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AMPATHCHAT

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Diagnosing Pulmonary TB

Introduction

According to the World Health Organisation (WHO) Global Tuberculosis Report of 2018, an estimated 10 million new cases of tuberculosis (TB) were reported in 2017. Although the synergism between *Mycobacterium Tuberculosis Complex* (MTBC) and HIV poses difficult diagnostic challenges due to an increased frequency of atypical presentations and smear-negative cases, the availability of molecular platforms have improved the laboratory diagnosis of active pulmonary tuberculosis (PTB) in this population. Consider PTB as part of the differential diagnosis in patients presenting with symptoms, clinical signs and epidemiologic risk factors as summarised in Table 1. Prompt diagnosis of active PTB facilitates timely therapeutic interventions and minimises community transmission.

Table 1: Clinical symptoms, signs and epidemiological factors suggestive of active TB infection

Symptoms	Clinical signs	Epidemiological factors
Cough > 2 weeks duration Fever Night sweats Unintentional weight loss Chest pain Dyspnoea Malaise Haemoptysis	Lymphadenopathy Tachypnoea Pyrexia Pleural effusion or consolidation Clubbing Wasting Immunological manifestations, e.g. erythema nodosum and phlyctenulosis	Health care workers Correctional services employees and prisoners Immunocompromised states (e.g. HIV and chronic corticosteroid therapy) Refugees/immigrants Previous history of TB Friends, family or co-workers with TB Mine workers and other congregate settings

Laboratory diagnosis

The diagnosis of PTB is definitively established by the isolation of MTBC from clinical specimens by means of TB culture. The submission of good-quality respiratory specimens lies central to a successful laboratory diagnosis (Table 2).

Additional diagnostic modalities, as summarised in Table 3, include sputum acid-fast bacilli (AFB) smear and nucleic acid amplification (TB PCR) testing. Interferon-gamma release assays (IGRA) play no role in the diagnosis of active PTB. A positive TB PCR from a sputum specimen (with or without AFB smear positivity) in a person at risk for PTB is considered sufficient evidence of MTBC infection unless the patient has a prior history of TB treatment. A positive TB PCR implies that the DNA of MTBC has been detected, but cannot distinguish between viable and dead MTBC. DNA from dead/non-viable AFBs can persist in the lungs for six months to two years following successful TB treatment, hence the need for a TB culture in patients with a history of previous TB.

The establishment of a definitive laboratory diagnosis of PTB may not be possible in 15 to 20% of patients with clinical PTB. Genotypic drug susceptibility testing (DST) can be performed where the most commonly known mutations are screened for with a PCR assay. This can be performed directly from clinical specimens that have sufficient amounts of MTBC DNA or from cultured isolates. Phenotypic DST can be performed on cultured isolates. This method will detect resistance, irrespective of the underlying mechanism. Figure 1 outlines a basic approach to a patient with suspected PTB.

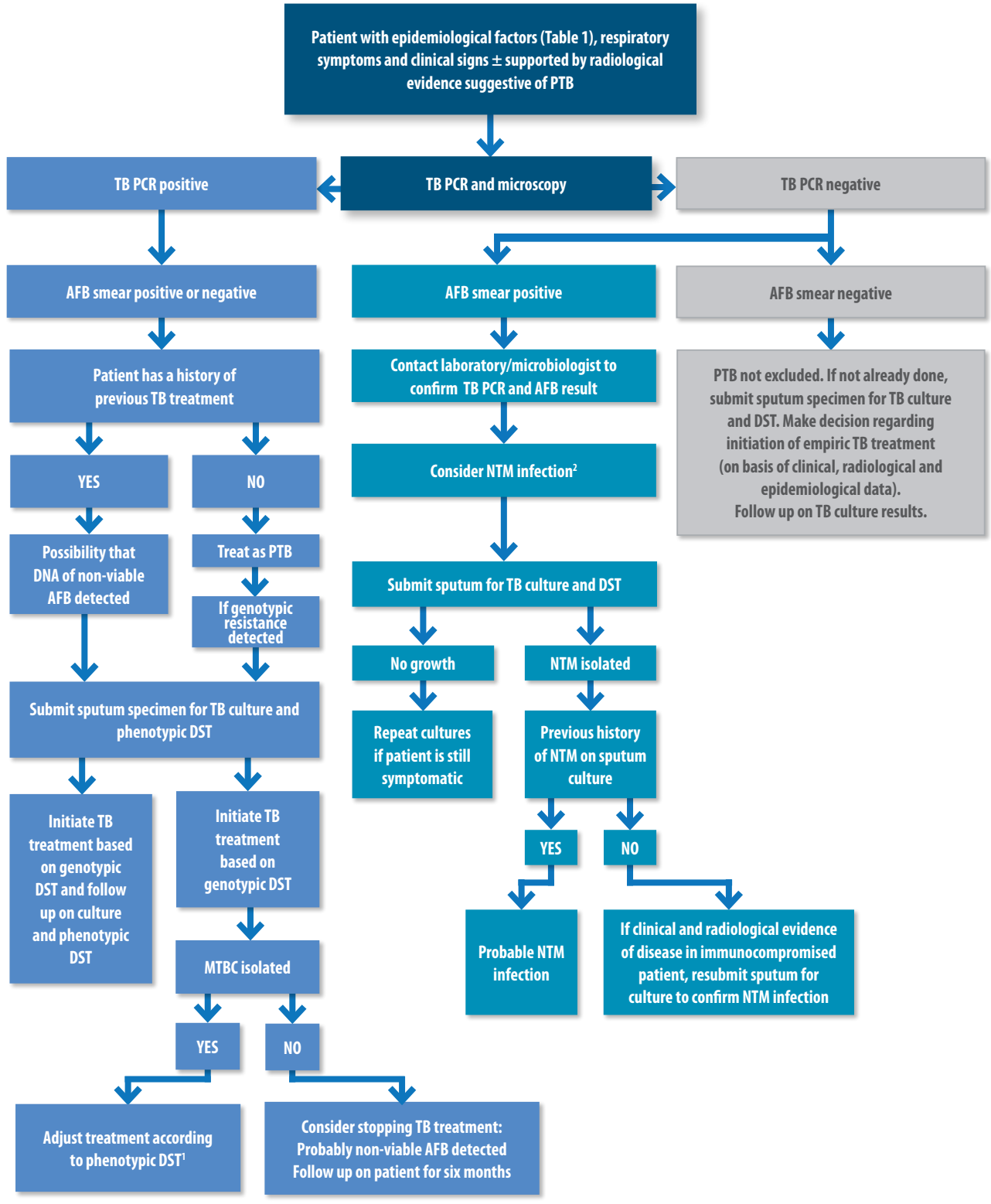
Table 2: Clinical specimen types to submit as part of the laboratory diagnosis of pulmonary TB

