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Spectrum of Pulmonary Nontuberculous Mycobacterial Infection[1]

PURPOSE: **To organize pulmonary nontuberculous mycobacterial (NTMB) infections into a classification system based on clinical and radiographic features.**

MATERIALS AND METHODS: **Scientific literature was reviewed and organized into a framework of clinical-radiographic syndromes of NTMB infection.**

RESULTS: **NTMB infection was classified into five clinical-radiographic syndromes. The "classical" form radiographically mimics tuberculosis. It is seen predominantly in white male patients with underlying chronic obstructive lung disease. "Nonclassical" disease radiographically appears as nodular infiltrates and bronchiectasis in a sporadic distribution. It characteristically occurs in elderly women without underlying chronic illness. Asymptomatic nodules are another manifestation. Immunocompromised individuals develop disseminated infection, often with few or no pulmonary symptoms but various chest radiographic manifestations. Patients with achalasia have a radiographic appearance that most often resembles aspiration pneumonia.**

CONCLUSION: **Most pulmonary NTMB infections can be classified into one of five categories, which helps in the understanding of these wide-ranging manifestations.**

Index terms: Acquired immunodeficiency syndrome (AIDS), 60.203, 60.2518 • Achalasia, 71.745 • Lung, infection, 60.20 • Mycobacteria, 60.203

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RESEARCH in the past decade has resulted in a broadened concept of pulmonary infections with nontuberculous mycobacteria (NTMB). As a consequence, the traditional radiographic conception of an infection that mimics the radiographic appearance of pulmonary tuberculosis is outdated. The radiographic manifestations of this infection can be subdivided into several clinical-radiographic syndromes that are discussed at length.

NTMB are increasingly recognized as causes of human disease. This has been particularly true in the acquired immunodeficiency syndrome (AIDS) epidemic but is also true in non-AIDS populations (1–3). As is evident from the high rate of exposure and the low rate of clinical infection (4), these organisms are low-grade pathogens that, in general, produce low-grade, chronic infections, often with minimal symptoms.

A. Cavitary lung disease
   1. Two or more sputum samples produce positive findings with an acid-fast bacillus smear or cultures with moderate to heavy growth of NTMB.
   2. Chest radiographic findings compatible with NTMB infection and other processes have been excluded.

B. Noncavitary lung disease
   1. Two or more sputum samples are positive with an acid-fast bacillus smear or cultures with moderate to heavy growth of NTMB.
   2. Chest radiographic findings compatible with NTMB infection and other processes have been excluded.
   3. *M. kansaii* or MAC is isolated, and sputum fails to clear with bronchial cleansing or within 2 weeks of instituting specific mycobacterial drug therapy.

C. Cavitary or noncavitary lung disease in which the sputum is nondiagnostic
   1. Transbronchial biopsy or open lung biopsy specimens yield NTMB organisms and histologic material characteristic of mycobacterial infection.
   2. Transbronchial biopsy or open lung biopsy specimens fail to yield NTMB organisms but have histologic features characteristic of mycobacterial infection with no history of other granulomatous infection. In addition, two or more positive cultures and other reasonable causes for granulomatous disease have been excluded.

Figure 1. Outline shows disease versus colonization versus contaminant according to American Thoracic Society criteria.

HISTORY

NTMB were first isolated in the late 1800s, soon after the discovery of tuberculosis by Koch (5). However, they were not recognized to be human pathogens until the 1950s, when Tempe and Runyon first provided evidence of the disease in humans (5). New species of NTMB continue to be discovered. *Mycobacterium malmoense* and *M hemophilum,* two rare species, were first discovered in 1977 and 1978, respectively (6,7).

SPECIES CLASSIFICATION

The species of mycobacteria were first classified by Runyon according to the morphologic characteristics of the colonies, their response to light, and their rate of growth (8). The Runyon classification scheme is as follows: Group I, photochromogens (*M kansasii* and others), grow slowly (appear in culture in 2–4 weeks), and the colonies become yellow with exposure to light. Group II, scotochromogens (*M scrofulaceum, M xenopi,* and others), grow slowly (appear in culture in 2–4 weeks) and produce yellow colonies that turn orange with exposure to light. Group III, nonchromogens (*M avium–intracellulare* complex [MAC] and others), grow slowly (appear in culture in 2–4 weeks) and produce white or beige colonies that do not change color with exposure to light. Group IV, rapid growers (*M fortuitum–chelonei* complex and others), grow rapidly (appear in culture in 3–5 days), and the colonies do not change color with exposure to light.

Although the Runyon classification initiates the process of identifying the species, definitive identification requires analysis of response to a vari-

Abbreviations: AIDS = acquired immunodeficiency syndrome, MAC = *Mycobacterium avium–intracellulare* complex, NTMB = nontuberculous mycobacteria.

