The acquired immune deficiency syndrome (AIDS) epidemic continues to outstrip global efforts to contain or eradicate it. Indeed, the total number of people living with human immunodeficiency virus (HIV) currently stands at 40.3 million, double the number in 1995. During the two and a half decades since the emergence of AIDS, many changes have occurred in the demographics, complications, and treatment of this epidemic. For example, the introduction of highly active anti-retroviral therapy (HAART) has been associated with a dramatic reduction in HIV-associated morbidity and mortality.

Pulmonary disorders, particularly respiratory infections, remain a common clinical presentation, and a source of significant morbidity and mortality among HIV-infected individuals throughout the world, even in the current era of potent anti-retroviral therapy. Interestingly, demographic and therapy changes of HIV infection have been accompanied by changes in the frequency and nature of the pulmonary complications of AIDS and their imaging features. In this article, we review the various infectious pulmonary complications of AIDS, with a particular emphasis on recent trends in imaging features of specific pulmonary infections as demonstrated on chest radiography and computed tomography (CT) examinations.

Demographics, Treatment, and Prophylaxis

Demographics

Following dramatic reductions in the number of AIDS cases and deaths in the United States in the mid-1990s, the number of new cases has stabilized. However, since people with HIV are now living longer, the total number of people living with HIV in the United States is still increasing, exceeding 1 million at the end of 2003. According to the latest data, male homosexuals continue to comprise a majority of people living with HIV in the United States, accounting for 63% of newly diagnosed HIV infections in 2003. Notably, during the time period of 1999 to 2003, there was a 40% increase in the rate of HIV infection among male homosexuals, which offset the previous decline in this risk group during the early and mid-1990s. At the end of 2003, an estimated 1,039,000 to 1,185,000 persons in the United States were living with HIV/AIDS, with 25% undiagnosed and unaware of their HIV infection.

Intravenous drug use remains a prominent channel for HIV transmission, accounting for about 20% of newly infected people in the United States. Notably, there is a racial disparity in HIV infection in the United States: although African Americans comprise only 12.5% of the country’s population, they account for nearly half of new HIV cases. In addition, African Americans have not experienced the same benefit from anti-retroviral therapy as white Americans. For example, in 2003, there were nearly twice as many deaths among African Americans from AIDS compared with white Americans.

Regarding women infected by HIV, unprotected heterosexual intercourse is the main mode of transmission for this subgroup. Following an increase in the late 1990s, the proportion of women among new annual infections has now stabilized at approximately 25%.

Although potent anti-retroviral therapies have transformed the AIDS epidemic in developed nations, the battle against AIDS looms large on a global basis, with continued growth of the epidemic in the setting of significant barriers to anti-retroviral therapy. Thus, when considering the AIDS epidemic, it is important to keep in mind that two-thirds of infected persons live in Africa, and one-fifth live in Asia. In these regions, unprotected sexual intercourse between men and women is the predominant mode of transmission of the virus. In Africa, the sub-Saharan area is the most affected region, where HIV prevalence rates have stabilized at acceptably high levels, exceeding 25% of the entire population in some countries, while in other African regions rates remain...
around 5 to 7%, or below. At best, only 1 person in 10 in Africa and 1 in 7 in Asia who is in need of anti-retroviral therapy would have received it in 2005. Thus, when reporting this disease, a split should be made between the developing world, where HAART has not been commonplace, and the developed world, where HAART has led to the management of HIV infection as a chronic disease, with life expectancy after diagnosis now measured in decades rather than years.

Treatment
Combination anti-retroviral therapy, or HAART, is the cornerstone of management of patients with HIV infection. By effectively suppressing viral replication, HAART results in a decrease in viral load and a rise in the CD4 lymphocyte count, with an associated reduced prevalence of various opportunistic infections and certain neoplasms. Anti-retroviral therapy is indicated for HIV-infected patients who are symptomatic, and for those who have AIDS (CD4 cell counts of less than 200 cells/mm³ or AIDS-defining conditions). Initiation of anti-retroviral therapy in asymptomatic pre-AIDS patients is usually recommended at CD4 levels below 350 cells/mm³.

