to 8% of patients (10). At CT, the incidence of lymph node enlargement is higher, with

40% of patients demonstrating hilar or mediastinal adenopathy in conjunction with lung abnormalities (39). Adenopathy results from regional spread of infection from pulmonary parenchymal foci to hilar or mediastinal lymph nodes that contain suppurative or granulomatous lesions. Mediastinal adenopathy occurs in cases of severe or prolonged lung infection, and paratracheal or other mediastinal adenopathy suggests a greater risk of disseminated disease (1,3). Adenopathy, particularly mediastinal, may persist or progress even after parenchymal abnormalities resolve.

A pulmonary nodule or mass with ipsilateral hilar or mediastinal adenopathy may simulate lung cancer. In addition, isolated hilar and mediastinal adenopathy can mimic such diseases as mycobacterial infection, other fungal infections, lymphoma, metastatic disease, or sarcoidosis (10). Prominent or persistent mediastinal adenopathy is an indication for antifungal treatment (3).

Pleural Effusion.—Pleural effusion occurs in approximately 15%–20% of patients with acute coccidioidomycosis (3,10,32). Pleural effusion may be transudative or exudative and is usually caused by contiguous spread of infection from adjacent parenchyma (1,32,33). Rupture of a subpleural granuloma, immune complex pleuritis, and hematogenous seeding are other causes of pleural effusion.

Pleural effusion occurs in isolation or in association with parenchymal disease (Fig 6) (1,40). It is usually unilateral and small and resolves within 1–8 weeks. Moderate or large pleural effusion is present in 2%–10% of acute cases, may clear over several weeks, or may persist for more than 1 year (10,23). A large pleural effusion may be seen at chest radiography, ultrasonography, or CT in as many as 45% of patients hospitalized with coccidioidomycosis (32). Pleural effu-
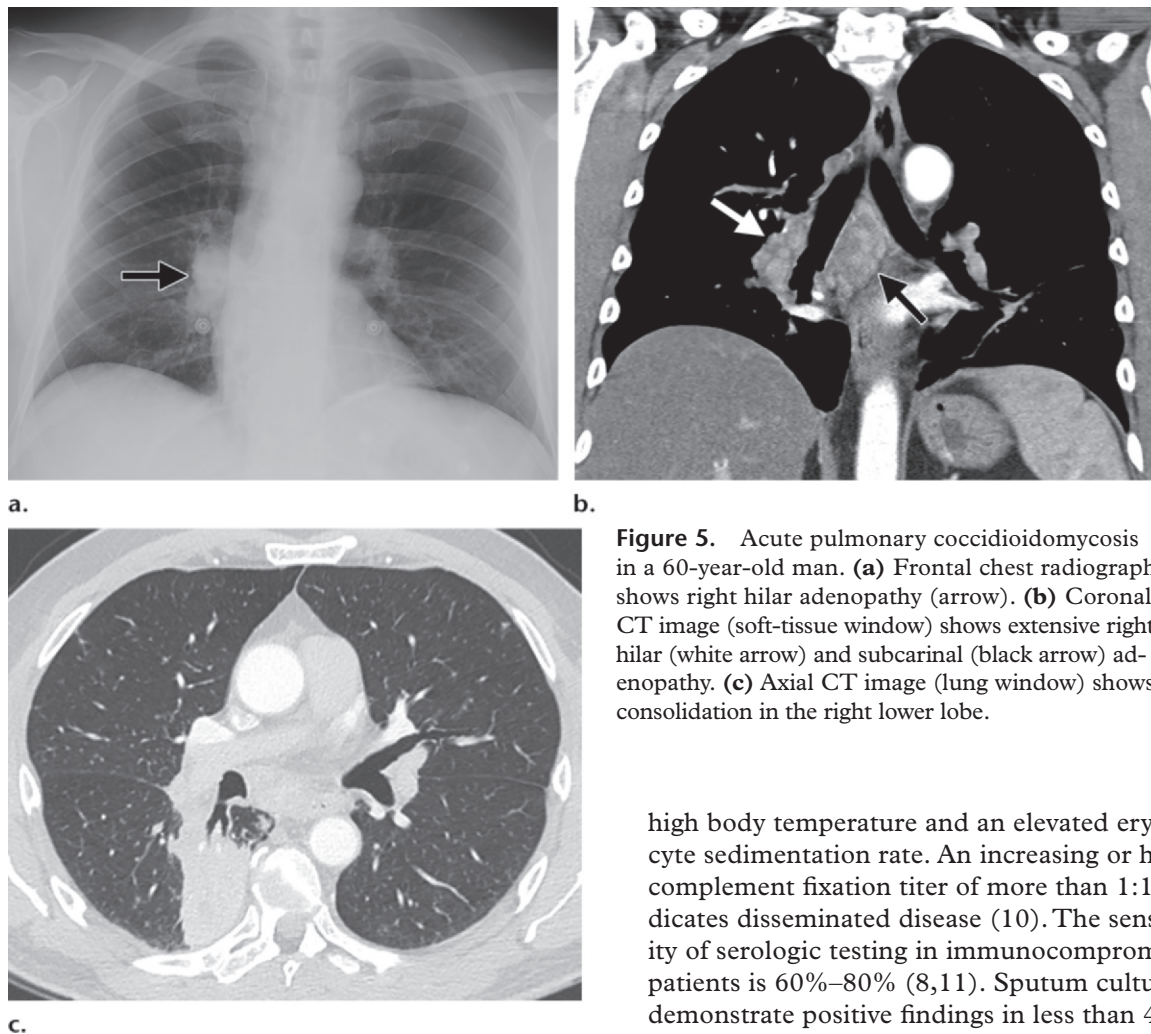
Figure 5.   Acute pulmonary coccidioidomycosis in a 60-year-old man. **(a)** Frontal chest radiograph shows right hilar adenopathy (arrow). **(b)** Coronal CT image (soft-tissue window) shows extensive right hilar (white arrow) and subcarinal (black arrow) adenopathy. **(c)** Axial CT image (lung window) shows consolidation in the right lower lobe.

sion can lead to development of an empyema in as many as 22% of hospitalized patients, necessitating thoracotomy (32). In children, a large pleural effusion is associated with severe disease and may suggest acute dissemination (41). Development of a pleural effusion is an indication for antifungal treatment (3).