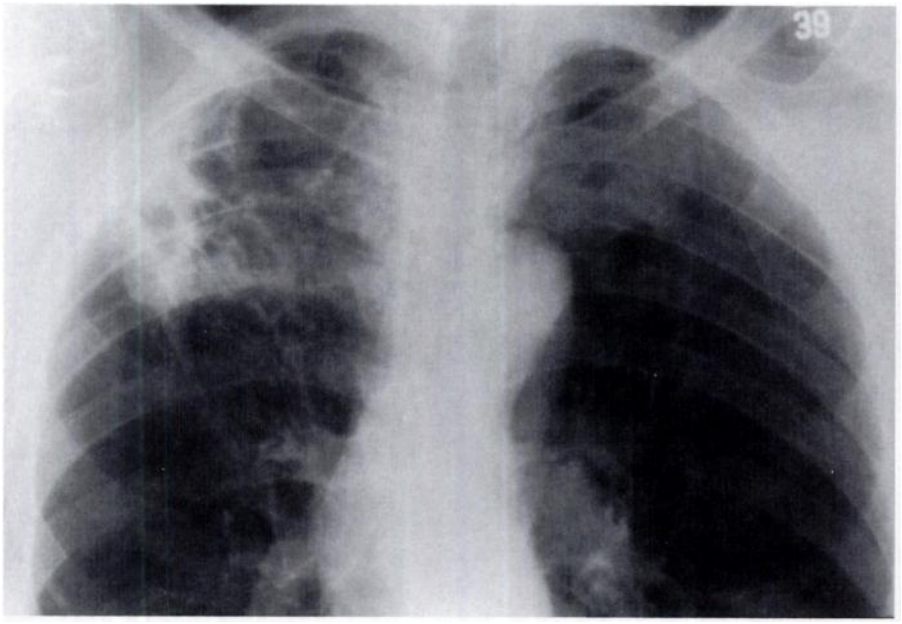
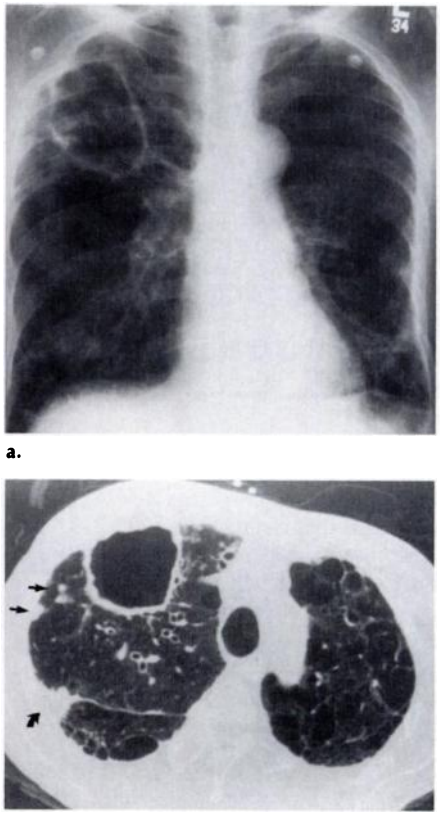


Figure 2. Classical form of disease associated with chronic obstructive pulmonary disease in an elderly man who developed chronic cough and constitutional symptoms. *M kansasii* was recovered from the sputum. Chest radiograph shows characteristic fibroproductive changes in the right lung apex. Chronic obstructive pulmonary disease is the most common predisposing condition in classical NTMB infection.



a.

b.

Figure 3. Classical form of disease associated with chronic interstitial disease due to scleroderma in a man who complained of chronic cough, night sweats, and weight loss. **(a)** Chest radiograph shows a thin-walled cavity in the right upper lobe, reminiscent of reactivation tuberculosis. Sputum cultures demonstrated MAC infection. **(b)** Computed tomographic (CT) scan through the upper lobe cavity demonstrates adjacent nodular areas of high attenuation (straight arrows), bronchiectasis, and pleural thickening (curved arrow).

ety of biochemical tests. These tests include assays that help detect nitrate, niacin, arylsulfatase and urease production, iron uptake, and the catalase response. Each species has a characteristic profile of responses to these tests (5).

More recently, DNA probes have been devised that specifically bind to the RNA of the various mycobacterial species. This binding is then detected photometrically (9–11). This is likely to be used increasingly often as the means of species identification.

At one time, there was hope that skin testing would provide a rapid means of identifying infection; however, there is substantial cross reactivity between species, which limits the usefulness of skin testing for epidemiologic surveys (5). Also, there is a large pool of asymptomatic individuals who respond to skin testing, and therefore this response does not indicate active infection (2,4).

