Nontuberculous *Mycobacterium* (NTM) Species
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Nontuberculous *Mycobacterium* (NTM) Species

Overview [2, 3, 4, 5, 6, 7]

The *Mycobacterium* genus comprises more than 120 different species and is distributed worldwide. Among them are pathogenic species which can cause serious diseases in humans and animals. Synonyms of "Nontuberculous Mycobacteria (NTM)", are "Mycobacteria Other Than Tuberculosis" (MOTT) or "Atypical Mycobacteria." NTM refers to all the species in the family of mycobacteria that may cause disease, other than the *Mycobacterium tuberculosis* (TB) complex [i.e. *M. tuberculosis, M. africanum, M. bovis, M. canettii, M. microti, M. caprae, M. orygis*, and *M. pinnipedii*,] and *M. leprae* which can cause Hansen's disease (leprosy).

Every year in the United States approximately two people per 100,000 population develop mycobacterioses caused by these lesser-known "cousins" of TB and leprosy. NTM produces the following major clinical disease syndromes: chronic bronchopulmonary disease, cervical or other lymphadenitis, skin and soft tissue disease, skeletal infection, disseminated infection, and catheter-related infections. Clinical features are dependent on the organism and the site of infection, but are usually chronic and have a progressive clinical course. Being classical opportunists, NTM predominantly infect patients already suffering from pulmonary diseases or immunodeficiency (e.g., HIV-infection) or other chronic antecedent illness. The number of mycobacterioses is increasing among immunocompetent person. Furthermore, NTM infections are emerging in previously unrecognized settings, with new clinical manifestations. Another major factor contributing to increased awareness of the importance of NTM as human pathogens is improvement in methodology in the mycobacteriology laboratory, resulting in enhanced isolation and more rapid and accurate identification of NTM from clinical specimens.

NTM may cause both asymptomatic infection and symptomatic disease in humans. Asymptomatic infection with NTM has not been shown to lead to latent infection, so that in contrast to TB, there is currently no evidence that NTM are associated with reactivation disease. Symptoms of mycobacterioses can include fever or chills, night sweats, weight loss, abdominal pain, fatigue, diarrhea, swollen glands and anemia. You may develop other problems such as blood infections, hepatitis, and pneumonia.

Many of the NTMs are ubiquitous and readily recovered from the environment. NTM are found in soil, dust, food, water (fresh and sea), animals, plant material, and birds. Most infections appear to be acquired by ingestion, aspiration, or inoculation of the organisms from these natural sources; however the specific source of individual infections is usually not identified. No evidence of person-to-person transmission has been reported. Tap water is considered the major reservoir for the most common human NTMs. Species from tap water include *M. gordonae, M. kansasii, M. xenopi, M. simiae, M. avium* complex, and rapidly-growing *Mycobacterium*, especially *M. mucogenicum. M. kansasii, M. xenopi*, and *M. simiae* are recovered almost exclusively from municipal water sources and rarely, if ever from other environmental sources.[4]

NTM infections (if treated) are treated with very strong antibiotics. Treatment may last a full year or two. The antibiotics used can cause severe side effects, so doctors carefully monitor

patients being treated for mycobacterioses. For a complete description of NTM refer to the following texts:

- American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases.* 29th ed; 2012.
- Mandell GL, Bennett JE, Dolin RD, eds. *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 7th ed; 2010.
- An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases January 2007.

2007 Case Definition – (1/15)[4]

NTM *Lung Disease - Clinical Description*

1. Pulmonary symptoms, nodular or cavitary opacities on chest radiograph, or an HRCT scan that shows multifocal bronchiectasis with multiple small nodules. **And**
2. Appropriate exclusion of other diagnoses.

NTM *Lung Disease - Laboratory Criteria for Diagnosis*

1. Positive culture results from at least two separate expectorated sputum samples. (If the results from the initial sputum samples are nondiagnostic, consider repeat sputum AFB smears and cultures.) **Or**
2. Positive culture results from at least one bronchial wash or lavage. **Or**
3. Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB) and positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) and one or more sputum or bronchial washings that are culture positive for NTM.

NTM *Lung Disease - Case classification*

Confirmed: A clinically compatible illness that is culture confirmed.

COMMENTS: Expert consultation should be considered when NTM are recovered that are either infrequently encountered or that usually represent environmental contamination. Patients who are suspected of having NTM lung disease but who do not meet the diagnostic criteria should be followed until the diagnosis is firmly established or excluded. Making the diagnosis of NTM lung disease does not, *per se*, necessitate the institution of therapy, which is a decision based on potential risks and benefits of therapy for individual patients.

NOTE*:** These criteria fit best with *Mycobacterium avium* complex (MAC), *M. kansasii*, and *M. abscessus*. There is not enough known about most other NTM to be certain that these diagnostic criteria are universally applicable for all NTM respiratory pathogens. ***Important: A patient that is positive with a NTM infection can have false positive PPD skin tests. NTMs are a reportable condition in Missouri, but are currently **not** a nationally notifiable disease.