Following initiation of the widespread use of HAART in the USA in 1996, marked declines have been noted in the incidence of most AIDS-defining conditions, resulting in improved survival and enhanced quality of life in patients with HIV infection. Currently, drugs for the treatment of HIV infection fall into three categories: those that inhibit the viral reverse transcriptase; those that inhibit the viral protease enzyme; and those that interfere with viral entry. Interestingly, following initiation of effective anti-retroviral therapy, a paradoxical worsening of preexisting, untreated, or partially treated opportunistic infections may be noted. The phenomenon is called “immune reconstitution disease.” It is particularly common in patients with underlying untreated mycobacterial infections. This entity is described in further detail later in this article.

Prophylaxis
Manifestations of HIV-related opportunistic infections can occur at virtually any level of CD4 cell count, but the incidence of serious and potentially life-threatening infections increases dramatically as the CD4 cell count drops below 200 cells/mm³. CD4 thresholds of 200, 100, and 50 cells/mm³ have been established as levels that demarcate the risks of opportunistic infections, lung abscess, and pulmonary complications of HIV infection. Currently, drugs for the treatment of HIV infection are classified into three categories: those that inhibit the viral reverse transcriptase; those that inhibit the viral protease enzyme; and those that interfere with viral entry. Interestingly, following initiation of effective anti-retroviral therapy, a paradoxical worsening of preexisting, untreated, or partially treated opportunistic infections may be noted. The phenomenon is called “immune reconstitution disease.” It is particularly common in patients with underlying untreated mycobacterial infections. This entity is described in further detail later in this article.

Approach to Imaging Diagnosis
Because the various pulmonary complications of HIV occur with different frequencies among patients with specific risk factors, different levels of immune compromise, and various prophylactic therapies, one should integrate these factors along with the clinical presentation and the recognized radiographic pattern to reach the most likely correct diagnosis. Of these parameters, the patient’s immune status, as reflected by the serum CD4 lymphocyte count, is considered the most important determinant for assessing the relative likelihood of various pulmonary infections. The threshold levels of CD4 counts and associated risk for developing various pulmonary infections are reviewed in Table 1. An important threshold is a CD4 count <200 cells/mm³, which is AIDS-defining in an HIV-infected individual even in the absence of an AIDS-defining illness, and places a patient at risk for opportunistic infections as well as certain malignancies.

Presenting symptoms, in association with the level of immunosuppression, may further guide the radiologist in providing a limited and relevant differential diagnosis. For example, pulmonary infections, in contrast to most malignancies (except lymphoma), typically present with fever. Among various infections, bacterial pneumonia is often associated with an acute onset of fever, often with pleuritic chest pain, productive cough, and purulent sputum. In contrast, PCP typically has a more insidious onset, with symptoms present for >1 week before presenting to medical attention with symptoms of dyspnea and dry cough. Unlike bacterial pneumonia, pleuritic chest pain is usually absent in patients with PCP unless it has been complicated by pneumothorax.

Individual demographic characterization of the infected patient may further narrow the differential diagnosis, as the incidence of certain complications varies among different populations. For example, among intravenous drug abusers with HIV infection, bacterial pneumonia rates are more than double those of other risk factor groups, regardless of the CD4 lymphocyte count. This group of HIV patients also shows an increased prevalence of septic emboli, recurrent Staphylococcus aureus infections, lung abscess, and pulmonary tuberculosis (TB) compared with other risk factor groups. On the other hand, cytomegalovirus (CMV) occurs more frequently in patients infected with HIV through sexual contact, while Kaposi’s sarcoma occurs almost exclusively in male homosexual patients. Interestingly, when controlling for HIV levels and use of anti-retroviral therapy, tobacco use was found to triple the risk for hospitalization with PCP and to double the risk for hospitalization with community-acquired pneumonia. The geographic location of a patient

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is also a significant factor. For example, analysis of surveillance data collected in the World Health Organization European region between 1993 and 2000 revealed that PCP was the most common opportunistic infection among all AIDS patients in Western Europe, whereas TB was the most common infection in Eastern Europe.26

Table 2 displays the characteristic clinical, demographic, laboratory, and radiographic findings in various pulmonary infections. These features are described in further detail in the following sections of this article.