SOURCE OF INFECTION

NTMB are ubiquitous organisms that constitute part of the normal environmental flora. They have been isolated from lakes, streams and other natural waters, soil, milk and other foodstuffs, and domestic animals (5). As a consequence, individuals are routinely exposed to these organisms. This has been confirmed with studies of military recruits in which up to one-third of all individuals and up to 70%–80% of individuals from rural environments were skin test–positive to purified protein derivative–B, an antigen from *M kansasii* (4).

Unlike tuberculosis, which is an obligate human parasite and is transmitted from human to human, there is no convincing evidence that NTMB infection can be acquired from other individuals. Instead, it appears to be acquired from the environment in which it is so ubiquitous. Inhalation of aerosolized water droplets appears to be the predominant means of pulmonary infection. This has most convincingly been demonstrated in MAC (2,12,13).

Recurrent aspiration in patients with stasis of food is also a rare means of infection. This appears to be predominantly, if not exclusively, caused by *M fortuitum–chelonei* complex and is best typified by NTMB infection in achalasia (14–17).

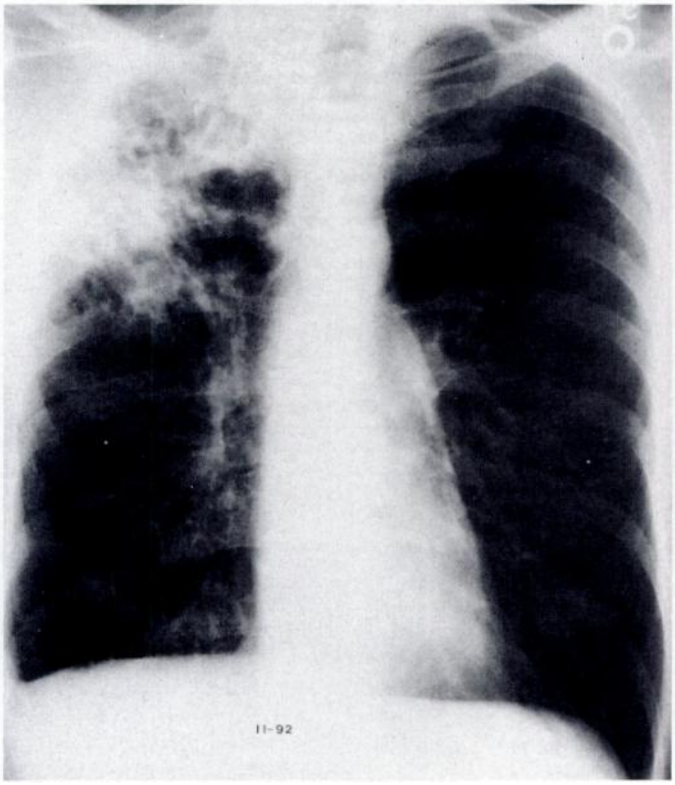
In patients with AIDS, the portal of entry appears to be the gastrointestinal tract rather than the respiratory system, as in most other patients (18–21). It appears as though the organism gains access to the lymphatic and vascular systems via the gut, resulting in bacteremia and disseminated infection.

DIAGNOSIS OF DISEASE: INFECTION VERSUS COLONIZATION VERSUS CONTAMINANT

Figure 1 shows the current American Thoracic Society criteria for the diagnosis of pulmonary NTMB infection (22). If any one of these criteria is met, the patient can be considered to have a pulmonary NTMB infection. These criteria are quite complicated because of the difficulty in separating true infection from nonsubstantial colonization of airways and from contamination in the microbiology laboratory.

Colonization may be seen in patients with underlying structural disease of the lung such as those with emphysema or bronchiectasis (23). Intensive bronchial cleansing with or without specific antimycobacterial therapy should clear NTMB from respiratory secretions. If this does not occur, the possibility of infection should be considered.

Contamination and colonization are potential confounding factors. As a consequence, American Thoracic Society criteria require demonstration



