Interim guidance on the use of nucleic acid amplification tests (including Cephiad Xpert® MTB/RIF assay) on making decisions related to airborne infection isolation (AII).

Background

The package insert for the Cephiad Xpert® MTB/RIF assay was recently changed to reflect approval from the U.S. Food and Drug Administration (FDA) for expanded claims within the product label of its Xpert MTB/RIF test related to airborne infection isolation (AII). This test is one of several nucleic acid amplification tests (NAAT) approved for the diagnosis of active tuberculosis. This label change was supported by new data collected and recently reported by the Centers for Disease Control and Prevention (CDC) on the use of the Xpert MTB/RIF in making isolation decisions. In the following document, we provide updated guidance regarding AII decision-making involving patients suspected to have TB disease.

New AII recommendations based on NAAT results

Recent data supports the use of two negative NAAT results from sputum* specimens (no matter the smear result) as sufficient for removing a patient suspected of having TB from isolation. This recommendation is based upon two recently published documents by CDC. In the Availability of an Assay for Detecting *Mycobacterium tuberculosis*, Including Rifampin-Resistant Strains, and Considerations for Its Use - United States, 2013, CDC recommended NAAT results could be interchangeable with sputum smear results, so a combination of three consecutive negative tests from either smear or NAAT would suffice to declare a patient noninfectious.[1] In the 2014 Revised Device Labeling for the Cepheid Xpert MTB/RIF Assay for Detecting *Mycobacterium tuberculosis*, CDC provided an overview of the label change approved by FDA supporting the use of the Xpert MTB/RIF in making decisions about AII.[2] The data used to support this label change were recently reported at an international conference. This data suggested 97% of patients with sputum smear positive TB were detected with one NAAT result, and 100% were detected when an additional NAAT was used.[3]

To rule out TB disease, we recommend at least three sputum specimens be obtained greater than eight hours apart (one of these obtained in the morning) for AFB smear and culture.[4] The first sputum should also be sent for NAAT.[5] If the first NAAT is negative, then a patient may be released from AII after either a second negative NAAT **or** a combination of three negative sputum smear and/or NAATs from different sputum specimens.

** Data does not support substituting bronchoalveolar lavage (BAL) for sputum specimens in decision making related to AII.*

Summary:

- **All TB suspects should have three sputum specimens obtained at least eight hours apart (one of these obtained in the morning) for AFB smear microscopy and AFB culture.**
- **At least one of these specimens should be submitted for NAAT.**
- **Patients with any combination of three negative sputum smears or NAATs collected at least eight hours apart can be released from isolation.**
- **Alternatively, patients with two negative NAATs, regardless of smear results, can be released from isolation. In such cases where smears are positive, they can be attributed to nontuberculous mycobacteria (NTM).**

Examples:

Results are:

Sputum #1 NAAT negative, smear positive, culture pending

Sputum #2 NAAT negative, smear positive, culture pending

Sputum #3 smear positive, culture pending

Conclusion: Most likely NTM. Consider discontinuing AII. If patient is highly suspected to have MTB or resides/works in a high-risk setting (e.g., correctional facility, homeless shelter) obtain additional NAAT results or consult with TB expert.

Results are:

Sputum #1 NAAT negative, smear not done, culture pending

Sputum #2 smear negative, culture pending

Sputum #3 smear negative, culture pending

Conclusion: Most likely noninfectious. Discontinue AII.

References

1. CDC. Availability of an Assay for Detecting *Mycobacterium tuberculosis*, Including Rifampin-Resistant Strains, and Considerations for Its Use — United States, 2013. MMWR 2013;62(41):821-824
2. CDC. Revised Device Labeling for the Cepheid Xpert MTB/RIF Assay for Detecting *Mycobacterium tuberculosis*, MMWR 2014; 64(07); 193.
3. Luetkemeyer A, Firnhaber C, Kendall MA, Wu X, Benator D, Mazurek G, Havlir D, Grinsztein B, Alland D. Xpert MTBI/RIF versus AFB Smear to Determine Respiratory Isolation of U.S. Tuberculosis Suspects. Poster presented at Conference on Retroviruses and Opportunistic Infections; 2015 February 23-26; Seattle, WA.
4. CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. MMWR 2005;54(No. RR-17).
5. CDC. Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. MMWR 2009;58:7–10.

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