### Imaging Methods

Chest radiography is usually the first imaging test obtained for the assessment of an HIV-infected individual with respiratory symptoms.27 Despite atypical manifestations and overlapping features among several entities, the chest radiograph is fairly accurate for diagnosing common complications. For example, in a blinded study that assessed the ability of radiologists to diagnose PCP, bacterial pneumonia, and pulmonary tuberculosis in HIV-positive patients, Boiselle and coworkers28 reported accuracies of 75, 64, and 84%, respectively. It is likely that an integrated approach to interpretation would have resulted in even higher accuracy. Importantly, even in asymptomatic HIV patients, an abnormal chest radiograph usually signifies an active process.29

**CT** is generally considered a second-line study for problems unresolved by chest radiography.30 The main indications for CT are listed in Table 3.7,30,31 With regard to evaluating for occult lung disease, it is important to be aware that a normal chest radiograph can be seen in a significant minority of HIV-positive patients with active pulmonary infection due to a variety of organisms, including *P. jirovecii* and mycobacterial, fungal, and viral organisms. CT, particularly, high-resolution CT, is usually positive in such patients.32 Additionally, high-resolution CT often reveals characteristic findings that can help to determine the most likely causative organism.32

With regard to the accuracy of CT, Hartman and coworkers33 have shown that this method is highly accurate in diagnosing certain complications, especially *Pneumocystis pneumonia* (94%) and Kaposi's sarcoma (90%). Importantly, CT also has a high negative-predictive value for excluding active disease.30,33

Other imaging modalities play a very limited role in imaging pulmonary complications of HIV infection. Although nuclear medicine gallium scanning was initially used in the assessment of PCP, it has been supplanted by high-resolution chest CT for this indication.34 Recently, positron emission tomography fluorine-18 fluorodeoxyglucose scanning was successfully used for localizing disease in AIDS patients with fever of unknown origin. However, this technology is unable to distinguish infection from tumor.35,36

### Bacterial Infections

Although HIV infection is most closely associated with alterations in cell-mediated immunity, there is evidence that AIDS also substantially impairs humoral immunity.23 Altered B-cell function and/or defects in neutrophil function place HIV-infected individuals at especially high risk for frequent infections with encapsulated bacteria such as *Streptococcus pneumonia*.12,23,37,38

Bacterial respiratory infections, including infectious airways disease and pneumonia, are currently the most common respiratory disease in HIV-infected individuals in developed countries.39,40 Moreover, they are frequently the first clinical manifestation of HIV infection. In a recent analysis of published reports on bacterial pneumonia,41 rates were 25-fold higher among HIV-infected individuals than in the general population, although in developed countries, HAART had shown a consistent effect on reduction of bacterial pneumonias.41

The significance of bacterial pneumonia in HIV infection is
underscored by the inclusion of two or more episodes of bacterial pneumonia within a 1-year period as an AIDS-defining illness for an HIV-infected individual, regardless of the CD4 cell count. Although bacterial pneumonia often occurs early in the course of HIV, the risk for this infection progressively increases with decreasing CD4 counts. For example, HIV-infected individuals with CD4 counts <200 cells/mm³ have a fivefold increased prevalence of bacterial pneumonia when compared with infected persons with CD4 counts greater than 500 cells/mm³. Bacterial pneumonia has been shown to accelerate the course of HIV. Among AIDS patients, bacterial pneumonia is associated with higher recurrence rates, and its occurrence is predictive of reduced survival time. Thus, it is not surprising that, in a recent autopsy series of 233 HIV-infected individuals, bacterial pneumonia was found to be the most frequent pulmonary complication.

Most episodes of pneumonia occur secondary to *S. pneumoniae* and *Haemophilus influenzae*, the same organisms that commonly cause community-acquired pneumonia in the general population. Nosocomial pneumonia, however, is mostly caused by *S. aureus* and Gram-negative agents, especially *Pseudomonas aeruginosa*. *Pseudomonas* has also been recognized as an important cause of pulmonary infection in AIDS among patients with a recent history of hospitalization, antibiotic use, or steroid therapy. Interestingly, “atypical agents” such as *Legionella pneumophila* and *Mycoplasma pneumoniae* are rarely diagnosed in HIV-infected patients with community-acquired pneumonia.