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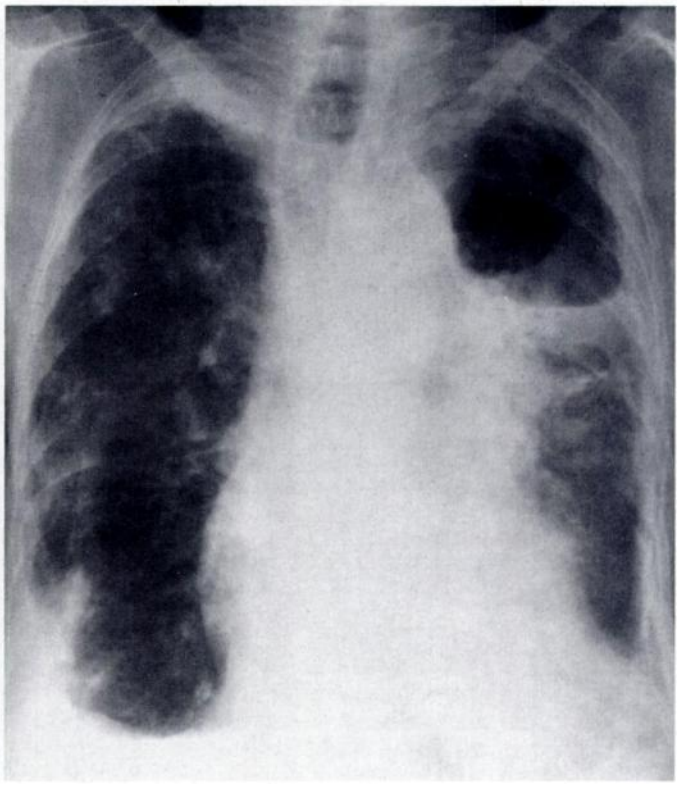

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Figures 4, 5. **(4)** Classical form of disease due to *M xenopi.* Chest radiograph shows that fibroproductive opacities in the right upper lobe caused by an uncommon organism, *M xenopi,* are identical to those caused by other NTMB. **(5)** Classical form of disease in an elderly woman who had undergone repeated pneumothoraces 40 years earlier as therapy for pulmonary tuberculosis. She presented with dyspnea, cough, and night sweats. Recurrent tuberculosis was suspected because of the left apical cavity, but multiple pure cultures of MAC infection were grown from her sputum. Chest radiograph shows that the cavity is thick walled and contains an air-fluid level. Note the extensive bilateral pleural thickening due to the previous therapeutic pneumothoraces.

of multiple positive cultures with heavy growth of the organism. Unfortunately, in some cases of true infection, the patient produces little sputum, and therefore exclusion of other causes of disease may not be possible; in addition, radiographic features compatible with disease may provide evidence of disease. Fiberoptic bronchoscopy may be useful in providing material for culture sputum and also may provide histologic evidence of granulomatous infection.

NTMB SPECIES AND PULMONARY INFECTION

Although there are numerous species that may potentially cause disease, MAC and *M kansasii* account for the bulk of NTMB pulmonary infections. The remainder of organisms fit into two groups: rare pathogens that predominantly cause pulmonary infection (such as *M xenopi, M szulgai, M malmoense,* and *M simiae*) and those that more commonly cause skin infection but rarely result in pulmonary disease (such as *M scrofulaceum, M fortuitum–chelonei,* and *M gordonae*).

Marked geographic variations have been demonstrated. *M kansasii* is most prevalent in the midwestern and southwestern United States, whereas MAC is most prevalent in the southeastern United States (2,3,5). *M xenopi* was shown to account for 17% of isolates found in patients in Ontario, Canada (3).

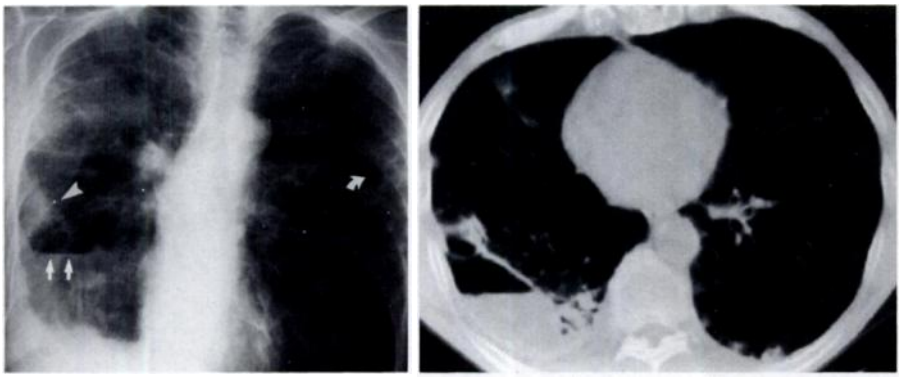
CLINICAL-RADIOGRAPHIC PULMONARY SYNDROMES

Although there is a potentially wide spectrum of clinical and radiographic findings among patients with nontuberculous pulmonary infections, there appear to be two paradigms that account for most cases in immunocompetent individuals. In this article, for purposes of identification, these forms of disease are called "classical" and "nonclassical." These are distinct clinical-radiographic complexes that affect various populations with different risk factors and clinical and radiographic features. Other clinical-radiographic syndromes include asymptomatic nodules, achalasia-associated NTMB infection, and disseminated disease in immunocompromised patients.

