

American College of Radiology ACR Appropriateness Criteria®

Clinical Condition: Acute Respiratory Illness in HIV-Positive Patient

Variant 1: Cough, dyspnea, chest pain, fever.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
X-ray chest	9		Min
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 2: Negative, equivocal, or nonspecific chest radiograph.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT chest without contrast	8		Med
NUC Ga-67 scan lung	2		High
NUC Tc-99m DTPA scan lung	2		Low

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Clinical Condition:**Acute Respiratory Illness in HIV-Positive Patient****Variant 4:****Positive chest radiograph, infection other than PCP suspected.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	6		Med
NUC Ga-67 scan lung	2		Low
NUC Tc-99m DTPA scan lung	2		High
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

Variant 5:**Positive chest radiograph, noninfectious disease suspected.**

Radiologic Procedure	Rating	Comments	RRL*
CT chest with or without contrast	8	If neoplasm suspected.	Med
NUC Ga-67 scan lung	2		High
NUC Tc-99m DTPA scan lung	2		Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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ACUTE RESPIRATORY ILLNESS IN HIV-POSITIVE PATIENTS

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Summary of Literature Review

Acute respiratory illness (ARI) constitutes a group of signs and symptoms that develop over a brief interval (hours to weeks), some of which are constitutional (such as fever, chills, and weight loss) and some of which are organ specific (such as cough, shortness of breath, and chest pain). In HIV-infected individuals with ARI, a wide variety of diseases can have a similar presentation. Clinical and demographic factors that help to rank the differential diagnosis include: the degree of immunosuppression as reflected by the patients' CD4 cell counts [1], whether or not they are being treated with highly active antiretroviral therapy (HAART) [2-4], their country or region of origin and travel history, and their HIV risk factor. Radiographic findings play a role in narrowing the differential diagnosis and in guiding further diagnostic testing or procedures.

The chest radiograph is a basic and widely accepted diagnostic imaging tool in HIV-infected patients. When an HIV-infected patient presents with ARI, after obtaining the history and performing a physical examination, obtaining a chest radiograph is usually the next step. The vast majority of processes that cause ARI in HIV-infected individuals are associated with chest radiographic abnormalities, and several studies support obtaining an initial chest radiograph in HIV-infected patients with ARI.

The nature and distribution of pulmonary findings on the chest radiograph will often suffice in suggesting a diagnosis or differential diagnosis. Bacterial pneumonia caused by infection with the usual organisms is the most common cause of ARI in AIDS patients [5]. The chest radiographic finding of focal or multifocal consolidation associated with fever, sputum production, and

leukocytosis is usually diagnostic. Viral pneumonia can also present with bilateral reticular opacities on chest radiographs. If the viral infection is cytomegalovirus, there will often be cytomegalovirus infection in other organs (eg, retinitis, esophagitis), and the patients will have very low CD4 cell count (less than 50/mm³). On computed tomography (CT), cytomegalovirus will often demonstrate small, ill-defined nodules, peribronchial thickening, and foci of bronchiectasis. Congestive heart failure due to AIDS cardiomyopathy can also show reticular interstitial opacities. If bilateral nodular or reticular opacities are present without lymphadenopathy or pleural effusion and the CD4 cell count is less than 200/mm³, a diagnosis of pneumocystis jiroveci (carinii) pneumonia (PCP) [6] can be suggested. Opravil et al [7] found that the severity of the radiographic abnormality correlated with both severity of illness and mortality in patients with PCP.

It is now accepted that a normal or only subtly abnormal chest radiograph can occasionally occur in patients with tuberculosis [8], cytomegalovirus pneumonia [9], and PCP [10], among other processes. If there is a high clinical suspicion of a pulmonary infection in the setting of a normal chest radiograph, a CT may be warranted to assess for subtle pulmonary parenchymal disease [11,12]. Miliary or disseminated tuberculosis or nodal disease can be readily evident on CT in the face of a normal or near-normal chest radiograph [8]. In the series by Aderaye et al [13] 7.2% of patients with HIV and TB had normal chest radiographs. Among patients with culture-positive TB and normal chest radiographs in this series, 90% had negative smears for acid-fast bacilli. Small airways disease with mild bronchiectasis, peribronchial thickening, foci of mucoid impaction, and air trapping may be evident only on CT [14]. Patients who have a normal chest radiograph and PCP will usually have focal areas of ground-glass opacity evident on CT [15]. Cysts, reticular opacities, nodules, or cavities are common additional findings in patients with PCP [16].