Patients with bacterial pneumonia typically present with an acute onset of fever and productive cough, with symptoms usually lasting less than 1 week before seeking medical attention. Most frequently, bacterial pneumonia in HIV patients presents radiographically as focal consolidation (Fig. 1), in either a segmental or a lobar distribution similar to non-HIV-infected patients, but with a higher propensity for multilobar and bilateral disease. In almost half of cases of bacterial pneumonia, however, a radiographic pattern other than focal consolidation is observed. Thus, it is not surprising that bacterial pneumonia has been found to be more difficult to diagnose radiographically than either PCP or pulmonary TB. For example, a bilateral pattern of alveolar and/or interstitial opacities may be observed in the setting of bacterial pneumonia, which can mimic PCP (Fig. 2). The identification of a segmental distribution can occasionally help differentiate bacterial pneumonia from consolidative PCP, which only rarely demonstrates a segmental pattern. Bacterial infections may also present as solitary or multiple lung nodules. A study regarding the etiology of pulmonary nodules in HIV-infected patients found bacterial pneumonia as the most common etiology, followed by tuberculosis. Pulmonary nodules due to bacterial and mycobacterial infections usually measure greater than 10 mm in diameter, whereas nodules associated with viral infection usually measure less than 10 mm in diameter.

Cavitary pulmonary lesions are an important radiological finding in HIV-infected patients. A bacterial etiology was found in 85% of cases of cavitary lung disease detected on

<table>
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<th>Infection</th>
<th>CD4 Threshold (cells/mm³)</th>
<th>Demographics</th>
<th>Duration of Symptoms before Presentation (days)</th>
<th>Lungs</th>
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<td>7 days</td>
<td>Focal consolidation; bilateral, symmetrical interstitial; ground glass on CT</td>
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<td>≥30 days</td>
<td>CD4 &gt;200: absent; CD4 &lt;200: common CT; low-density centers with peripheral enhancement</td>
</tr>
<tr>
<td>Pneumocystis</td>
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<td>All groups</td>
<td>&gt;7 days</td>
<td>Patchy consolidation; nodules</td>
</tr>
<tr>
<td>TB</td>
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<td>All groups, especially endemic areas</td>
<td>Variable</td>
<td>Ground glass, consolidation; nodules</td>
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<td>CMV</td>
<td>&lt;100</td>
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<td>Variable</td>
<td>Patchy consolidation; nodules</td>
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Abbreviations: TB = tuberculosis; CMV = cytomegalovirus
Thoracic infections in HIV/AIDS

Table 3 Indications for Chest CT Imaging in HIV/AIDS

1. Evaluating for radiographically occult lung disease in symptomatic patients with normal or equivocal chest radiographs
2. Further characterizing nonspecific patterns of abnormality on chest radiographs
3. Assessing for complications of pneumonia, such as abscess and empyema
4. Staging AIDS-related malignancies
5. Assessing extent and characterization of enlarged intrathoracic lymph nodes
6. Planning and guiding biopsy procedures

Parapneumonic pleural effusions are seen in a significant minority of cases of bacterial pneumonia and are usually small in size (Fig. 1).45 Thoracic empyema is more common in intravenous drug abusers and usually presents as multiple cavitary nodules. Other bacterial causes of cavitary nodules or cavitary consolidation include Nocardia asteroides and Rhodococcus equi infections. Mycobacterial and fungal infections are important differential diagnostic considerations for these findings. Mediastinal and/or hilar lymphadenopathy are more frequently associated with mycobacterial infection than bacterial infection.49,53,54 Thus, when cavitary lesions are accompanied by lymphadenopathy, mycobacterial infection should be favored over bacterial infection.

Parapneumonic pleural effusions are seen in a significant minority of cases of bacterial pneumonia and are usually small in size (Fig. 1).45 Thoracic empyema is more common in intravenous drug abusers, but surprisingly has an overall low prevalence.45 Although intrathoracic lymph node enlargement is not usually evident on chest radiographs, mildly enlarged nodes are not infrequently seen on CT scans of patients with bacterial pneumonia.49,56

HIV-infected individuals with uncomplicated bacterial pneumonia due to typical pathogens usually have a clinical and radiographic response to antibiotic therapy with a time course similar to normal hosts undergoing treatment for community-acquired pneumonia.48 In contrast to normal hosts, however, bacterial pneumonia in AIDS tends to progress more rapidly, is more often complicated by abscess formation, and is more frequently associated with bacteremia.46

AIDS patients with advanced immune suppression are also vulnerable to a host of unusual infections, including N. asteroides, R. equi, Bartonella henselae, and Bartonella quintana.57 Nocardia is a soil-borne aerobic actinomycete, acquired by inhalation. It usually occurs in southern and rural regions of the United States, possibly reflecting differential exposure to soil-borne pathogens compared with urban areas.21 The lung is the most commonly involved organ in HIV-related nocardiosis.48 R. equi pneumonia is typically seen in patients with advanced immune suppression. Affected patients usually present with an indolent course of cough, fever, and dyspnea. Radiographically, R. equi pneumonia usually presents with one or more foci of cavitary consolidation, often with an upper lobe predominance; additional features may include empyema and lymphadenopathy.21