Classical Form of Infection

Christensen and colleagues (24–26) provided detailed descriptions of the radiographic features of pulmonary MAC and *M kansasii* infections in a large group of patients from the southwestern United States. These studies provided the initial framework for the radiographic diagnosis of pulmonary NTMB infection. In retrospect, their patient population represented only one form of pulmonary NTMB infection. This clinical-radiographic syndrome is the most common manifestation of pulmonary NTMB infection and was the first to be rigorously defined. Thus, this can be called the classical form of the disease.

These patients initially demonstrate complex fibronodular or fibroproductive apical opacities that are indistinguishable from reactivation tuberculosis (Figs 2–5). Cavitation occurs in the majority of cases (80%–95%), and there is frequently associated apical pleural thickening (37%–56%) (Fig 2). Bronchogenic spread is also common (40%–70% of cases) and may involve both the ipsilateral and contralateral lung, relative to the dominant apical



a. b.

Figure 6. Classical form of disease with a bronchopleural fistula in an older man with chronic obstructive pulmonary disease. He was admitted to the hospital with fever, malaise, and weight loss. **(a)** Chest radiograph demonstrates an air-fluid level (straight arrows). Fibronodular opacities are seen in the right upper lobe. Additional patchy alveolar disease is seen in the right lower lobe (arrowhead) and is probably due to bronchogenic spread. Indistinct nodular opacities are seen in the peripheral left lung (curved arrow). **(b)** CT scan reveals the air-fluid level in the pleural space, indicating the presence of a bronchopleural fistula. Cultures of the pleural fluid demonstrated MAC infection.

- Underlying lung disease (33%–82%)
  - Chronic obstructive pulmonary disease (25%–72%)
  - Previous tuberculosis (20%–24%)
  - Interstitial lung disease (6%)
    - Idiopathic pulmonary fibrosis
    - Silicosis
    - Asbestosis
- Other risk factors
  - Smoking (>30 pack-years) (46%)
  - Alcohol abuse (40%)
  - Cardiovascular disease (36%)
  - Chronic liver disease (32%)
  - Previous gastrectomy (especially *M xenopi*) (18%)

Figure 7. Outline shows the predisposing factors for NTMB infection. Numbers in parentheses represent the percentage of individuals with that predisposing condition. (Percentages are derived from references 3, 24–29.) Interstitial lung disease was found in miners, welders, sandblasters, and painters.

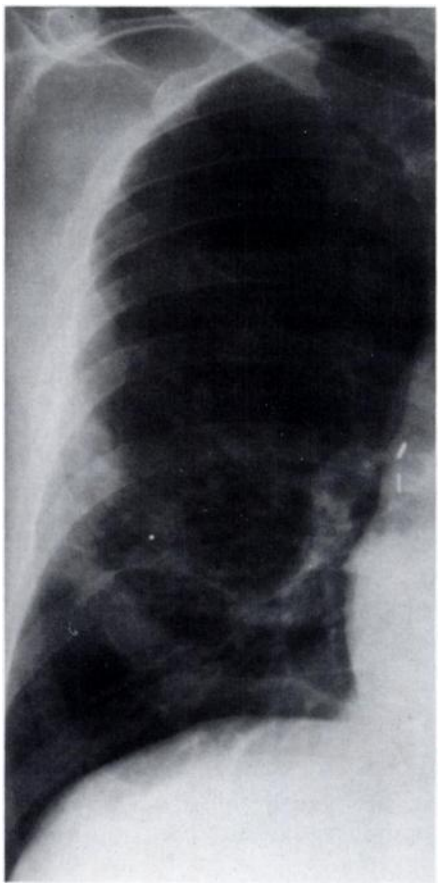


Figure 8. Nonclassical form of disease in an elderly woman without other medical problems, who for several years had a nonproductive cough and fatigue. Sputum cultures were repeatedly positive for MAC infection. Radiograph of the right lung demonstrates multiple nodular and linear opacities in the middle and lower lobe. Similar findings were seen in the left lung. No upper lobe disease was present.

focus (Fig 6). This usually appears as patchy nodular alveolar opacities, although at times may appear to be interstitial. Adenopathy, as detected at chest radiography, is distinctly uncommon (0%–4%), and pleural effusions are also less common (5%–20% of cases). Bronchopleural fistulas, a known manifestation of tuberculosis, may also occur with NTMB infections (Fig 6).