Adults		
Sputum (5 ml–10 ml)	**Expectorated sputum** – if able to voluntarily cough Instruct patients on the proper procedure (naso-pharyngeal discharge and saliva **not** desirable)	At least **three single specimens** should be collected over eight-hour intervals, of which one must be an early-morning specimen prior to eating
	Induced sputum – if unable to voluntarily cough Hypertonic saline nebulisation (3%) under supervision in a well-ventilated area	
Children		
Sputum (5 ml–10 ml)	**Induced sputum** is preferred to expectorated sputum Heated saline and salbutarol nebulisation plus suctioning	At least **three single specimens** should be collected over eight-hour intervals, of which one must be an early-morning specimen prior to feeds
Gastric aspirates (GA)	Useful in young children or where induction failed Perform lavage with 25–50 ml chilled, sterile, distilled water and place in sterile container	At least **three early morning** specimens collected on different days prior to child eating/ambulating
Adults and children		
Tracheal aspirate **Bronchoalveolar lavage/Bronchial brush** Minimum volume – 3 ml	BAL is useful if sputum specimens were inadequate and/or repeatedly negative in cases of high clinical suspicion of TB Collect washings or aspirates in sputum traps Place brushes in a sterile, leak-proof container with 5 ml sterile saline	Bronchoscopy performed in bronchoscopy theatre as outpatient/inpatient by pulmonologist

Table 3: Laboratory tests available for the diagnosis of pulmonary TB

Test	Sensitivity/limit of detection	Advantages	Disadvantages
Microscopy Ziehl Neelsen or Auramine stain	30–78% (Depending on HIV status) ≥10 000 bacilli/ml sputum	Rapid Inexpensive Used to monitor response to therapy	Lacks sensitivity in paucibacilliary cases (HIV and paediatric patients) Does not distinguish MTBC from other AFBs such as non-tuberculous mycobacteria and Nocardia Does not distinguish viable from dead AFBs Does not provide susceptibility information
TB PCR	63–95% (Depending on HIV status, PCR platform and specimen type) 50–100 bacilli/ml sputum	Rapid Genotypic susceptibility testing can be performed if sufficient DNA present	Relatively high cost Poor sensitivity in smear negative specimens Detects presence of MTBC DNA and not the presence of viable MTBC
		Performing a second TB PCR on a follow-up specimen from a pulmonary site if the first TB PCR is negative may increase sensitivity. Any further TB PCR testing from a pulmonary site cannot be justified and these samples must be submitted for TB culture	
Culture	80–85% 10–100 bacilli/ml sputum	Reference test Detects presence of viable AFBs Used for treatment monitoring Best option to diagnose MTB in HIV patients/children Species identification and phenotypic susceptibility testing possible	Turnaround time 1–6 weeks

Figure 1: Pulmonary Mycobacterium tuberculosis (PTB) diagnostic algorithm



[1] **Treatment failure:**
If AFB smear is positive at the end of the two-month induction phase of treatment, continue treatment for one more month. If AFB smear is still positive after three months, submit a specimen for culture and DST.

[2] **NTM diagnostic criteria:**
Clinical: Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or a high-resolution CT scan that shows multifocal bronchiectasis with multiple small nodules **and** appropriate exclusion of other diagnoses.
Microbiological: Positive culture results from at least two separate expectorated sputum samples; if the results are non-diagnostic, consider repeat sputum AFB smears and cultures **or** positive culture results from at least one bronchial wash or lavage **or** transbronchial or other lung biopsy with compatible histopathological features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histopathological features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture-positive for NTM.