Bacillary angiomatosis, an infection caused by B. henselae and B. quintana, is characterized by a neovascular proliferation involving multiple sites in the body including skin, liver, spleen, lymph nodes, and lung. Exposure to cats, cat fleas, and lice are the main risk factors for this infection. Affected patients typically present with angiomatous skin lesions that mimic Kaposi’s sarcoma. Clinical symptoms include fever, night sweats, cough, and occasional hemoptysis. Bacillary angiomatosis has several radiographic manifestations in the chest, including endobronchial lesions, parenchymal nodules, pleural effusions, and densely enhancing lymphadenopathy and chest wall masses. One should strongly consider this treatable infection in patients with suspected Kaposi’s sarcoma who lack the typical risk factor (homosexual contact) for this neoplasm.37,59

HIV-infected patients are also at increased risk for developing infectious airways disease such as bacterial tracheobronchitis and bronchiolitis. The most common bacterial organisms responsible for infectious airways disease include H. influenzae, P. aeruginosa, Streptococcus viridans, and S. pneumoniae.50,61

HIV-positive patients with pyogenic infectious airways diseases typically present with dyspnea, fever, and productive cough.62 Chest radiographs of patients with acute bacterial bronchitis are usually normal, but may demonstrate bronchial wall thickening.

Extensive bronchiolitis may create an apparent interstitial pattern of reticulonodular opacities which represent impacted bronchioles.8 This is typically symmetrically distrib-

Figure 1 Bacterial pneumonia with typical radiographic features. Frontal chest radiograph demonstrates focal right lower lobe consolidation and small parapneumonic right pleural effusion.
PCP

PCP has historically been one of the leading causes of morbidity and mortality among persons with AIDS. The introduction of highly active anti-retroviral therapy and widespread PCP prophylaxis in industrialized nations has brought about dramatic declines in the incidence of PCP, although it is still the single most common opportunistic pulmonary infection in patients with HIV infection in the United States, responsible for approximately 25% of cases of pneumonia in HIV infection.  

Approximately 25% of cases of HIV-associated PCP occur in patients who are unaware of their HIV status. In view of the increasing prevalence of drug-resistant HIV infections, possible drug-resistant PCP, and the tremendous number of AIDS cases in developing countries, PCP remains the most common cause of life-threatening infection pulmonary infection in HIV-positive patients.

Patients who develop PCP almost always have less than 200 CD4 cells/mm³, and often less than 100. Affected patients generally present with an insidious onset of fever, dry cough, and dyspnea. Symptoms are usually present for roughly 30 days before patients present to medical attention. With respect to laboratory data, an elevated serum lactate dehydrogenase level is highly sensitive for PCP, but it is not very specific. Because P. jirovecii cannot be grown in

Figure 2 Bacterial pneumonia with atypical features that mimic PCP. Frontal chest radiograph shows bilateral perihilar parenchymal opacities. This distribution is highly suggestive of PCP, but proved to be due to bacterial pneumonia in this patient.

Figure 3 Bacterial small airways disease and pneumonia. CT sagittal oblique reformation image using maximal intensity projection demonstrates small Y- and V-shaped opacities in the left lower lobe (arrows), consistent with small airways disease. Also note small loci of adjacent consolidation (asterisk).
culture, a diagnosis is made by morphologic identification of the organism, usually from specimens obtained from induced sputum or bronchoalveolar lavage.66,70

The classic chest radiographic presentation of PCP is a bilateral perihilar or diffuse symmetric interstitial pattern, which may be finely granular, reticular, or ground glass in appearance (Fig. 4A).66,69-72 If left untreated, the parenchymal opacities may progress to airspace consolidation.66 Radiographic improvement usually lags at least a few days behind the clinical improvement; thus, frequent chest radiographs may not be necessary during treatment for patients who demonstrate clinical signs of response to therapy.73

