Proposed Investigation/Reporting Thresholds and Outbreak Definition for Extrapulmonary Nontuberculous Mycobacteria (NTM)
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A. Background
The thresholds and outbreak definition presented below are based on available scientific resources and expert opinion and intended only as guidance; states and localities may have their own outbreak definitions and reporting requirements.

Nontuberculous mycobacteria (NTM) are opportunistic pathogens that can be difficult to diagnose and treat. Pulmonary disease, the most common clinical manifestation of NTM infection, often affects individuals with underlying lung disease. Although extrapulmonary NTM infections are less common than pulmonary infections, they are often associated with severe disease and poor outcomes, even among immunocompetent individuals. Outbreaks of extrapulmonary NTM infections in the United States have been increasingly linked with healthcare exposure, and healthcare-associated outbreaks have been associated with medical devices, cosmetic procedures, dental procedures, and contaminated parenteral medications, among other sources. Non-healthcare settings associated with extrapulmonary NTM outbreaks include tattoo parlors, nail salons, and spas. Given the nonspecific symptomatology and lengthy delay between exposure and symptom onset, outbreaks of extrapulmonary NTM infections can be difficult to detect. Early detection can be facilitated by the use of outbreak definitions and case thresholds for investigation and reporting. Early detection, in turn, can speed implementation of interventions to prevent disease spread.

Importantly, a case definition and investigative/reporting thresholds should be applied regardless of location of disease onset, whether in a healthcare facility or community-based setting.

NOTE: The following definitions and thresholds may be applied across all types of healthcare facilities, including acute care hospitals, critical access hospitals, long-term acute care hospitals, long-term care facilities with vented patients, long-term care facilities, dialysis facilities, outpatient facilities, emergency departments.

B. Outbreak Detection and Reporting

1. Case Definition:
NTM are mycobacterial species other than *M. tuberculosis* complex species and *M. leprae*. An extrapulmonary NTM infection is indicated by a positive culture or positive molecular test result, such as findings from polymerase chain reaction (PCR) or 16S ribosomal RNA gene sequencing (16S) of organisms taken from at least one of the following extrapulmonary sites:
   - Skin or soft tissue
   - Lymph node
   - Urine
   - A normally sterile body site, such as blood, spinal fluid, bone marrow, abdominal fluid, pleural fluid, or bone.

The following *cannot* be used as the basis for confirming a case of NTM infection:
   - Cultures or molecular evidence positive for *M. tuberculosis* complex or *M. leprae*
• Cultures or molecular evidence from lower respiratory specimens, including sputum, bronchial alveolar lavage, tracheal aspirate culture, or lung tissues
• Cultures or molecular evidence from stool specimens

2. Proposed Investigation/Reporting Thresholds and Outbreak Definition for Extrapulmonary Nontuberculous Mycobacteria

Investigative/Reporting Thresholds for all Healthcare Settings:
• Threshold for additional investigation by facility:
  o 1 case of extrapulmonary NTM
• Threshold for public health reporting:
  o 1 case of extrapulmonary NTM, excluding advanced HIV with disseminated mycobacterium avium complex

Outbreak Definitions for all Healthcare Settings:
• ≥2 cases of epidemiologically-linked extrapulmonary NTM (excluding advanced HIV with disseminated mycobacterium avium complex) within a one-year period. Evidence of epidemiological linkage includes, but is not limited to, shared water sources, similar surgical procedures, usage of common medical devices or equipment, similar medications. Multiple species of Mycobacteria may be involved in the same outbreak.

3. Points for Consideration:
• When a healthcare-associated case is identified, the healthcare facility should prepare a line list of exposures.
• Medical tourism should be considered a possible source of extrapulmonary NTM infection and requires additional investigation and collaboration with federal, state and/or local partners.6
• Extrapulmonary NTM infection outbreaks have been associated with medical devices, cosmetic procedures, contaminated parenteral medications, medical tourism, tattoo parlors, nail salons, and spas. These infections are a cause of both sporadic and healthcare-associated infections in the United States.
• Although the Council of State and Territorial Epidemiologists standardized case definition for extrapulmonary NTM includes clinical evidence of infection, the thresholds and definitions used in this document do not necessarily include clinical evidence to allow detection of potential pseudo-outbreaks.4 Initial thresholds for identifying extrapulmonary NTM infection include laboratory evidence only, since clinical evidence may not be available until additional facility investigation is underway.
• Pediatric lymph node infections with NTM are common and typically do not require further investigation unless related to a dental surgery or invasive procedure.3
• M. gordonae is known to be a contaminant in pulmonary specimens. However, less is known about whether M. gordonae is more often a pathogen versus a contaminant in extrapulmonary specimens; rare case reports of M. gordonae causing extrapulmonary disease exist. Health jurisdictions may consider including detection of M. gordonae in extrapulmonary specimens as the basis for a clinical case in order to better understand the clinical and epidemiological significance of these findings. However, it is unclear whether the
benefit of *M. gordonae* reporting to identify NTM outbreaks merits the resources required to investigate these cases.\textsuperscript{4}

C. **Key Resource:**

D. **References:**

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