Disseminated Disease
Disseminated disease is the most severe manifestation of coccidioidomycosis. It occurs in less than 1% of cases overall and in as many as 11% of hospitalized patients (1). Disseminated lung disease occurs most commonly as a complication of acute disease and occasionally develops from chronic progressive pneumonia or extrathoracic disease (8). The origin of hematogenous spread is thought to be infected, necrotic tracheobronchial lymph nodes.

Diagnosis of Disseminated Coccidioidomycosis.—Disseminated coccidioidomycosis is diagnosed according to clinical symptoms, serologic findings, and tissue diagnosis. Patients have

high body temperature and an elevated erythrocyte sedimentation rate. An increasing or high complement fixation titer of more than 1:16 indicates disseminated disease (10). The sensitivity of serologic testing in immunocompromised patients is 60%–80% (8,11). Sputum cultures demonstrate positive findings in less than 40% of cases, and lung biopsy is often required for diagnosis of miliary nodules (21,42). Patients with risk factors or confirmed disseminated disease should receive antifungal treatment (3,18).
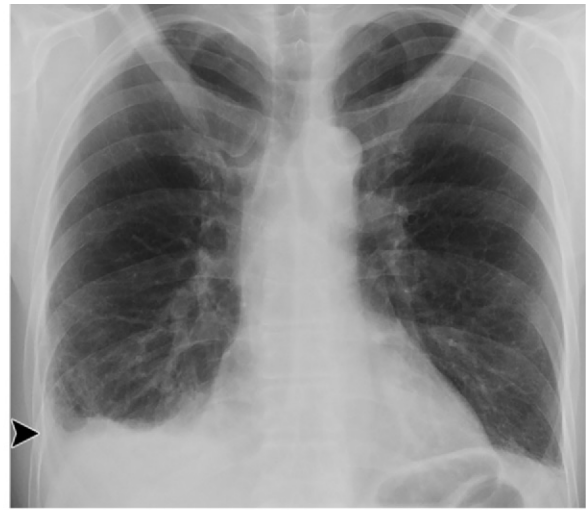
Imaging of Disseminated Coccidioidomycosis.—
The classic pulmonary manifestation of disseminated coccidioidal infection is miliary nodules caused by hematogenous spread (Fig 7) (10). The original focus of parenchymal consolidation is seen occasionally, and hilar and mediastinal adenopathy is usually present. The lung nodules often progress to confluent opacities (1). Acute respiratory distress syndrome (ARDS) is an infrequent complication that usually occurs in immunocompromised hosts (38).

Patients with AIDS are at increased risk of fungemia and ARDS (43). Diffuse or dependent lung opacities may be seen with ARDS (Fig 8). Even with antifungal and supportive therapy, these patients have a high mortality rate, approaching 100%. ARDS may also occur in immunocompetent patients or in individuals with other preexisting conditions, such as diabetes or renal failure, with a mortality rate of 40%–60% (44,45).
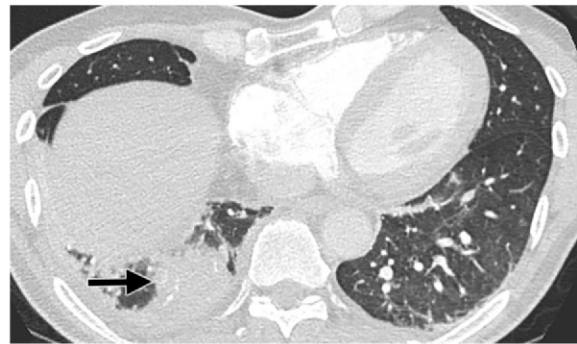
Teaching Point

Figure 6.   Acute pulmonary coccidioidomycosis in a 54-year-old man. **(a)** Frontal chest radiograph shows a small right pleural effusion (arrowhead). **(b)** Axial CT image (soft-tissue window) shows a small right pleural effusion (∗) and subcarinal adenopathy (arrow). **(c)** Axial CT image (lung window) shows consolidation in the right lower lobe (arrow).
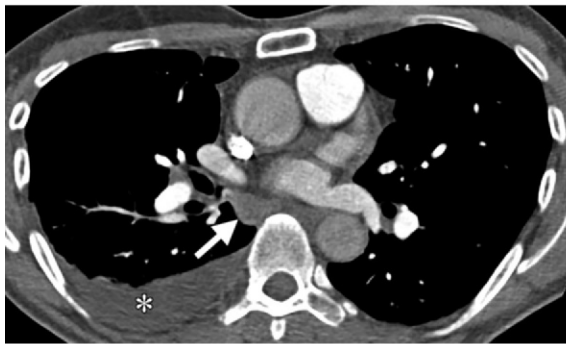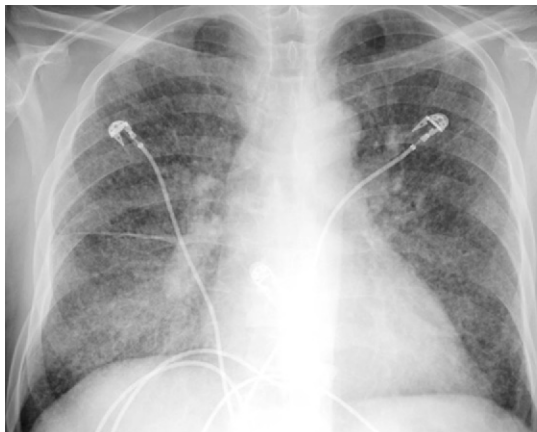

Figure 7.   Disseminated pulmonary coccidioidomycosis in a 54-year-old man with a renal transplant. Frontal chest radiograph **(a)** and axial CT image **(b)** show diffuse micronodules consistent with a miliary pattern.