Advances in the prevention and treatment of PCP have been associated with an increased frequency of unusual manifestations and a trend toward more subtle radiographic presentations.66,67,72,74 Importantly, the chest radiograph may be normal in up to 39% of cases at the time of presentation, especially in those patients with severe impairment in immune status.73 CT, particularly high-resolution CT, is more sensitive than chest radiographs for detecting PCP and thus may be helpful in evaluating symptomatic patients with normal or equivocal radiographic findings.66,69,72,74 The classic high-resolution CT finding in PCP is extensive ground-glass attenuation (Fig. 4C), which corresponds to the presence of intra-alveolar exudate, consisting of surfactant, fibrin, cellular debris, and organisms.32,66 It is often distributed in a patchy or geographic fashion, with a predilection for the central, perihilar regions of the lungs.32,66 When interlobular septal thickening and intralobular linear opacities are superimposed over the ground-glass opacities, the resulting pattern is referred to as “crazy paving.” Although nonspecific in the acute setting, this pattern is closely associated with alveolar proteinosis when chronic in nature.32 Importantly, it has recently been shown that, when a tree-in-bud appearance
is present on high-resolution CT, PCP infection is very unlikely.\textsuperscript{39} Several features that were once considered unusual manifestations of PCP are now considered as typical manifestations.\textsuperscript{66} These features include upper lobe distribution of parenchymal opacities and cystic lesions, which may result in spontaneous pneumothorax (Fig. 5).\textsuperscript{32,76,77} Some of the cysts have been shown to be secondary to tissue invasion by \textit{P. jirovecii} followed by necrosis.\textsuperscript{32} Residual interstitial fibrosis is not uncommon.\textsuperscript{32,66,69,74} Interestingly, interstitial fibrosis has also been reported as the primary radiographic finding in a subset of patients with PCP who experienced relatively stable symptoms over months to years. This subset has been referred to as chronic PCP.\textsuperscript{78}

**Tuberculosis**

It has been estimated that HIV-infected individuals have a 50- to 200-fold increased risk of mycobacterium TB compared with the general population.\textsuperscript{79} Patients at particularly high risk for TB include intravenous drug abusers and patients from areas where TB is endemic. The interplay between infection with the two pathogens TB and HIV is complex: TB can be associated with accelerated progression and higher mortality in HIV infection, possibly due to increased HIV replication and mutation in the lung,\textsuperscript{67} whereas HIV infection increases the risk of developing active TB and TB recurrence, at least among patients not receiving HAART.\textsuperscript{80,81} As TB is both contagious and highly curable (except for multi-drug-resistant strains), prompt diagnosis and treatment are essential.\textsuperscript{81} TB may occur at any stage of HIV infection.\textsuperscript{81} In fact, TB is often one of the initial manifestations of HIV infection. Presenting symptoms may include cough, night sweats, and weight loss. Symptoms are often present for more than 7 days before patients seek medical attention.\textsuperscript{48}

In comparison to the general population, patients with HIV infection and TB more commonly demonstrate “atypical” radiographic patterns (eg, lymphadenopathy, pleural effusions, and mid and lower lung zones consolidation), irrespective of the time from acquisition of the infection to the development of clinical disease. Using molecular fingerprinting, it has recently been shown that the “atypical” radiographic pattern is a result of altered immunity and may thus represent either recent infection or reactivation of a latent infection.\textsuperscript{82} Moreover, the radiographic pattern observed in HIV-infected individuals with TB is dependent on the level of immune suppression at the time of overt disease.\textsuperscript{83-85} Early in HIV infection, when the CD4 count is >200 cells/mm\textsuperscript{3}, the imaging features are typically those associated with reactivation TB, including parenchymal opacities with associated cavitation, often located within the apical, posterior, and superior segments of the lungs.\textsuperscript{83-85} In contrast, as the patient’s immune level decreases, one will observe findings typically associated with primary TB, including mid and lower lung consolidation and lymph node enlargement.\textsuperscript{83-85} This pattern is usually observed in patients with CD4 counts <200 cells/mm\textsuperscript{3}. On CT, enlarged TB lymph nodes frequently demonstrate low-density centers and peripheral contrast enhancement.\textsuperscript{8,83,84}

In comparison to normal hosts, AIDS patients with TB are more likely to present with diffuse lung disease (Fig. 6), bronchogenic spread, miliary disease, and extrapulmonary disease.\textsuperscript{83-85} These manifestations increase in frequency with

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**Figure 5** Cystic PCP complicated by pneumothorax. Portable chest radiograph demonstrates large cyst in right lung, which was complicated by a basilar right pneumothorax, with slight shift of the mediastinum to the left, suggestive of tension. Note diffuse bilateral hazy “ground-glass” opacities, in keeping with PCP.