Other Mycobacterioses - Case classification

Confirmed: A clinically compatible illness that is culture confirmed.

Information Needed for Investigation

Many of these species are ubiquitous and are found in soil, food, water and animals, and are not transmittable person-to-person. If the person is on a public water system please document the water district information (e.g. Water District #12; Anywhere, Mo) on the lab slip or on Disease Case Report (CD-1).

Notification

NTM infections or (MOTT) are a Category III condition and should be reported within three (3) days of first knowledge or suspicion by telephone, facsimile or other rapid communication to the local health authority or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7).

Control Measures[2, 4, 6]

General Recommendations[2]

Control measures include chemoprophylaxis for high risk patients with HIV infection, avoidance of tap water contamination of central venous catheters, surgical wounds, skin antisepsis, or endoscopic equipment, and use of sterile equipment for middle-ear instrumentation, including otoscopic equipment. Additional information is available at: An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases and:

- American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases.* 29th ed; 2012.
- Mandell GL, Bennett JE, Dolin RD, eds. *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 7th ed; 2010.

NTM *Lung Disease*[4]

The minimum evaluation of a patient suspected of NTM lung disease should include (*1*) chest radiograph or, in the absence of cavitation, chest HRCT scan; (*2*) three or more sputum specimens for AFB analysis; and (*3*) exclusion of other disorders such as tuberculosis (TB) and lung malignancy. In most patients, a diagnosis can be made without bronchoscopy or lung biopsy.

Disease caused by *M. tuberculosis* is often in the differential diagnosis for patients with NTM lung disease. Empiric therapy for TB, especially with positive AFB smears and results of nucleic acid amplification testing, may be necessary pending confirmation of the diagnosis of NTM lung disease.[4] For additional information on TB see MDHSS' Tuberculosis Case Management Manual.

Laboratory Procedures

NTM are often isolated when testing for *M. tuberculosis*. The Missouri State Public Health Lab (MSPHL) processes NTM and encourages specimen submission to their facilities located in Jefferson City, MO. Clinical specimens may take up to 6 weeks before a final report is released. Reference isolates submitted for identification purposes may only take up to 2 weeks before a final report is released. Currently the MSPHL performs this testing at no charge to the

submitting laboratory. ***NOTE***: Information on the collection and/or shipment of specimens for NTM testing by the MSPHL may be viewed at: http://health.mo.gov/lab/hplc.php.

Reporting Requirements

Nontuberculous mycobacteria (NTM) or (MOTT) are a Category 3 disease and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services (MDHSS) within three (3) calendar days of first knowledge or suspicion.

NTM is **not** a nationally notifiable condition.

1. For all reported cases – [see the Information needed for Investigation section].
2. Entry of the completed information into WebSurv negates the need for the paper CD-1 or lab report to be forwarded to the District Health Office.
3. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).
4. If an outbreak is associated with the consumption or use of water for drinking, or with ingestion, contact, or inhalation of recreational water, a CDC 52.12 form (National Outbreak Reporting System - Waterborne Disease Transmission) is to be completed and submitted to the District Communicable Disease Coordinator at the conclusion of the outbreak.
5. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

References

1. American Public Health Association. *Diseases Due to Other Mycobacteria*. In D. Heymann (Ed.), *Control of Communicable Diseases Manual*. 19th ed. Washington, DC: American Public Health Association; 2008: 659-660.
2. American Academy of Pediatrics. *Diseases Caused by Nontuberculous Mycobacteria*. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases.* 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012: 759-767.
3. Churchill Livingstone Elsevier. *Infections Due to Nontuberculous Mycobacteria Other than Mycobacterium avium-intracellularei.* Brown-Elliott, BA and Wallace Jr., RJ, In: Mandell GL, Bennett JE, Dolin RD, eds. *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 7th ed; 2010: 3191-3198.
4. An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases. This Official Statement of the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) was adopted by the ATS Board Of Directors, September 2006, and by the IDSA Board of Directors, January 2007. (1/15).
5. Centers for Disease Control and Prevention. National Center for Emerging and Zoonotic Infectious Diseases, Division of Foodborne, Waterborne, and Environmental Diseases. In: *Other Mycobacterium Species.* http://www.cdc.gov/nczved/divisions/dfbmd/diseases/nontb_mycobacterium/technical.html (1/15).

6. American Lung Association. Illinois, United States. In: Lung Disease. *Nontuberculosis Mycobacterium.* http://www.lung.org/lung-disease/nontuberculosis-mycobacterium/ (1/15).
7. Hain Lifescience GmbH. Tübingen, Germany. In: Microbiology, *Mycobacteria*. http://www.hain-lifescience.de/en/products/microbiology/mycobacteria/mycobacteria.html (1/15).