

In people with HIV and CD4 counts <200 cells/mm³, the chest radiographic findings of pulmonary TB are markedly different, with infiltrates showing no predilection for the upper lobes, and cavitation uncommon.^{100,103,104} Normal chest radiographs can be seen in some people with respiratory symptoms and positive sputum cultures. Thoracic CT scans may demonstrate mild reticulonodular infiltrates despite a normal chest radiograph.¹⁰⁵

With increasing degrees of immunodeficiency, extrapulmonary (especially lymphadenitis, pleuritis, pericarditis, and meningitis) or disseminated TB are more common. In people with HIV who are markedly immune-suppressed, TB can be a severe systemic disease with high fevers, rapid progression, and features of sepsis.¹⁰⁶ Clinical manifestations of extrapulmonary TB in people with HIV are not substantially different from those described in people without HIV. TB must be considered in disease processes involving any site in the body,¹⁰⁷ especially in those with central nervous system (CNS) disease, when early TB treatment is essential to improve outcomes.¹⁰⁸⁻¹¹¹

After initiation of ART, immune reconstitution can unmask subclinical TB disease, resulting in pronounced inflammatory reactions at the sites of infection (see [Unmasking TB-IRIS](#) below).

Diagnosis

Initial diagnostic testing for TB disease should be directed at the anatomic site of symptoms or signs (e.g., lungs, lymph nodes, urine, cerebrospinal fluid).¹⁷ Pulmonary involvement is common at all CD4 counts.^{99,112} The initial evaluation of a person suspected of having HIV-related TB should always include chest imaging, even in the absence of pulmonary symptoms or signs. However, chest radiography is an imperfect screen for pulmonary TB, particularly among individuals with advanced immunodeficiency who can have TB culture-positive sputum despite normal chest radiographs.^{113,114} Therefore, sputum acid-fast bacilli (AFB) smear, nucleic acid amplification (NAA) testing, and AFB culture should be performed in people with HIV with symptoms of TB disease who have a normal chest radiograph, as well as in those with no pulmonary symptoms but evidence of TB disease elsewhere in the body.¹⁷

Sputum culture yield is not affected by HIV or the degree of immunodeficiency. Sputum smear-negative, culture-positive TB disease is common among people with HIV, particularly those with advanced immunodeficiency and non-cavitary disease.^{115,116} NAA tests have a higher sensitivity for culture-positive disease than smear.^{17,117} Smear and culture of three sputum specimens is recommended based on a large study in people with HIV that showed a 10% incremental yield for broth culture between the second and third specimens.¹¹⁸ Additionally, up-front NAA testing for *M. tuberculosis* can expedite diagnosis.¹⁷

Lymph node involvement is common in HIV-related TB, and the combined yield of histopathology, smear, and culture from needle aspirates of enlarged lymph nodes is quite high.^{119,120} While NAA testing on specimens other than sputum is an off-label use of the test, a positive NAA test result can be useful as evidence of extrapulmonary TB and for clinical decision-making.¹²¹ Histopathologic findings also are affected by the degree of immunodeficiency. People with relatively intact immune function have typical granulomatous inflammation associated with TB disease. With progressive immunodeficiency, granulomas become poorly formed or can be completely absent.^{101,122}

Pleural fluid, pericardial fluid, ascites, and cerebrospinal fluid should be sampled if there is clinical evidence of involvement. Polymerase chain reaction (PCR) testing to aid with molecular identification of *M. tuberculosis* on formalin-fixed tissue is available through reference laboratories