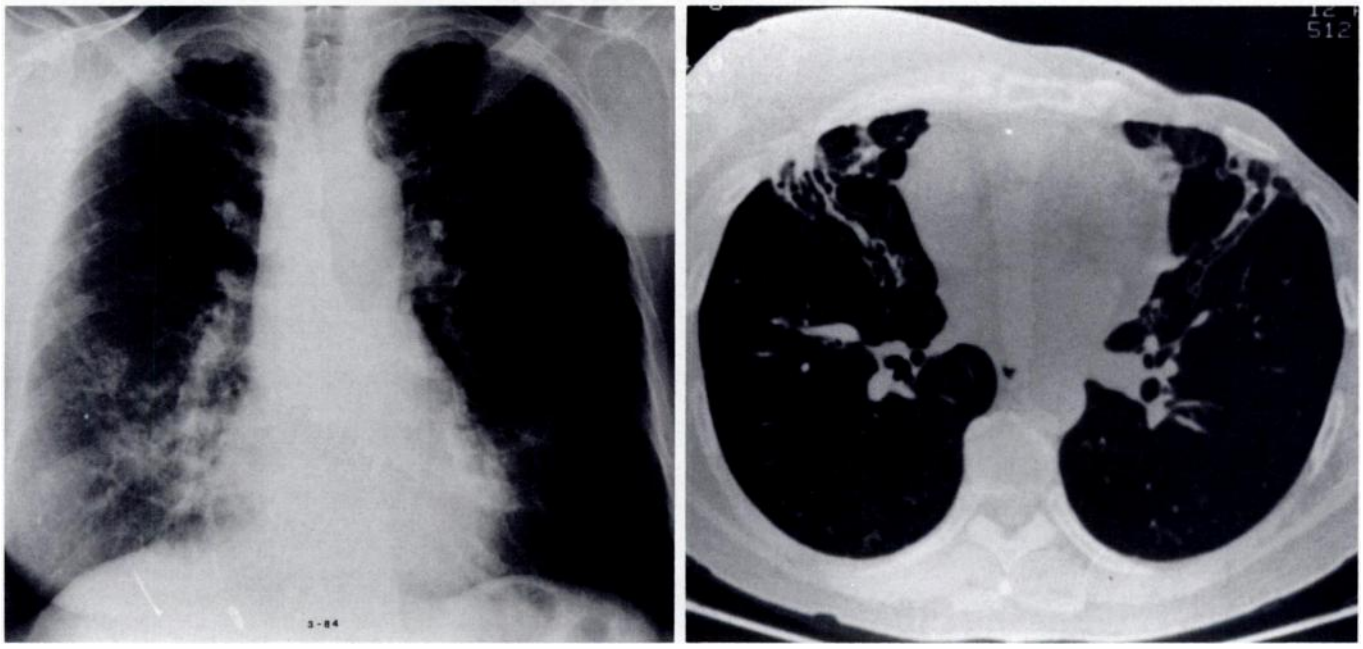
CT examination demonstrates complex foci of high attenuation in the apical portions of the lung. Cavities may be round or oval and smooth or irregular in appearance (Fig 3b). There is often bronchiectasis in regions of the most severe lung disease. Pleural thickening is also frequently present adjacent to parenchymal disease. Small (0.5–2.0-cm) nodules, a common feature of NTMB infection on CT scans, may often be demonstrated in regions of the lung distant to the dominant focus of infection (Miller WT Jr, unpublished data, 1992).

This form of infection is seen predominantly in men, whereas women predominantly have the nonclassical forms of infection. Unlike tuberculosis, which is seen largely in non-white populations in the United States, NTMB infections are seen in the white population in approximately 80%–90% of cases (24–27). This is a disease of older individuals, most commonly in their sixties and seventies. Many patients have predisposing ailments, most often chronic obstructive pulmonary disease or other pulmonary disorders. A list of the more common predisposing conditions and the relative frequency of their presence is seen in Figure 7. The presence of at least one risk factor has been reported in 25%–80% of cases (3,26–29).

The most important of the risk factors are the chronic lung diseases, both obstructive and restrictive (Figs 2, 3). Various occupations increase the likelihood of infection largely because of their propensity to produce chronic interstitial lung diseases such as asbestosis and silicosis. Previous pulmonary tuberculosis is also associated with NTMB infection (Fig 5). Patients with chronic disability, such as cirrhosis and heart disease, also appear to be predisposed to developing NTMB infection. Smoking and alcoholism are risk factors, probably because of their association with chronic obstructive lung disease and cirrhosis, respectively.

Symptoms are often insidious and include cough (60%–100%), hemoptysis (15%–20%), and constitutional symptoms such as weight loss and weakness (up to 50%) (1,3,14,19,23, 27,28,30). Of note, fevers, distinctly uncommon in all forms of nontuberculous pulmonary infections, are seen in only 10%–13% of cases; therefore, their absence should not dissuade the physician from entertaining the diagnosis of nontuberculous infection.