Extrapulmonary dissemination occurs frequently and most commonly involves the skin, lymph nodes, bones and joints, and central nervous system (1,8). Vertebral disease may extend into the soft tissues, forming a paraspinal phlegmon or psoas abscess (Fig 9). Hematogenous dissemination has a mortality rate of 28%–56%, even with correct diagnosis and aggressive antifungal therapy (8).

Chronic Disease

Chronic pulmonary coccidioidomycosis is diagnosed when clinical symptoms or imaging abnormalities persist beyond 6 weeks and occurs in approximately 5% of patients. Seventy-five percent of cases of chronic infection occur in patients who did not have classic symptoms of acute disease (10).
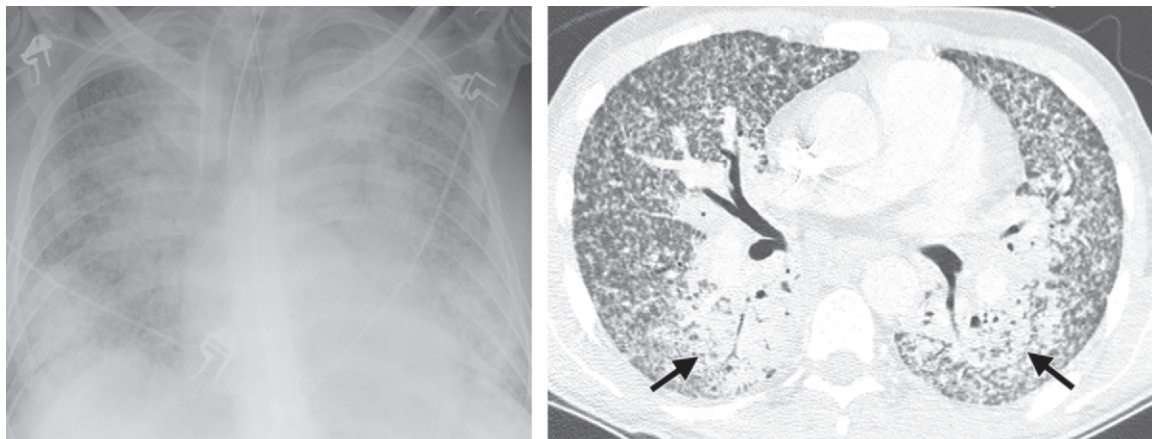
Figure 8. ARDS due to disseminated pulmonary coccidioidomycosis in a 42-year-old man with AIDS. **(a)** Frontal chest radiograph shows diffuse bilateral opacification that required intubation. **(b)** Axial CT image shows diffuse miliary nodules and dependent consolidation (arrows), consistent with ARDS. The patient later died.
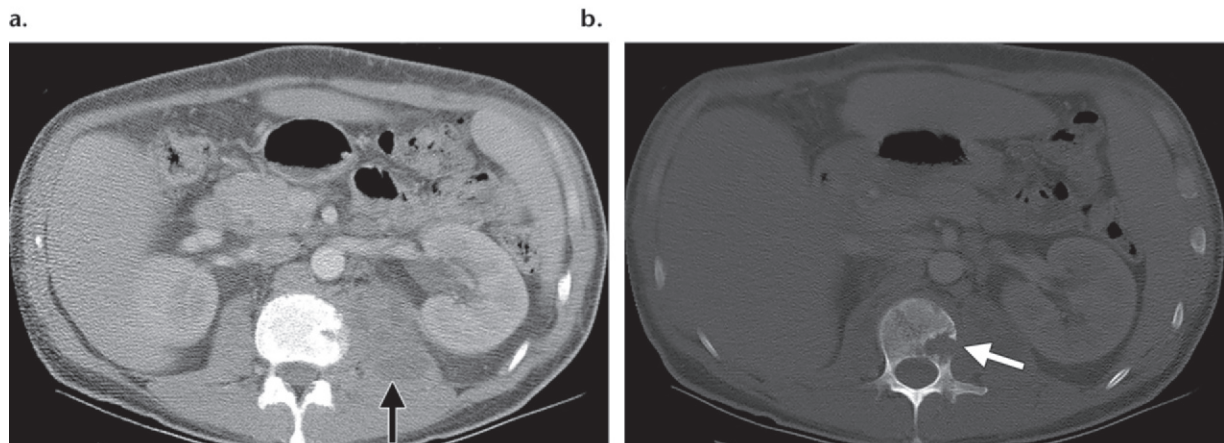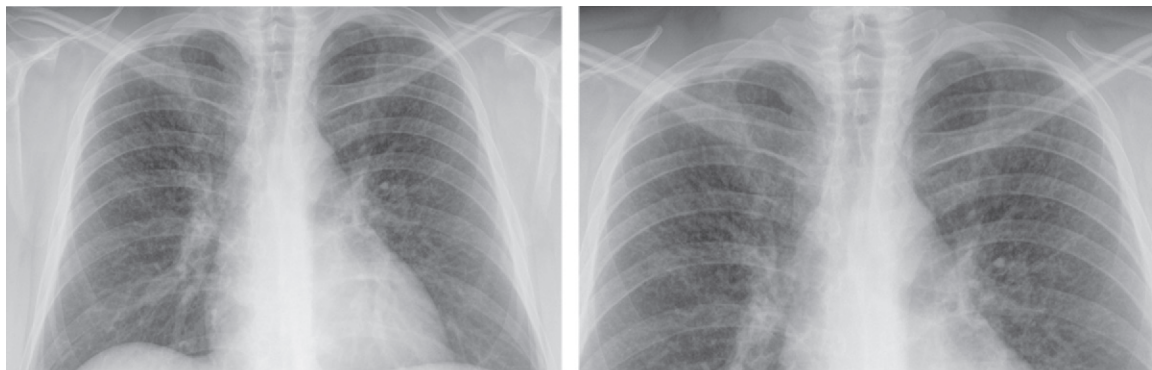