**Figure 6** Tuberculosis in a Haitian man with several months of cough, weight loss, and night sweats. Chest radiograph shows bilateral ill-defined nodular opacities predominately in the upper lung zones. Expectorated sputum was positive for \textit{M. tuberculosis}, and the patient was simultaneously found to be HIV positive, with CD4 count of 273 cells/mm\textsuperscript{3}.
increasing degrees of immune suppression. At advanced levels of immune suppression, it has been estimated that up to 20% of HIV-positive patients with TB have normal chest radiographs.86 These patients often have a reduced colony count of Mycobacterium tuberculosis. The combination of a normal chest radiograph and negative sputum smears in HIV patients may result in delays in diagnosis and treatment, increasing the risk of fatality.87

In contrast to radiographs, CT scan of such patients usually reveal subtle abnormalities, including small nodules and lymph node enlargement.83 Tuberculous bronchitis and bronchiolitis frequently occur in HIV-positive and AIDS patients, even in those without cavitary disease. Endobronchial spread caused by either M. tuberculosis or Mycobacterium avium complex may have identical CT appearances, typically resulting in a tree-in-bud pattern.27,83

In HIV-positive patients with drug-susceptible TB, the administration of a standard 6-month regimen usually results in a prompt response to therapy, similar to the non-HIV population; however, a longer course of treatment for 9 to 12 months has been advocated for patients who show a slow clinical or bacteriologic response to therapy.81 Directly observed therapy improves outcome and reduces the rate of multi-drug-resistant TB.81 Tuberculosis prophylaxis is usually administered to patients with history or symptoms of TB, a purified protein derivative (PPD) of at least 5 mm, or a possible false-negative PPD.5

In the past few years, there have been a growing number of cases of patients on HAART exhibiting a paradoxical symptomatic deterioration of presumably preexisting subclinical opportunistic infections that become symptomatic following HAART-induced recovery of the immune response. The phenomenon is referred to as immune reconstitution (IRD).88,89 A low baseline CD4 count below 50 cells/mm³ represents a risk factor for IRD.90 Mycobacteria are the most commonly implicated infectious organisms in IRD, accounting for almost 40% of the cases reported up to 2002.91 With regard to mycobacterial infections, manifestations of IRD in the affected HIV-infected patient who is successfully treated with HAART may be as subtle as fever and minor lymph node enlargement, or as dramatic as respiratory failure or neurological deterioration.91 Imaging findings include thoracic and abdominal lymphadenopathy (Fig. 7), lung parenchymal abnormalities (such as consolidation, nodules, micronodules), and/or pleural effusions.88,92,93 This syndrome is associated with restoration of cutaneous delayed type hypersensitivity reaction to tuberculin.90 Several diagnostic criteria have been proposed for establishing the diagnosis of IRD, including atypical presentation of opportunistic infections in patients responding to anti-retroviral therapy, decrease in plasma HIV RNA levels, and increased blood CD4 count. The differential diagnosis of IRD includes progressive disease due to nonadherence to treatment, single- or multi-drug-resistant mycobacterial infection, adverse drug reaction, and concurrent opportunistic infection or malignancy.88,92,90,93 Treatment is symptomatic; antimicrobial therapy should be started or continued, and antiinflammatory therapy using steroids may provide benefit.90

Atypical Mycobacterial Infections

Atypical mycobacterial infections in AIDS patients are usually secondary to Mycobacterium avium-intracellulare (MAI) and less commonly due to Mycobacterium kansasii.8,85,94 Because MAI is a less virulent organism than M. tuberculosis, it is usually encountered in the setting of more advanced immunosuppression (CD4 <50/mm³).8,85,94 Thoracic MAI involvement usually occurs in the setting of disseminated disease, with the gastrointestinal tract serving as the main entry site in most cases. A recent review of hospitalization charts in HIV-infected patients admitted to a large metropolitan hospital during 2001/2002 reported that nontuberculous mycobacteria was the third most common causative agent (after bacterial pneumonia and PCP), accounting for 11% of hospitalizations. In the majority of patients, the nontuberculous mycobacterial infection was disseminated, with half of the patients demonstrating respiratory tract involvement.95 Imaging findings in the lungs are variable and include multifocal patchy consolidation, ill-defined nodules (Fig. 8B), and cavities (Fig. 9).8,90 Lymphadenopathy is frequently present (Fig. 8A), but is observed less frequently than in patients with TB. Importantly, a normal chest radiograph may be observed in roughly 20% of patients with documented pulmonary infection with MAI.90 With regard to M. kansasii infection, the most common finding is focal alveolar consolidation.94
IRD has also been described in association with MAI, mostly in profoundly immunosuppressed individuals who have demonstrated an excellent response to HAART. Affected patients present with an acute febrile reaction accompanied by new or enlarging peripheral, intrathoracic, or abdominal lymphadenopathy. Interestingly, the development of paratracheal lymphadenopathy may cause upper airway compression. Pulmonary disease is the second most common manifestation, with variable manifestations, including consolidation, cavitary lesions, lung nodules, atelectasis, and tree-in-bud opacities. Affected patients usually respond to appropriate antibiotic therapy, but adjunctive steroids may be considered for severely symptomatic patients.

