

THE PATHCARE NEWS

OPTIMIZING TB DIAGNOSTICS: PRIORITIZING MOLECULAR TESTING & CULTURE

We would like to highlight an update in the diagnostic approach to tuberculosis (TB) investigation. While smear microscopy for acid fast bacilli (AFB) has long been used for *Mycobacterium tuberculosis* complex (MTB) detection, it is no longer recommended as the initial rapid diagnostic test due to its low sensitivity and inability to distinguish MTB from non-tuberculous mycobacteria (NTM).

According to the World Health Organization (WHO), smear microscopy can miss a significant number of TB cases, particularly in individuals with low bacillary load such as children, people living with HIV, and those with extrapulmonary TB. Microscopy also does not detect drug resistance. The WHO now recommends **rapid molecular tests, TB PCR (e.g. GeneXpert)**, as the initial diagnostic test for all individuals being evaluated for TB, offering improved sensitivity and specificity, rapid identification of MTB and the detection of rifampicin and/or isoniazid resistance. However, **a negative PCR result does not rule out TB**, especially in cases with low bacterial load or extrapulmonary involvement. In such cases, **TB culture** remains essential.

TB culture remains the most sensitive method for the detection of MTB, particularly in cases where PCR results are negative, despite ongoing high clinical suspicion. It enables definitive diagnosis in paucibacillary disease, facilitates detection of all mycobacterial species including NTM, and allows for drug susceptibility testing (DST) of MTB isolates to guide appropriate therapy.

Important note on healthcare funders and reimbursement

Healthcare funders and medical aids are increasingly aligning their reimbursement policies with updated TB diagnostic guidelines. Therefore, only correctly motivated and guideline-aligned test requests are reimbursed. This implies:

- If only AFB smear microscopy (standalone) is requested, this will be re-imbursed. However, TB PCR and culture will not automatically be performed despite being the most appropriate tests for suspected new TB cases.
- TB PCR testing should always be the initial diagnostic test requested in suspected new TB cases.
- Culture is essential for TB PCR-negative or follow-up cases and must be specifically requested.
- Non-compliant or unjustified test requests may be declined by funders, leading to delays in care and unnecessary additional costs.

PathCare's TB Diagnostic Offerings

To support best practice and funder compliance, we offer the following structured TB diagnostic services as per the current General Request Form

TB	
MTBLAMAG	☐ MTB LAM Ag (urine)
Specimen type:	
Pulmonary TB:	
MTAURC	☐ Concentrated Auramine
C5057+MTBR	☐ GeneXpert & Culture
MTBR	☐ Follow up (Microscopy, culture, PCR ID & susceptibility if culture +)
Extra-pulmonary TB:	
MTBR	☐ Microscopy, culture, PCR ID & susceptibility if culture +
C5057+MTBR	☐ GeneXpert & Culture
MTBR	☐ Culture for BCG; PCR ID if culture +

1. MTB LAM Antigen (Urine) - MTBLAMAG

- Urine-based testing recommended in people living with HIV and advanced immunosuppression (CD4 <200)
- Unable to distinguish between MTB and NTM, and drug resistance detection

2. Smear Microscopy for AFB (Concentrated Auramine - MTAURC)

- Reserved for monitoring smear conversion in previously confirmed smear-positive cases
- Not suitable for initial diagnosis

3. TB Investigation: TB PCR (e.g. GeneXpert) & Culture - C5057 + MTBR

- Recommended for all new suspected TB cases
- Aligns with WHO and national guidelines

4. TB Culture only (Follow-up - MTBR)

- For follow-up testing (e.g., monitoring culture conversion after treatment initiation)

In addition, we also offer testing for determination of TB exposure and/or infection including both blood-based Interferon Gamma Release Assay (IGRA - K5150, QuantiFERON Gold®) and tuberculin skin testing (Mantoux - G4765).

WHO-Aligned testing policy: MTB Detected and Rifampicin-Susceptible

In accordance with WHO guidelines, if MTB is detected by PCR and rifampicin susceptibility is confirmed on sputum, no further diagnostic testing is required, and the laboratory will not proceed with culture in these cases. This supports rapid treatment initiation and reduces unnecessary laboratory processing. If culture is clinically indicated despite this result, please contact the laboratory for further testing.

Additional testing for NTM cases and Rifampicin-Resistant MTB

- For MTB cases where rifampicin resistance is detected, genotypic susceptibility to isoniazid, the fluoroquinolones, ethionamide and second-line injectables will be done once the culture is positive. In selected cases, clinicians may request direct testing on the original specimen. can only be done if concentration of MTB > low level detected.
- All culture-positive MTB isolates with rifampicin resistance will undergo routine testing for phenotypic resistance to selected antimicrobials (bedaquiline and linezolid +/- pretomanid) as recommended by national guidelines."
- If a non-tuberculous mycobacterium (NTM) is isolated on culture, the laboratory will proceed with identification to species level in medical aid funded patients', to guide appropriate clinical management.

If you have any questions or require support with test selection, please contact our microbiology team.

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On behalf of the PathCare Mycobacteriology Expert Group