Figure 9. Disseminated pulmonary coccidioidomycosis with vertebral body involvement in a 42-year-old man with AIDS. **(a, b)** Frontal chest radiograph **(a)** and coned-down view of the upper chest **(b)** show miliary nodules, consistent with disseminated disease. **(c, d)** Axial CT images at soft-tissue **(c)** and bone **(d)** windows show a left paraspinal abscess (arrow in **c**) and bone destruction (arrow in **d**).

Imaging of Chronic Pulmonary Coccidioidomy-cosis.—Imaging manifestations of chronic coccidioidomycosis include residual nodule, chronic cavity, persistent pneumonia with or without adenopathy, pleural effusion, and regressive changes. Uncommon complications of a cavitary lesion are mycetoma, abscess formation, and bronchopleural fistula (10,38).

Residual Pulmonary Nodule or Coccidioi-doma.—Residual pulmonary nodule is present in 5%–7% of patients after acute infection and

Teaching
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Figure 10.   Residual pulmonary nodule due to chronic pulmonary coccidioidomycosis in a 52-year-old man with diabetes mellitus and ischemic cardiomyopathy. **(a)** Frontal chest radiograph shows patchy consolidation in the left lung. **(b, c)** Frontal chest radiograph **(b)** and axial CT image **(c)** after 10 months of antifungal therapy show a residual dominant nodule (arrow) with small satellite nodules (arrowheads in **c**) in the left upper lobe.
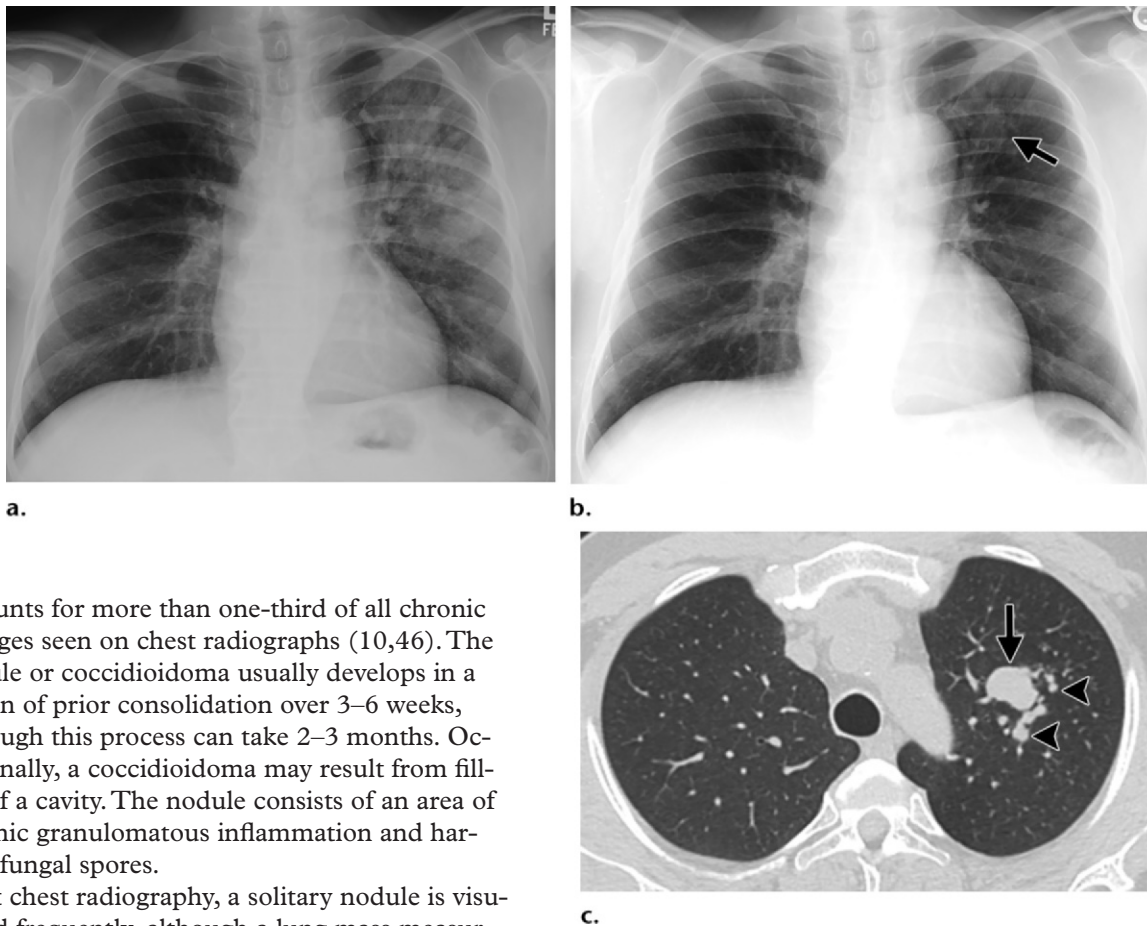
accounts for more than one-third of all chronic changes seen on chest radiographs (10,46). The nodule or coccidioidoma usually develops in a region of prior consolidation over 3–6 weeks, although this process can take 2–3 months. Occasionally, a coccidioidoma may result from filling of a cavity. The nodule consists of an area of chronic granulomatous inflammation and harbors fungal spores.

