

GUIDELINES FOR THE DIAGNOSIS OF PULMONARY NONTUBERCULOUS MYCOBACTERIAL DISEASES—2008

April 2008

The Nontuberculous Mycobacteriosis Control Committee
of the Japanese Society for Tuberculosis
The Scientific Assembly for Infection and Tuberculosis
of the Japanese Respiratory Society

Introduction

The American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) revised the Guidelines for Nontuberculous Mycobacterial (NTM) Lung Diseases after an interval of ten years and published the revised Guidelines in March 2007¹⁾.

The Nontuberculous Mycobacteriosis Control Committee of the Japanese Society for Tuberculosis found substantial amendments in the revised US version of the Guidelines mentioned above and, with an aim of maintaining international consistency, decided it necessary to review the Japanese diag-

nostic criteria for nontuberculous mycobacteriosis that were released in 2003²⁾. The Committee then performed a survey by questionnaire of the councilors of the Japanese Society for Tuberculosis. All responders (126 responders; response rate 63%) recognized the necessity of revision and many of them expressed a demand for simple diagnostic criteria.

Under these circumstances, review and revision works were initiated. The Diagnostic Criteria of Pulmonary Nontuberculous Mycobacteriosis, established jointly by the Japanese Society for Tuberculosis and the Japanese Respiratory Society, are described here.

Table 1 Diagnostic criteria of pulmonary nontuberculous mycobacteriosis (established jointly by the Japanese Society for Tuberculosis and the Japanese Respiratory Society)

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- A. Clinical criteria (The two criteria stated below must be met.)
1. Chest imaging examinations (including high resolution computed tomography [HRCT]) indicate one or more findings of the following: nodular opacities, dissemination of small nodular or branching opacities, homogeneous opacities, cavitary opacities, or bronchiectasis or bronchiolectasis.
However, this criterion does not apply if opacities due to any preceding lung diseases have already existed.
 2. Other diagnoses can be excluded.
- B. Bacteriologic criteria (One of the criteria listed below must be met irrespective of the NTM species.)
1. Positive culture results from at least two separate expectorated sputum specimens are obtained.
 2. Positive culture results from at least one bronchial washing sample are obtained.
 3. In the case of transbronchial lung biopsy or other lung biopsied tissue, both histologic findings indicative of mycobacteriosis and positive culture results from at least one tissue specimen, bronchial washing sample or sputum specimen are obtained.
 4. For a species that is rarely encountered or frequently isolated from the environment, irrespective of the sample type, at least two positive culture results and tests for species identification will be necessary as a rule, and in addition, expert consultation will be required.

The above-stated criteria A and B must be met.

Table 2 Nontuberculous mycobacteria that have been reported to cause infections in humans in Japan

NTM species that are frequently noted.

M. avium, *M. intracellulare*, *M. kansasii*, *M. abscessus*

NTM species that are relatively rarely noted.

M. fortuitum, *M. chelonae*, *M. szulgai*, *M. xenopi*, *M. nonchromogenicum*, *M. terrae*, *M. scrofulaceum*,
M. gordonae, *M. simiae*, *M. shimoidei*, *M. thermoresistibile*, *M. heckeshornense*, *M. intermedium*, *M. lentiflavum*,
M. ulcerans subsp. *shinshuense*, *M. malmoense*, *M. branderi*, *M. celatum*, *M. genavense*, *M. haemophilum*,
M. triplex, *M. goodii*, *M. marinum*, *M. mageritense*, *M. mucogenicum*, *M. peregrinum*

Note: *M. avium* and *M. intracellulare* are similar to each other in properties and are frequently referred to collectively as the *M. avium* complex (MAC).

Notice:

1. On the basis that NTM diseases can be diagnosed prior to the occurrence of clinical symptoms in regular medical checkups and thorough physical examinations in Japan currently, due to the advancement in diagnostic imaging, nucleic acid-based diagnostic techniques and other relevant technologies, "the presence of clinical symptoms" was excluded from the present diagnostic criteria.
2. In the traditional diagnostic criteria, it was understood by unspoken consent that the time at which the diagnostic criteria were met was regarded as the time of treatment initiation. In the revised diagnostic criteria, however, as in the 2007-ATS/IDSA criteria, the time of establishing the diagnosis is separated from the time of initiating treatment.
3. At the time of treatment initiation, although relevant evidence may not have yet been accumulated, attention should be paid to the fact that when the post-diagnosis strategy is to monitor a clinical course without any other interventions performed, the monitoring alone will miss a chance of starting early treatment, including surgical intervention, and of achieving an outcome regarded as a quasi-healing status.
4. In the 2007-ATS/IDSA criteria, only a HRCT scan showing "multifocal bronchiectasis with disseminated small nodules" was included. However, in the revised diagnostic criteria, the imaging criteria capable of fitting more extensive phenomena are stipulated in consideration of patients who are diagnosed early as having the disease, who have already started to receive chemotherapy, or who show a solitary pulmonary nodule.
5. In accordance with the principle of diagnosing infectious diseases, a diagnosis solely based on imaging findings will never be accepted, even for a patient showing typical radiological features. In addition, attention should be paid to the fact that even if radiological findings from a particular patient are strikingly similar to those with NTM diseases, the patient may not suffer from NTM disease.
6. One of the reasons why the present diagnostic criteria stipulate positive culture results from at least two separate expectorated sputum specimens is that the criterion is in accordance with the study of Tsukamura in 1991³⁾ and the other reason is consistency with the 2007-ATS/IDSA criteria.
7. In the revised diagnostic criteria, the requirement for a bacillary dose in smear and culture specimens was abolished, again for the purpose of maintaining consistency with the 2007-ATS/IDSA criteria. In addition, the abolishment is based on the considerations of the following facts: for the nontuberculous mycobacteria in particular, a bacillary dose itself is substantially affected by pretreatment; and because of the spread of liquid media, a cultured bacillary dose is not reported. (Culture of a NTM species should as a rule use both liquid and solid media in accordance with the 1997 ATS recommendations. However, it is considered reasonable that the combined use is only accepted if it is feasible in an actual clinical setting.)
8. Positive results from nucleic acid amplification testing using the nucleic acid directly obtained from NTM species are useful for identification of a species but will not be substituted for positive culture results.
9. The bacteriologic criterion of the revised diagnostic criteria includes requirements for species that are rarely encountered and, accordingly, unlike the 2007-ATS/IDSA criteria, the bacteriologic criteria themselves of the revised diagnostic criteria will apply irrespective of the type of species.
10. For bronchoscopic specimens, the procedures for disinfecting bronchoscopes should comply with the Guidelines provided by The Japan Society for Respiratory Endoscopy⁴⁾, since there are substantial influences of contamination through automatic endoscope washers.
11. For specimens not derived from the respiratory system or lesions, aseptic body cavity fluids should be used generally. Although gastric juice is an obviously useful specimen for diagnosis of tuberculosis, it is not suitable for diagnosis of NTM diseases since high amounts of bacteria reside in the gastrointestinal juice. Therefore, meeting the criterion of "positive culture results from at least two different sputum specimens" should be a minimum requirement.
12. Species identification is not always required for both specimens, in consideration of coverage limitations by the Japanese health insurance scheme. In the case of species that are rarely encountered or those that are frequently isolated from the environment (e.g., *M. gordonae* and *M. chelonae*), however, at least two tests for species identification are necessary.

References

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