In general, the radiographic appearance of infection is not influenced by the species of atypical mycobacterium (Fig 4). The chronic indolent nature of all forms of this disease cannot be overemphasized. Delays in diagnosis are frequent, and radiographs may remain unchanged for years. In one series, an average of 6.4 years passed before the radiographic changes were demonstrated (29). With positive cultures for atypical mycobacterial species, the presence of a stable chest radiograph is not sufficient evidence to exclude infection. Delays in diagnosis are also related to the similarity of clinical symptoms of nontuberculous infec-



a. b.

Figure 9. Nonclassical form of disease in an older woman with a diagnosis of chronic bronchitis for several years because of a chronic cough and malaise. Finally, cultures were positive for MAC infection, and the correct diagnosis of NTMB infection was made. **(a)** Chest radiograph reveals irregular interstitial opacities in the right middle lung and lung bases. **(b)** CT scan shows bronchiectasis, one of the most common features of nonclassical NTMB infections. The middle lobe and lingula are the most common sites of disease. Irregular alveolar hyperattenuation is also seen in the right middle lobe.

tions with associated pulmonary disorders such as chronic obstructive lung disease (29). Therefore, high degrees of clinical and radiographic suspicion are often necessary to make the diagnosis, particularly in the early stages of disease.

The response of NTMB infection to drug therapy is often incomplete. It is not uncommon for antituberculous medication to arrest the progression of disease, only to have it recur months to years after treatment. This is especially true for MAC infections because this organism is characteristically resistant to most antituberculous medications. Recurrence of disease is uncommon for *M kansasii.* This mycobacterium is very sensitive to rifampin and therefore is usually cured with rifampin-based drug therapy.

Nonclassical Form of Infection

In 1985, Albelda et al (27) were among the first to realize that a substantial number of cases did not fit the traditional concepts of infection as described by Christensen and colleagues (24–26). Four years later Prince et al (1) defined a new clinical-radiographic syndrome associated with NTMB infection. I have chosen to call this form of disease nonclassical because the term "nontuberculous mycobacterial infection in patients without predisposing conditions" is too cumbersome. This pattern may be seen in 20%–30% of cases of atypical mycobacterial pulmonary infections in nonimmunocompromised patients (1,27–29). To my knowledge, this form of infection has to date been described only with MAC infection and may be exclusive to this organism. However, there are still only a relatively few reported cases of this syndrome, and it may later be found that other NTMB infections may produce similar clinical and radiographic manifestations.

Unlike the classical form of infection, women predominate among patients with the nonclassical form of infection, constituting approximately 80% of cases (1,28). The nonclassical form of infection is seen predominantly in the white population (86% of cases) (1). As previously noted, these patients do not have the traditional predisposing factors that are commonly seen in the classical form of disease (1,27,28). This is an infection that most commonly afflicts elderly patients, usually in their 7th and 8th decades of life.

Clinical symptoms are quite similar to those of the classical form of infection. Onset of disease is insidious. Chronic cough is the most frequent symptom, and fever is rare, occurring in only 14% of patients. Hemoptysis is seen in approximately 14% of patients. Unlike the more classical form of infection, constitutional symptoms are thought to be uncommon (1).

Radiographically, patients with nonclassical infection are quite distinct from those with classical disease. This pattern of infection is characterized by multiple bilateral opacities. These are most often nodular and irregular interstitial opacities in a haphazard distribution throughout both lungs. Prince et al (1) described multiple tiny pulmonary nodules as being most common (Fig 8). Nonclassical infection also often appears as irregular curvilinear opacities resembling bronchiectasis, as was first reported by Albelda et al (27) (Fig 9). In many instances, CT helps confirm the presence of bronchiectasis. In the nonclassical form of atypical mycobacterial infection, there is no predominant focus of disease. In particular, the apical pattern resembling reactivation tuberculosis is not present. In fact, the infiltrates are often most predominant in the lower lung zones, particularly the middle lobe and lingula (27,28) (Figs 8, 9).