At chest radiography, a solitary nodule is visualized frequently, although a lung mass measuring up to 6 cm may be seen (21). The nodule commonly occurs in the lung periphery and is round and well circumscribed (10). At CT, it usually measures 1–2 cm and has various margin characteristics, including smooth, spiculated, and lobulated. The nodule has homogeneous attenuation and is occasionally surrounded by ground-glass opacity, consolidation, or satellite nodules (Fig 10) (5). Cavitation may occur, and calcification may occur rarely. A residual pulmonary nodule may resolve, remain stable for an extended period, or grow slowly. In cases of altered immunity, a coccidioidoma may result in reactivation of infection and cause local or disseminated disease (10,21).

The differential diagnosis for a coccidioidoma includes primary lung malignancy, solitary metastasis, or other granulomatous infection. Coccidioidoma may occur in the anterior segment of the upper lobe and rarely calcifies. These features help distinguish it from tuberculous nodule but are not useful for differentiating it from lung cancer. In endemic regions, as many as 50% of solitary pulmonary nodules represent a coccidi-

oidoma (42). A coccidioidoma may be followed up with serologic testing and serial imaging. Approximately 60%–70% of patients have a low titer (<1:4) of complement-fixing antibodies (7,42). Identification of spherules in the smear or positive fungal cultures in tissue obtained with transthoracic fine-needle aspiration or biopsy is often required for definitive diagnosis (1,21,28). Occasionally, coccidioidoma is diagnosed after resection of the nodule (7). A coccidioidoma usually requires no antifungal treatment.

Chronic Coccidioidal Cavity.—A chronic cavitary lesion is seen radiographically in 2% of patients, whereas at CT it may be seen in 11% of cases (5). Most patients are asymptomatic, with approximately 60% of cavities discovered incidentally on routine chest radiographs. Mild or intermittent hemoptysis occurs in symptomatic patients (42). Diabetes mellitus is a risk factor for chronic cavity formation (17). A coccidioidal cavity often harbors hyphae, the saprophytic form of the organism.

Figure 11. Ccoccidioidal cavity due to chronic pulmonary coccidioidomycosis in a 40-year-old woman. Frontal chest radiograph **(a)** and coronal CT image **(b)** show a thick-walled cavity in the right upper lobe (arrow).
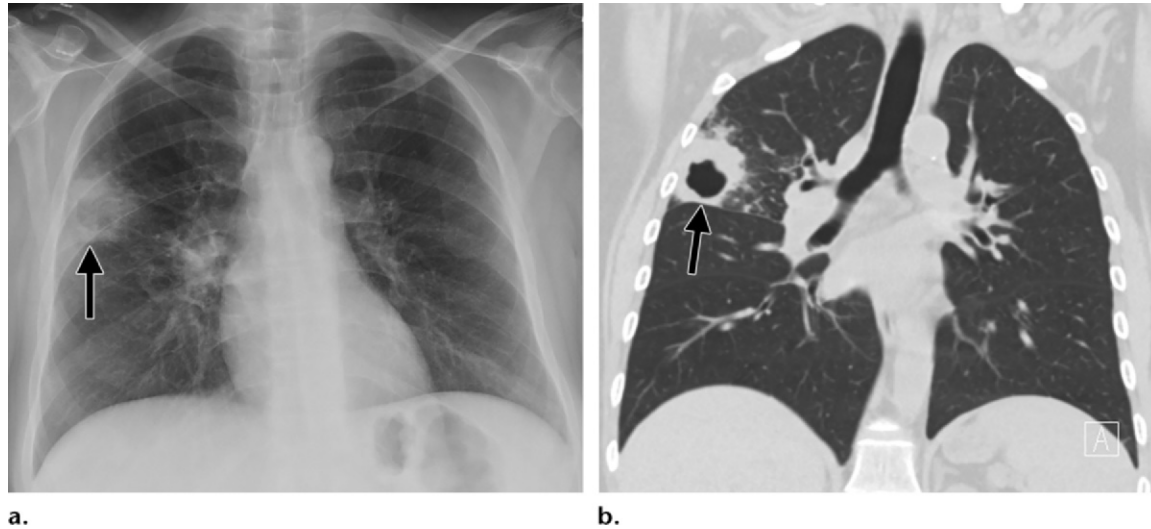

a.

b.

Figure 12. Coccidioidal cavity with mycetoma due to chronic pulmonary coccidioidomycosis in a 36-year-old man with diabetes mellitus who was noncompliant with antifungal therapy. **(a)** Frontal chest radiograph shows bilateral upper-lobe cavities (arrows). **(b)** Axial CT image shows bilateral apical cavitary lesions and small nodules. A cavity in the left upper lobe contains a fungus ball (arrow).

a.