Exercise desaturation, an elevated lactate dehydrogenase (LDH), and a low diffusion capacity [17] are all associated with PCP and add supportive evidence to a typical chest radiographic appearance. Sputum induction will often confirm the diagnosis [18]. In the setting of a negative sputum induction, some practices treat empirically for PCP if the chest radiographic and clinical findings are typical. Otherwise, fiberoptic bronchoscopy (FOB) with bronchoalveolar lavage and/or biopsy is the usual practice. Gruden et al [10] proposed some compelling arguments for using CT early in the diagnostic evaluation of PCP. When the presence or absence of ground glass opacity on CT was used as the diagnostic criterion, patients were classified as "possible PCP" or

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“not PCP.” CT had a high sensitivity and specificity. This result is supported by the findings of Hidalgo et al [19] who found ground glass, reticular, and cystic changes in the lung on high resolution CT (HRCT) in patients with PCP. In contrast, those with tree-in-bud nodules had other diagnoses. The authors concluded that patients with “possible PCP” should go on to direct testing (induced sputum, BAL) whereas a diagnosis of “not PCP” can be used to avoid empiric treatment and direct testing. They also pointed out that CT has higher sensitivity and specificity and is cheaper than gallium scanning and provides an immediate result, in contrast to the 48-72-hour delay for gallium. There is, however, literature supporting the utility of performing DTPA-Tc and gallium 67 lung scans in patients with suspected PCP and negative or atypical chest radiographs. In two different studies, gallium lung scans were positive (94% and 100%, respectively) in patients with PCP [20]. Leach et al [21] noninvasively detected 34 of 36 patients with PCP using a combination of DTPA lung scanning while inducing sputum, and they were thus able to reduce the need for bronchoscopy.

CT is widely accepted when noninfectious AIDS-related intrathoracic diseases are suspected, when the chest radiograph shows findings atypical for PCP, or when FOB is not diagnostic. The CT findings can frequently suggest the diagnosis, or at least limit the diagnostic possibilities, and may identify optimal sites for obtaining a biopsy [22]. According to Hartman et al [22] in their series of 128 AIDS patients, CT was 93% accurate in excluding disease and 94% and 93% accurate in rendering confident diagnoses of PCP and Kaposi sarcoma, respectively. Abdel-Dayem et al [23] demonstrated the utility of thallium and gallium scanning for diagnosing Kaposi sarcoma. In their series, a thallium-positive, gallium-negative pattern had a high specificity of 95% for diagnosing Kaposi sarcoma. However, the sensitivity decreased from 89% to 37% in patients who had opportunistic infections.

If lung nodules or masses [24] with or without cavitation are present on the chest radiograph and the sputum is unrevealing, a chest CT should be performed. CT better delineates the distribution and morphology of the parenchymal disease and can demonstrate additional important findings. Nyamande et al [25] found that CT revealed pathology not visualized by chest radiography in 82% of patients, including mediastinal lymphadenopathy, ground-glass opacities, and pleural or pericardial effusions. The differential diagnosis for lung nodules and masses depends in part on the patient’s immune status and HIV risk factors. Bacterial infection can occur at any level of immunity, although its frequency increases as CD4 cell count declines, and it occurs more often in HIV-infected patients whose risk factor was intravenous drug use.

In the series by Jasmer et al [24] bacterial infection was the most common etiology of lung nodules seen on CT. Tuberculosis was second. In areas where fungal infections are endemic, that diagnosis rises in the differential diagnosis. Jasmer et al [24] noted that nodule size less than 1 cm, fever, and cough favored an infectious etiology for the nodules. Neoplasms also can cause nodules and masses. In cases in which masses are present and necrotizing pneumonia is suspected, limited evidence [26] suggests that T2-weighted magnetic resonance imaging (MRI) of the lungs may detect necrotizing pneumonia in immunocompromised patients before CT signs are present.

