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***Using Rapid DNA Tests (NAATs) Effectively for Rapid
Mycobacterium Tuberculosis Detection***

Division of Public and Behavioral Health

DPBH Tuberculosis (TB) Program in Conjunction with
Nevada's Local Health Department TB Program Partners



7/21/2022

Helping people. It's who we are and what we do.



Preface

Please use this presentation along with the Technical Bulletin, [Rapid NAA Tests for MTB Detection](#), published by the Division of Public and Behavioral Health Tuberculosis Program in April 2022.

The Technical Bulletin can be found on the DPBH TB Program website and the references and resources for this presentation can be accessed through this bulletin.

After a brief review of NAATs, 3 clinical case scenarios will be presented for consideration, questions, and answers.

Acknowledgment:

This presentation was supported by the Nevada State Department of Health and Human Services through Grant Number NU52PS910224 from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Department nor the Centers for Disease Control and Prevention.





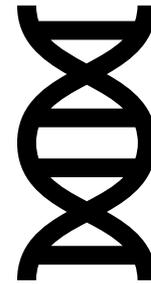
Definition of a NAAT

- NAAT is an acronym for Nucleic Acid Amplification Test.
- It is a rapid molecular test to detect the presence of DNA specific to MTB (or other organisms), results within 24-48 hours.
- Similar rapid molecular test names:
 - PCR, Polymerase Chain Reaction;
 - “DNA rapid test”, an everyday term;
 - XpertMTB/Rif[®], a proprietary test from Cepheid that additionally detects Rifampin resistance.



Goals of NAATs in MTB Detection

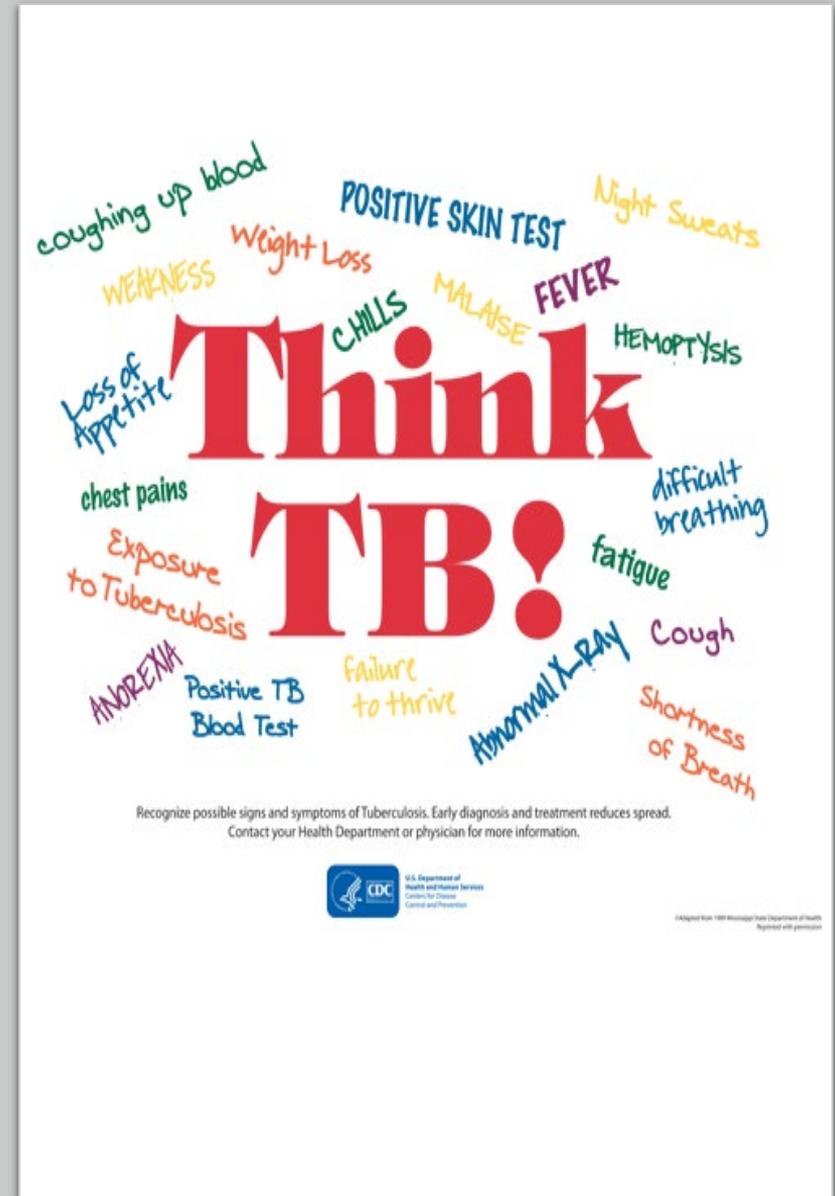
- To be the *standard of care* for use as a rapid molecular test to detect *Mycobacterium tuberculosis* (MTB) in sputum specimens when tuberculosis (TB) disease is being considered.
- To facilitate initiation of anti-TB therapy earlier.
- For identification of non-tuberculous mycobacterium (NTM) rapidly and the subsequent modification to the patient's airborne isolation.