b.
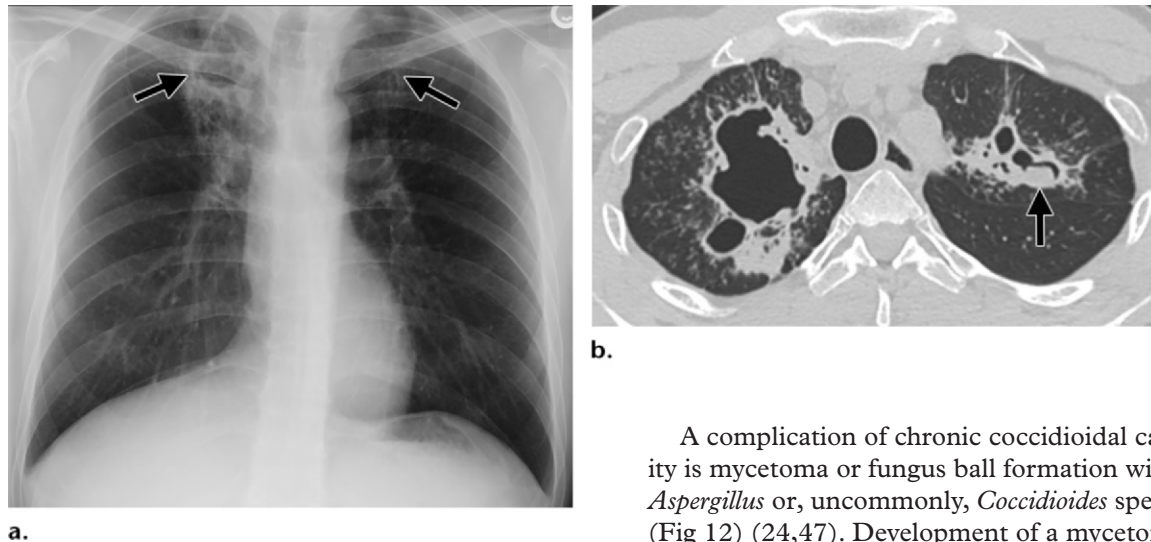
The cavity may develop in an area of prior consolidation, resulting in a thin-walled "grape-skin" cavity, or it may develop from excavation of a nodule, forming a thick-walled cavity (3,10). Ninety percent of cavities are solitary (Fig 11) (42). The cavities are usually round and well-circumscribed and measure 2–4 cm in diameter. The size of a cavity may vary because of rapid inflation and deflation due to a check-valve mechanism. This dynamic feature is highly suggestive of coccidioidal infection. Most cavitary lesions resolve spontaneously, within 2 years in up to 50% of cases (24,42). Even when the cavitary lesion persists, extrathoracic dissemination of infection is rare.

A complication of chronic coccidioidal cavity is mycetoma or fungus ball formation with *Aspergillus* or, uncommonly, *Coccidioides* species (Fig 12) (24,47). Development of a mycetoma is associated with low-grade fever, weight loss, and hemoptysis. Occasionally, bacterial superinfection of a cavity causes pyogenic lung abscess with an air-fluid level (1). Rarely, an enlarging, peripherally located cavity may rupture into the pleural cavity, resulting in pneumothorax, pyopneumothorax, or bronchopleural fistula (Fig 13) (3,21). Rupture of a coccidioidal cavity occurs most commonly in young, healthy, athletic men (48).

Routine follow-up of cavitary lesions is recommended with serologic testing and serial imaging. In as many as 50% of patients with a coccidioidal cavity, serum complement fixation titers are low (<1:4) or have negative findings; however, sputum cultures demonstrate positive results in most patients (11,34). Antifungal treatment is indicated for a symptomatic cavitary lesion (3).

Figure 13. Chronic pulmonary coccidioidomycosis in a 72-year-old man. Axial CT image shows a bronchopleural fistula in the right lower lobe (arrow) and an air-fluid level in the pleural space (arrowhead) secondary to pyopneumothorax.
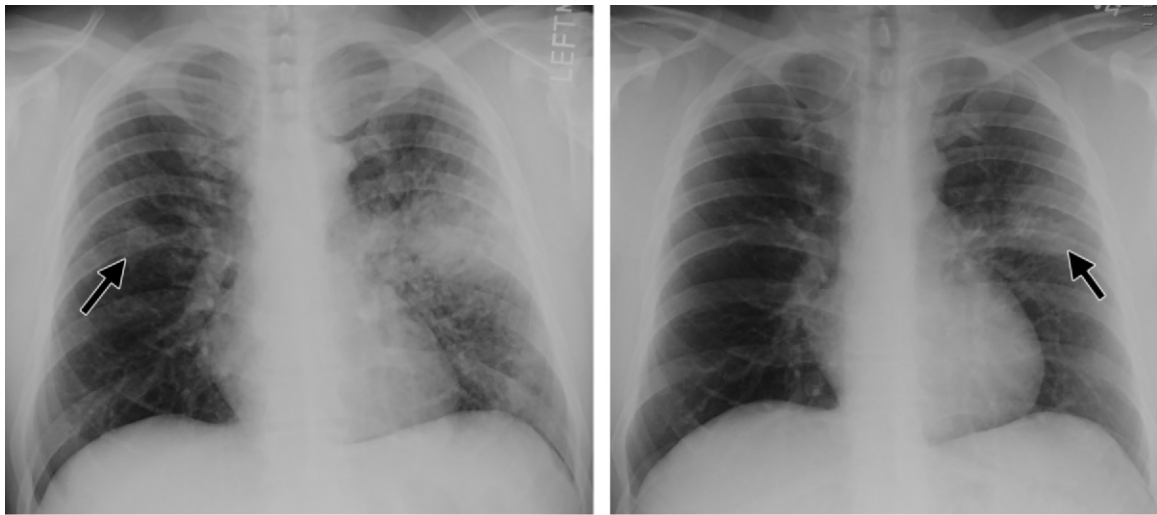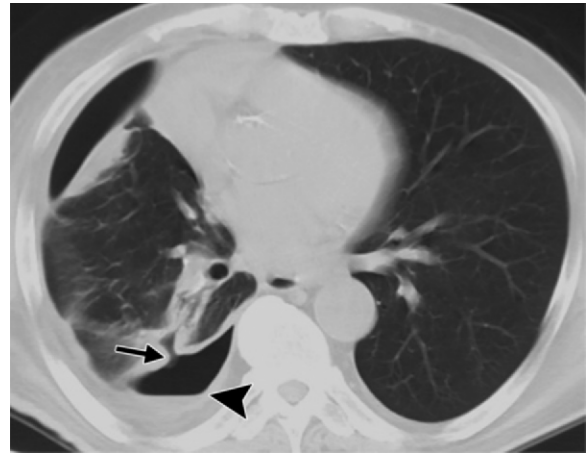

a.

b.