**Fungal Infections**

With the exception of PCP, fungal organisms are a relatively uncommon cause of pulmonary infection in AIDS patients, but are more prevalent in endemic areas. The most common fungal pathogen to involve the lungs in AIDS patients is *Cryptococcus neoformans*. Less common fungal infections include aspergillosis and the endemic fungi including histoplasmosis, blastomycosis, and coccidiomycosis.

**Figure 8** Atypical mycobacterial infection with nonspecific imaging findings. (A) Contrast-enhanced CT (soft-tissue window) at level of aortic arch demonstrates right paratracheal lymphadenopathy. (B) Lung window setting image at level of lung apices shows a poorly defined ground-glass nodule in the right apex.

**Figure 9** Atypical mycobacterial infection mimicking tuberculosis. Frontal chest radiograph (A) shows biapical complex cavitary lesions, which are shown to better detail on an axial CT image (B). Tuberculosis could produce an identical radiographic appearance.
Pulmonary cryptococcal infection usually occurs in the setting of advanced immunosuppression (CD4 < 100/mm³). More than half of patients are fungemic, and 90% of patients have concomitant CNS infection. Imaging findings are non-specific and include reticular or reticulonodular opacities, nodules (Fig. 10), and foci of consolidation. Parenchymal abnormalities may be accompanied by lymph node enlargement and pleural effusion. Although infection with Aspergillus is uncommonly encountered in AIDS, its incidence is increasing. This infection occurs almost exclusively in HIV-positive individuals with neutropenia (usually acquired from drugs such as zidovudine or ganciclovir) or steroid use. Affected patients generally have advanced immune suppression, with CD4 counts < 50 cells/mm³. Patients with angioinvasive aspergillosis may demonstrate cavitary disease with an upper lobe predominance, or multifocal areas of alveolar consolidation or nodules with a halo of peripheral ground glass. Airway invasive aspergillosis is another form of pulmonary Aspergillus infection, which includes tracheobronchitis, bronchiolitis, and bronchopneumonia. Chest radiography may be normal in tracheobronchitis, or it may show bronchial wall thickening. On high-resolution CT, bronchiolitis is characterized by a tree-in-bud pattern.

**Viral Infections**

CMV is the most common viral pulmonary pathogen in AIDS patients. Although it is frequently recovered from the lungs, CMV is not considered a significant pathogen in most cases. Isolated clinically relevant cases of CMV pneumonitis may occur, however, and generally affect patients with advanced levels of immunosuppression (CD4 < 100/mm³). Most patients have documented extrathoracic CMV infection. Interestingly, CMV infection occurs most frequently in patients infected with HIV by sexual contact, either heterosexual or homosexual.

The most common CT findings of CMV pneumonitis are ground-glass opacities and alveolar consolidation, which may mimic PCP. Other imaging findings include nodules, masses, and small airways disease. In a series of 21 AIDS patients with CMV pneumonia, McGuinness and coworkers reported that nodules or masses were present in a majority of cases. The latter findings are not typically associated with PCP, and their identification may thus be helpful in distinguishing between these two infections.

**Summary**

Pulmonary infections remain an important complication of HIV infection, even in the current era of potent anti-retroviral therapies.
therapy. Employing an integrated approach that combines radiographic pattern recognition with knowledge of a patient’s clinical symptoms, laboratory data, immune status level, demographic information, and drug therapy can enhance the interpretation of imaging studies in HIV-infected patients. Although chest radiography remains the mainstay of imaging the HIV-positive patient with respiratory symptoms, CT plays an increasingly important secondary role in selected cases. 

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