Alabama Department of Public Health
Alabama Emergency Response Technology (ALERT)
Health Alert Network (HAN)
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TB Molecular Diagnostics

The Alabama Department of Public Health (ADPH), Bureau of Communicable Diseases, Division of Tuberculosis Control, encourages the use of Rapid Molecular Diagnostic Testing in sputum within the initial workup for patients suspected of pulmonary tuberculosis. ADPH is providing the following information to assist in earlier diagnosis of tuberculosis and of potential antibiotic resistance; so that effective treatment can be quickly initiated, and additional cases can be prevented.

ADPH has a dedicated team of TB professionals, committed to management of TB cases and TB infection, including a full time, board certified infectious disease physician. TB is a notifiable disease in Alabama, and ADPH encourages early consultation of our TB Team, in order to provide optimal outcomes and evidence-based management.

ADPH TB Control maintains an up-to-date website with a number of resources for professionals, as well as the public. For more information, please visit: https://www.alabamapublichealth.gov/tb/index.html.

ADPH Division of Tuberculosis Control

Rapid Molecular Diagnosis of Pulmonary and Meningeal Tuberculosis

Tuberculosis Xpert MTB/RIF (real-time PCR)

Nucleic acid amplification tests (NAAT) have been developed for rapid diagnosis of pulmonary tuberculosis (TB) in patient's sputum. They are also recommended to be used in cerebrospinal fluid (CSF) for diagnosis of TB meningitis.

Xpert MTB/RIF is one rapid molecular test recommended by the Centers for Disease Control (CDC) and the World Health Organization (WHO) for joint diagnosis of active tuberculosis and detection of rifampin (RIF) resistance in people suspected of having TB.

The test is available through the Alabama Department of Public Health, Bureau of Clinical Laboratories (BCL).

https://www.alabamapublichealth.gov/bcl/assets/bcl-requisition-form.pdf

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What is the role of Xpert MTB/RIF in the diagnostic work up?

Provides quick information: Xpert MTB/RIF simultaneously detects *Mycobacterium tuberculosis* complex (MTBC) and resistance to RIF in less than 2 hours. In comparison, standard cultures can take 2 to 6 weeks for MTBC to grow. Phenotypic drug resistance tests can add 3 more weeks.

Can detect the presence of MTBC among cases of sputum-acid-fast bacilli (AFB) smear negative: The pooled sensitivity of the test is 67% among patients whose smear was negative.

An additional diagnosis tool: Xpert MTB/RIF is not intended to replace the roles of AFB smear and culture in the diagnostic algorithm for TB; rather, it is complementary.

Results must be interpreted in conjunction with AFB smear and culture, along with clinical evaluation, imaging, and other laboratory studies.

MTBC culture remains the gold standard for TB diagnosis, drug susceptibility testing and genotyping.

When to use Xpert MTB/RIF?

It can be used in all individuals suspected of having TB, both children and adults.

It is especially useful for individuals suspected of having TB who are at risk of harboring drug-resistant TB, including adults and children who have been previously treated with anti-TB drugs and in whom TB has again been diagnosed.

It can be used for individuals suspected of having HIV-associated TB.

It can be used on adults suspected of having TB but who are not at risk of multidrug resistant (MDR)-TB or HIV associated TB.

NOTE: Xpert MTB/RIF can be used in cerebrospinal fluid (CSF) as an initial diagnostic test for TB meningitis, alongside CSF cytology, chemistry, and AFB smear microscopy and culture.

Xpert MTB/RIF can allow rapid initiation of TB treatment for either drug sensitive or MDR-TB

Xpert MTB/RIF sensitivity and specificity for pulmonary tuberculosis and RIF resistance

Xpert MTB/RIF sensitivity for TB detection is 85% (95% CI[1]:70-93%). Its specificity is 99% (95% CI: 97-99%).

The test is more sensitive for TB in smear-positive than smear-negative individuals and in HIV-negative as compared to HIV-positive persons.

Tuberculosis detection

Xpert MTB/RIF: Pooled sensitivity (among culture positive patients)		
Sputum	**Smear**	**HIV**
85%	(+): 98%	(+): 81%
	(-): 67%	(-): 88%

Xpert MTB/RIF has high sensitivity and specificity for the detection of RIF resistance.

Rifampicin resistance detection

X-pert MTB/RIF		
Pooled Sensitivity	96%	
Pooled Specificity	98%	

[1] CI: Confidence Interval

How to collect sputum

- Patients suspected of pulmonary TB disease must be placed in an airborne infection isolation (AII) room.
- Collect raw sputum or sputum sediment samples following your institution's standard procedures. The patient should be seated or standing.
- Sputum quality is critical both for the diagnosis of pulmonary TB and for the performance of the Xpert MTB/RIF assay.
- Xpert MTB/RIF is FDA-approved only for sputum from patients who have received no, or fewer than 3 days, anti-tuberculosis therapy.
- Spontaneously expectorated sputum should be representative of secretions from the lower respiratory tract; it usually appears purulent.
- Induced sputum: purulence is desirable, but induced sputum may have the appearance of saliva due to the saline that is used for its generation.

CSF volume & storage

- Send at least 3 mL of CSF.
- CSF that has less than 1mL volume will be QNS (quantity not sufficient) for smear, should be so noted on the smear slip, and the culture will still be performed.
- CSF specimens should remain at 15-25º C while in transit. Do not refrigerate.

Specimen Transport:

Follow ADPH BCL guidelines:
https://www.alabamapublichealth.gov/infectiousdiseases/assets/bcl_shipping_guidance.pdf

Table with adequate specimen volume

Required Specimen Volume	
	Volume x 1 test
Sputum	5-10 mL
Bronchial wash/ BAL	5-10 mL
CSF	3 mL

Sputum submission for Xpert:

Collect 3 sputum samples separated by 8 hours. One of them preferably a first morning, good quality sputum.

Submit for Xpert testing, regardless of the smear result.

Storage

Sputum sediment: Store resuspended sediments at 2–8 °C for up to seven days.

Raw sputum: Transport and store specimens at 2–8 °C before processing whenever possible. Raw sputum specimens should be transported to the BCL within 24 hours and not to exceed 3 days from collection.

CSF: Transport and store specimens at 15-25° C, preferably within 24 hours of collection.

All specimens should be transported/shipped following Department of Transportation (DOT) guidelines.

Where to send the sputum or CSF?

Bureau of Clinical Laboratories
204 Legends Court
Prattville, AL 36066

References

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7. Xpert MTB/RIF for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Infectious Diseases Group. 2019
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