Figure 14. Persistent coccidioidal pneumonia due to chronic pulmonary coccidioidomycosis in a 34-year-old man with diabetes mellitus. **(a)** Frontal chest radiograph shows significant consolidation in the left lung and patchy consolidation in the right lung (arrow). **(b)** Frontal chest radiograph after 18 months of antifungal treatment shows decreased but persistent consolidation in the left lung (arrow).

Pulmonary resection is recommended for a cavitary lesion complicated by mycetoma or hemoptysis or for a peripheral enlarging cavity at risk for rupture. In young otherwise healthy patients, a ruptured cavity with pneumothorax, pyopneumothorax, or bronchopleural fistula is treated with surgical resection and decortication. If the diagnosis of a ruptured cavity is delayed by more than 1 week or the patient has a coexisting disease, management consists of antifungal therapy followed by surgery or chest tube drainage without surgery (7,28,34).

Persistent Coccidioidal Pneumonia or Adenopathy.—Persistent coccidioidal pneumonia usually occurs in cases with dense segmental or lobar consolidation or with extensive parenchymal disease (Fig 14) (23). Associated hilar or mediastinal adenopathy is occasionally present and may

persist after parenchymal abnormalities resolve (10). Persistent adenopathy is associated with an increased risk of disseminated disease (1).

The host immune status is often used to predict the clinical course of persistent coccidioidal pneumonia. Immunocompetent hosts usually have indolent symptoms, with resolution of parenchymal abnormalities over 6–8 months (23). Patients with a compromised immune system demonstrate severe clinical symptoms with high mortality. Serologic titers of complement-fixing antibody correlate with disease severity and are used to monitor treatment response, in conjunction with sputum cultures (11). Persistent coccidioidal pneumonia requires a prolonged course of antifungal treatment.

Persistent coccidioidal pneumonia may progress to chronic fibrocavitary pneumonia in less than 1% of cases (23). The incidence is higher in certain ethnic groups, including African-Americans,
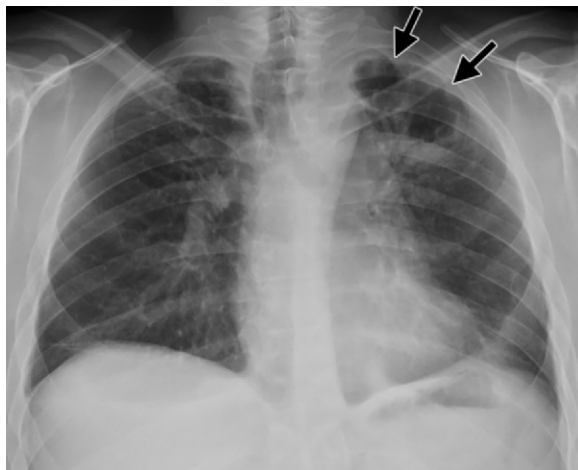
a.
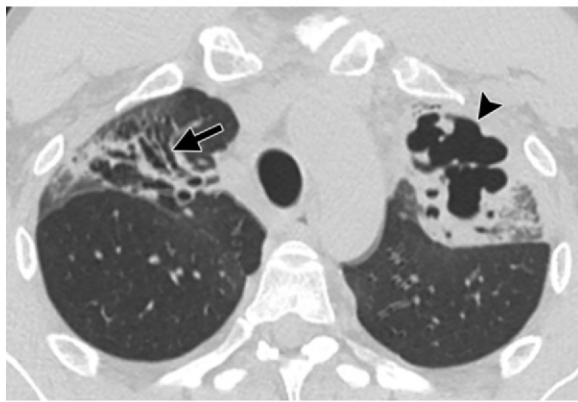
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Figure 15. Chronic fibrocavitary pneumonia due to chronic pulmonary coccidioidomycosis in a 37-year-old man with systemic lupus erythematosus. **(a)** Frontal chest radiograph shows cavitary lesions in the left upper lobe (arrows) and bilateral apical fibrosis with hilar elevation. **(b)** Axial CT image shows left-upper-lobe cavities (arrowhead) and consolidation, right-upper-lobe bronchiectasis (arrow), and bilateral upper-lobe volume loss.

Filipinos, Latinos, or American Indians, and in patients with diabetes (21,23). In these patients, disseminated disease may occur. Clinically and radiologically, chronic fibrocavitary pneumonia simulates reactivation pulmonary tuberculosis (10,23). Sputum cultures are persistently positive for *Coccidioides* species, and serum titers of complement-fixing antibodies are high. The imaging findings primarily involve the lung apices and consist of multiple cavities, nodules, calcified lesions, and fibrosis associated with volume loss (Fig 15). Long-standing disease may result in significant residual abnormalities, as described later in the discussion of regressive changes. These patients require a prolonged course of antifungal therapy. Surgical resection may be considered for a localized refractory lesion or in a patient with substantial hemoptysis (28).

Figure 16. Acute pulmonary coccidioidomycosis in a 39-year-old man with immunoglobulin A deficiency. Axial CT image shows bilateral bronchiolar dilatation and wall thickening (black arrows) and scattered centrilobular nodules (white arrows). The chest radiographs (not shown) were interpreted as normal.

Pleural Effusion.—Chronic pleural effusion occurs in approximately 3% of patients (10,21). The size of the effusion varies and may fluctuate over time, ranging from small to massive. A chronic pleural effusion may be complicated by empyema.

Regressive Changes.—The end-stage disease of pulmonary coccidioidomycosis resembles tuberculosis or histoplasmosis. Imaging findings are localized fibrosis, bronchiectasis, and calcifications (10,21). Calcification of nodules and regional lymph nodes is less common than other granulomatous infections. Disseminated infection may occur from calcified nodules and lymph nodes, which often contain viable organisms.