When to order NAATs

A NAAT should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established.

- First respiratory specimen: Order AFB, culture, & NAAT; *note*: a minimum of 5 ml of the specimen must be collected.
- Second NAAT: When higher suspicion of TB disease exists, order along with second AFB & culture.
- A total of 3 respiratory specimens, collected 8-24 hours apart, should be tested for AFB & culture (a 3rd NAAT is not necessary).



Interpretation of NAAT MTB Results



AFB Result	NAAT Result		Action
AFB (+)	NAAT (+)		Presume TB disease and initiate anti-TB treatment; a total of 3 specimens for AFB/cultures should be obtained
AFB (-)	NAAT (+)		Order 2 nd NAAT along with AFB/culture
2 nd AFB (-)	2 nd NAAT (+)		Presume TB disease and initiate anti-TB treatment
AFB (+)	NAAT (-)		Order 2 nd NAAT with AFB/culture
2 nd AFB (+)	2 nd NAAT (-)		Presume infected with non-tuberculous mycobacterium (NTM); airborne isolation may be discontinued if consistent with other clinical findings
AFB (-)	NAAT (-)		Order 2 nd NAAT with AFB/culture
2 nd AFB (-)	2 nd NAAT (-)		Unlikely TB disease; airborne isolation may be discontinued if consistent with other clinical findings



Case Scenario 1

(Answers are provided in the following slide.)

A previously well 58-year-old security officer who works in the correctional system is admitted to the hospital; he presents with:

- Complaint of a cough, fatigue, and a 20-pound weight loss over the past two months.
- He is a type 2 diabetic on Metformin with a hemoglobin A1C of 9%.
- A chest x-ray demonstrates a nodular lesion in the right upper lobe with central lucency confirmed by a CT scan to represent cavitation.
- He is placed in airborne respiratory isolation. Antibiotic therapy with azithromycin and ceftriaxone is initiated.
- Three specimens are sent for AFB stains and the results are negative.
- There is no improvement on antibiotic therapy after one week.

Questions:

- 1) Are signs and symptoms consistent with active TB disease?**
- 2) The next most appropriate step in the management of this patient is:**
 - A) Arrange for diagnostic bronchoscopy
 - B) Order a NAAT for detection of *M. tuberculosis*
 - C) Add anti-fungal therapy directed at Coccidioidomycosis



Scenario 1 Answers

1. Are signs and symptoms consistent with active TB disease?

Yes.

Symptoms consistent with TB: Cough > 3 weeks, unexplained weight loss, fatigue

Signs consistent with TB: Chest x-ray & CT scan demonstrate upper lobe involvement and suggestive of TB, cavitory lesion

2. The next most appropriate step in the management of this patient is:

Order a NAAT; NAATs performed on expectorated sputa will detect 60-70% of culture-positive pulmonary TB cases that are AFB smear-negative.

Takeaways from Case 1: AFB (-)/NAAT (+)

Obtaining a NAAT on the initial workup would have greatly expedited diagnosis and avoided unnecessary treatment and prolonged hospitalization. A bronchoscopy is unnecessary as expectorated sputum can be obtained and anti-TB treatment initiated immediately after positive NAAT results.