Kaposi sarcoma has its highest prevalence in HIV-infected gay men. In that population, especially if the patient has a low CD4 cell count and cutaneous or oropharyngeal Kaposi sarcoma, lung nodules and masses will often be due to Kaposi sarcoma [22]. The radiographic findings can mimic infection. Acutely, patients with Kaposi sarcoma can present with hemoptysis. FOB with bronchial inspection will reveal the typical violaceous endobronchial lesions in most cases. AIDS-related lymphoma is predominantly an extranodal disease. Lung nodules and masses are often present if there is thoracic involvement. These patients are often acutely ill with “B” symptoms. CT will often show lymphadenopathy or abdominal visceral involvement that is not evident on the chest radiograph.

Lymphadenopathy may be evident on chest radiographs, although CT is much more sensitive in its detection. When an HIV-infected patient is acutely ill and has lymphadenopathy, the differential diagnosis includes tuberculosis, other mycobacterial infections, fungal infection, and lymphoma among the more common etiologies [27,28]. In patients with tuberculosis who are evaluated with contrast-enhanced CT, central low-attenuation lymphadenopathy is highly suggestive of the correct diagnosis [29]. The pattern of associated parenchymal and pleural disease, described above, will also help prioritize the differential diagnosis.

Several authors have described different imaging manifestations of TB in HIV-infected patients. Aderaye et al [13] found that HIV-positive patients with TB were significantly less likely to have cavitory disease and more likely to have interstitial opacities, miliary patterns, or pleural effusions than patients without HIV. In addition, in a series by Busi Rizzi et al [30] patients on highly active antiretroviral therapy (HAART) were more likely to develop a postprimary pattern, defined as upper-lobe consolidation with or without cavitation, or bronchogenic spread, than patients not on HAART. HAART-naïve patients were more likely to develop a primary pattern, defined as adenopathy, pleural effusion, middle-lobe or lower-lobe consolidation, or interstitial changes. These authors also point out that CD4 cell count is an

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independent predictor of pattern of pulmonary infection. Sixty-one percent of patients in the study with a CD4 cell count of less than 200/mm³ had a primary pattern of TB, while 84% of patients with a CD4 cell count of more than 200/mm³ had a postprimary pattern.

Several uncommon conditions can mimic infectious pathology in HIV patients. New-onset sarcoidosis can cause lymphadenopathy and acute pulmonary and constitutional symptoms. In a small series by Morris et al [31], CD4 cell counts of patients with HIV and new-onset sarcoidosis were all below 200 mm³. Castleman's disease can also present with symptoms mimicking respiratory infection in HIV patients. Common patterns on chest radiography and CT include lymphadenopathy, reticular and/or nodular interstitial opacities, and pleural effusions [32].

Immune reconstitution syndrome (IRS) has been recognized as a source of worsening respiratory symptoms in patients with opportunistic infection after initiation of HAART. Shelburne et al [33] found that IRS was most common in patients who were HAART naïve, were diagnosed with opportunistic infections close to the time of beginning HAART, and/or who experienced a rapid drop in HIV-1 RNA. MAI, TB, and fungal infections are among the most common pathogens linked to IRS; PCP is much less common [34]. Rajeswaran et al [35] reported imaging findings of IRS including axillary or mediastinal lymphadenopathy, parenchymal nodules, and pleural effusions.

Pleural effusions are rarely present in patients with PCP. Bacterial pneumonia [5], tuberculosis, and fungal infections all can be associated with pleural effusions. Kaposi sarcoma may have effusions in the later stages [36]. Kaposi sarcoma effusions are often hemorrhagic. Pleural involvement with AIDS-related lymphoma is not rare. Patients can have effusions or masses. While the chest radiograph usually is adequate to demonstrate the presence of a pleural effusion, if the patient does not respond to antibiotic therapy or develops a complicated effusion, CT may be helpful in guiding the choice of a site for biopsy or drainage.

Recommendation

Chest radiography is indicated early in the evaluation of AIDS patients with ARI. Most respiratory diseases will be associated with abnormal chest radiographic findings. If the radiograph is normal or equivocal and clinical suspicion for disease is high, CT can be performed to evaluate for subtle pulmonary abnormalities and lymphadenopathy. CT also plays a role in weighting a differential diagnosis and guiding diagnostic and therapeutic procedures in patients with abnormal chest radiographs. Nuclear scintigraphy including gallium 67 and DTPA-Tc can be helpful in diagnosing PCP, and the

combination of thallium and gallium scanning has shown utility in the diagnosis of Kaposi sarcoma.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

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