Role of CT
Acute disease is mostly evident at chest radiography; CT is useful in select cases (10). Small or subtle parenchymal opacities, hilar or mediastinal adenopathy, and mild bronchial involvement are better characterized at CT, and additional lung lesions are frequently seen (5,21,39,49). CT also plays an important role in detection of radiographically occult disease and is indicated in evaluation of high-risk patients with a normal appearance or subtle abnormalities on chest radiographs (Figs 16, 17). CT has several advantages in acute pleural disease, including recognition of small pleural effusion, better assessment of underlying parenchymal disease, differentiation of empyema from lung abscess, and guidance for thoracentesis and thoracostomy tube placement (32,39).

In disseminated disease, CT is better able to characterize the extent of miliary nodules and pulmonary findings suggestive of ARDS, as compared with chest radiography.

In chronic disease, CT is useful for characterizing and monitoring residual nodules, chronic cavity, persistent pneumonia, intrathoracic adenopathy, and pleural effusion (5,10,27,49). Complications of a chronic cavity, including mycetoma, lung abscess, pneumothorax, pyopneumothorax, and bronchopleural fistula, are more readily characterized at CT (24,26,47,50). CT is useful for preoperative planning when resection of a residual nodule or chronic cavity is indicated (47).

Conclusion

The incidence of pulmonary coccidioidomycosis in the endemic areas of the southwestern United States has increased substantially over the past decade, and symptomatic cases are encountered frequently beyond the endemic regions. The infection is acquired by inhalation of spores and results in symptomatic disease in 40% of patients, primarily involving the lung. There is a wide spectrum of pulmonary manifestations in the acute, disseminated, and chronic forms of the disease. At radiography and CT, coccidioidomycosis may be indistinguishable from bacterial pneumonia, other granulomatous infections, and malignancy. Immune status, comorbid conditions, and ethnicity correlate with severity of disease. Familiarity with the imaging characteristics and corroboration with clinical and laboratory findings are necessary for prompt diagnosis and appropriate management of coccidioidomycosis.

a.

b.

Figure 17. Acute pulmonary coccidioidomycosis in a 29-year-old man who had undergone bone marrow transplantation. **(a)** Frontal chest radiograph shows subtle haziness in the right lower medial lung (arrow). **(b)** Axial CT image shows ground-glass opacification in the right lower lobe.

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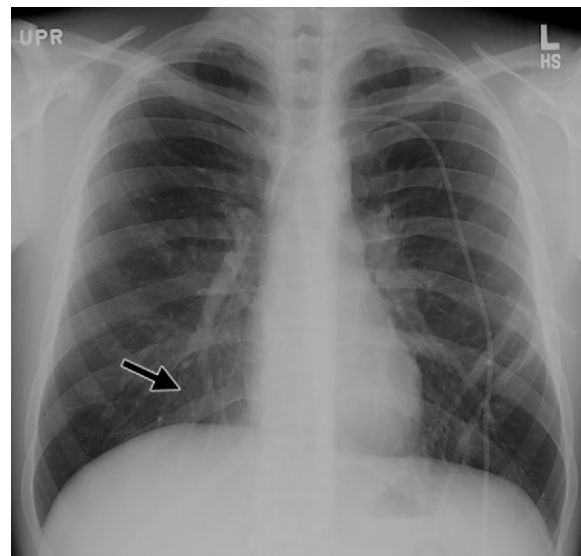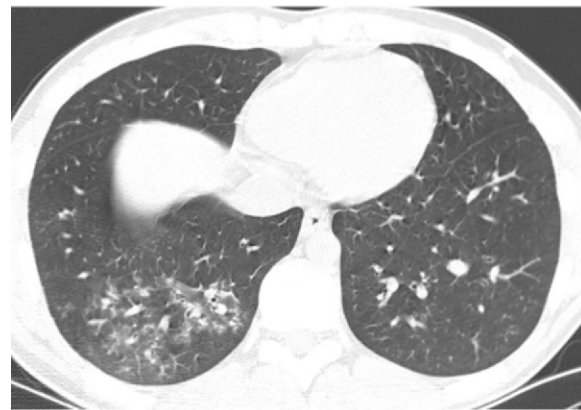
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RadioGraphics

Pulmonary Coccidioidomycosis: Pictorial Review of Chest Radiographic and CT Findings

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The lungs are the target organ in coccidioidomycosis and are involved in a wide spectrum of clinical and imaging manifestations that are categorized as acute, disseminated, or chronic disease. Acute coccidioidomycosis is responsible for up to 29% of cases of community-acquired pneumonia in endemic areas and is mostly self-limited. Disseminated or chronic disease occurs in a minority of cases and is associated with significant morbidity and mortality.

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Suppression of cellular immunity is a major risk factor for increased disease severity and dissemination. The most substantial risk factors are HIV infection, immunosuppressive medications, and high-dose glucocorticoid administration.

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Thoracic manifestations of acute coccidioidomycosis include pulmonary parenchymal abnormalities, intrathoracic adenopathy, and pleural effusion. Pulmonary parenchymal abnormalities occur in most symptomatic cases and consist of consolidation, nodules, cavities, and peribronchial thickening.

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The classic pulmonary manifestation of disseminated coccidioidal infection is miliary nodules caused by hematogenous spread. The original focus of parenchymal consolidation is seen occasionally, and hilar and mediastinal adenopathy is usually present. The lung nodules often progress to confluent opacities. Acute respiratory distress syndrome (ARDS) is an infrequent complication that usually occurs in immunocompromised hosts.

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Imaging manifestations of chronic coccidioidomycosis include residual nodule, chronic cavity, persistent pneumonia with or without adenopathy, pleural effusion, and regressive changes. Uncommon complications of a cavitary lesion are mycetoma, abscess formation, and bronchopleural fistula.