

and, in special situations, through the CDC. Clinical providers and pathologists should contact their state or local health department for consultation with the CDC (tbinfo@cdc.gov) and the CDC-funded [TB Center of Excellence](#) for assistance with referring specimens for evaluation. The yield of mycobacterial urine and blood cultures depends on the clinical setting; among people with HIV and advanced immunodeficiency, the yield of culture from these two readily available body fluids can be relatively high^{101,107} and may allow definitive diagnosis and be the only source of an isolate for drug-susceptibility testing (DST).¹²³

Nucleic-Acid Amplification Testing

NAA tests provide rapid diagnosis of TB, and some assays also provide rapid detection of drug resistance. NAA assays, if positive, are highly predictive of TB disease when performed on Acid-Fast Bacillus (AFB) smear-positive specimens. However, because nontuberculous mycobacterial infections (NTM) may occur in people with HIV with advanced immunodeficiency, negative NAA results in the setting of smear-positive specimens may indicate NTM infection and can be used to direct further workup and guide decisions about the need for respiratory isolation.

NAA tests are more sensitive than AFB smears, being positive in 50% to 80% of smear-negative, culture-positive sputum specimens^{124,125} and up to 90% when three NAA tests are performed. Therefore, it is recommended that for all patients with suspected pulmonary TB, an NAA test be performed on at least one sputum specimen.^{17,126} NAA tests also can be used on extrapulmonary specimens with the caveat that the sensitivity is often lower than with sputum specimens.¹⁷ Importantly, a smear-negative specimen with a negative NAA test result does not rule out active TB disease.

The Xpert MTB/RIF assay is an automated NAA test that can detect both *M. tuberculosis* and mutations in the *rpoB* gene associated with rifampin resistance. It has been implemented widely in resource-limited settings with high TB prevalence and as a frontline TB diagnostic test in people with HIV.¹²⁷ This assay combines simple processing requirements in the laboratory and rapid turnaround (results within 2 hours). In a meta-analysis, the overall sensitivity and specificity of the Xpert MTB/RIF assay were 88% (95% confidence interval [CI], 83% to 92%) and 98% (95% CI, 97% to 99%), respectively. The assay is somewhat less sensitive among people with HIV overall,¹²⁸ however, this may be, in part, attributed to a higher prevalence of smear-negative disease in people with HIV.¹²⁹ In one key study from South Africa, the sensitivity of Xpert MTB/RIF a relationship with CD4 count was demonstrated, indicating higher sensitivity among people with HIV as the CD4 count declined below 500 cells/mm³.¹³⁰ Importantly, patients in this study with the lowest CD4 count (<100 cells/mm³) actually had higher rates of smear-positivity and higher markers of severe TB disease (C-reactive protein, anemia, and WHO symptom screen).

Xpert MTB/RIF sensitivity in extrapulmonary specimens is up to 95% in smear-positive specimens and 69% in smear-negative specimens.¹³¹ Median sensitivity varied by specimen type, with higher yield from lymph nodes (96%), cerebrospinal fluid (85%), and gastric aspirates (78%) and lower yield from pleural fluid (34%) and other non-pleural serous fluids (67%). Xpert MTB/RIF also has been applied with excellent diagnostic accuracy to stool specimens in people with pulmonary TB,¹³² which may provide an alternative for people with HIV who are being evaluated for TB and unable to expectorate.

The next-generation Xpert MTB/RIF Ultra improved the sensitivity of the existing test platform, but it is not currently approved by the U.S. Food and Drug Administration (FDA) or available in the