Case Scenario 2

A 57-year-old high school French teacher undergoes her initial cancer CT chest screening and is found to have a left upper lobe cavitory lesion.

History:

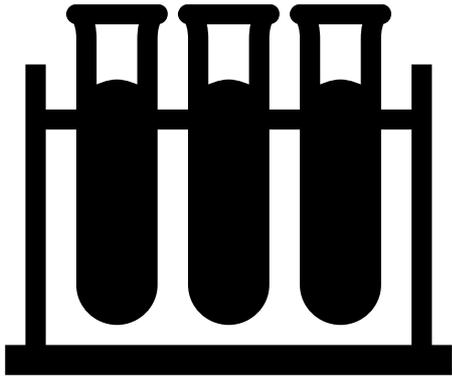
- 50 pack-year smoking
- Travel outside of the U.S. to vacation in France for two weeks, 10 years ago
- 10 pounds involuntary weight loss
- Respiratory symptoms – chronic morning cough
- Past TB skin test negative
- Recent TB blood test, IGRA, negative

Hospital Admission:

- Placed on respiratory isolation
- Upon admission 1st sputum specimen was obtained, and a 2nd sputum specimen was obtained the next morning; AFB, culture, and NAATs ordered
- By evening day 2 in the hospital, both specimens are AFB and NAAT negative

Question:

Can this patient be safely removed from respiratory isolation on the evening of hospital day 2?



Scenario 2 Answer

Can this patient be safely removed from respiratory isolation on the evening of hospital day 2?

Yes.

This patient has repeated negative testing in the past for latent TB infection and has no significant risk factors for ongoing or recent exposure.

Therefore, a low clinical probability of TB disease.

For patients with a low to low-intermediate clinical probability of TB, a negative NAAT on a good quality expectorated sputum specimen, confirmed by a second negative specimen, has a 99% negative predictive value for TB, thus enabling removal from airborne respiratory isolation and pursuit of an alternative diagnosis.

Note: In patients with a high clinical risk for TB disease and in whom an alternative diagnosis has not been established, additional testing may be appropriate before removing from isolation.

Takeaways from Case 2: AFB (-)/NAAT (-)

A patient with low clinical risk for TB despite a suggestive chest x-ray illustrates how obtaining NAATs on initial evaluation can facilitate early removal from airborne respiratory isolation.



Case Scenario 3

A 61-year-old female is evaluated for a chronic productive cough for years.

History:

- Always a non-smoker
- Works from home as a travel agent
- Medication(s): OTC multivitamin
- Prior treatments with antibiotics, empiric asthma regimens, and GERD regimens have not improved symptoms
- No family history of lung disease

Current diagnostics:

- Chest CT scan demonstrates central bronchiectasis which has progressed over the past year.
- Expecterated sputum analysis: 2 specimens, both AFB positive and NAAT for MTB negative.

Question: Which of the following is most likely correct for this patient?

- A) The patient has pulmonary tuberculosis.
- B) The positive AFB stains are false positives and should be disregarded.
- C) The patient has an active non-tuberculous mycobacterial infection (NTM).





Scenario 3 Answer

Which of the following is most likely correct for this patient?

Answer: C, non-tuberculous mycobacterial infection

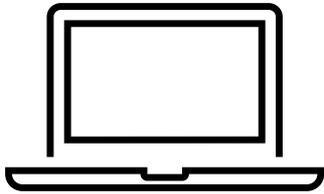
Repeated negative NAATs in specimens that are AFB positive imply colonization or infection with a non-tuberculous mycobacteria (NTM). This case meets the criteria for an active infection and the sputum specimen isolates should be characterized (identified) by culture and sensitivity testing.

In the U.S., NTM infections are more common than TB disease.

Takeaways from Case 3: AFB (+)/NAAT (-)

Obtaining NAATs early in the workup facilitates a diagnosis of NTM disease.





For More Information

- Contact the Division of Public and Behavioral Health Tuberculosis Program Manager, Susan McElhany, DMD, at smcelhany@health.nv.gov
- Visit the [Centers for Disease Control and Prevention Tuberculosis website](#)
- Visit the Division of Public and Behavioral Health's [Tuberculosis website](#)
- Contact your local health department's Tuberculosis Program