Haphazard arrangement of bronchiectasis is the most common CT manifestation. The most common location for bronchiectasis is the middle lobe and lingula (30,31) (Fig 9b). Small nodular areas of high attenuation, usually less than 1 cm, are also common (Fig 10). In most instances, these hyperattenuating areas are probably

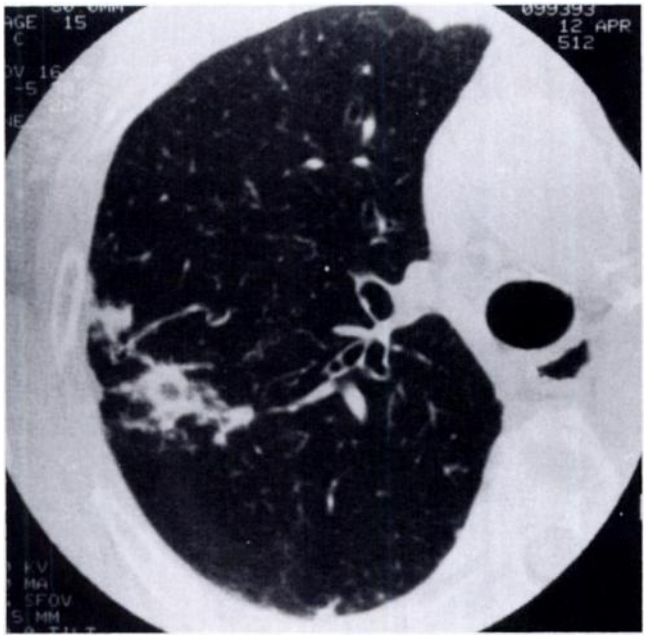


Figure 10. Nonclassical form of disease. CT scan of the right middle lung demonstrates nodular and irregular alveolar hyperattenuation, which is also common in nonclassical NTMB infection.

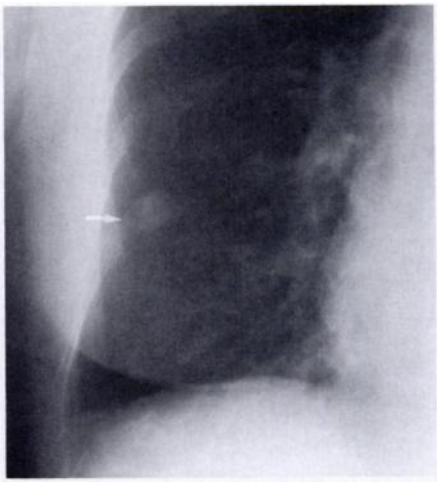


Figure 11. Asymptomatic nodule in a woman with breast carcinoma. Chest radiograph demonstrates a right middle lobe nodule (arrow). Histologic evaluation of a thoracoscopic biopsy specimen to exclude metastasis demonstrated noncaseating granulomas, which produced MAC in cultures.

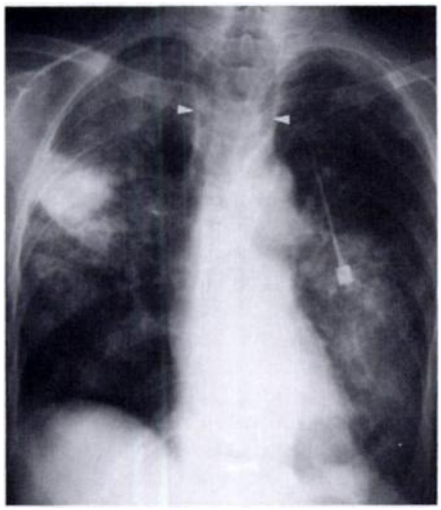


Figure 12. Long-standing achalasia and *M fortuitum–chelonei* complex in a woman who developed an acute onset of aspiration pneumonia. Cultures demonstrated *M fortuitum–chelonei* complex. Chest radiograph shows bilateral alveolar opacities and a dilated esophagus (arrowheads).

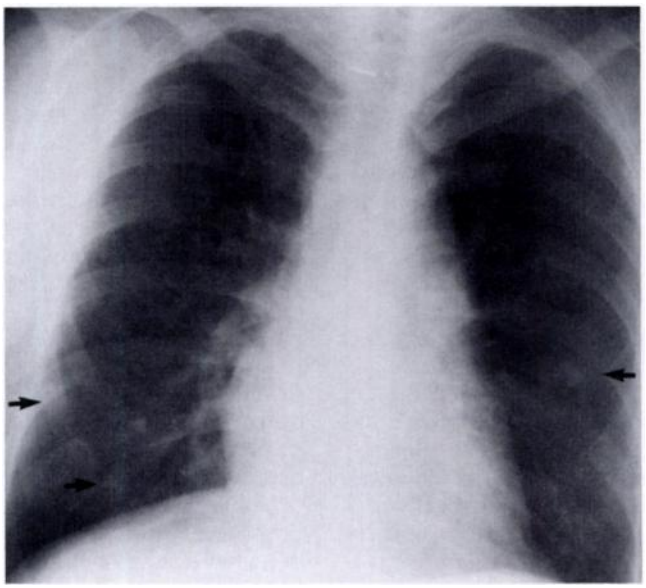
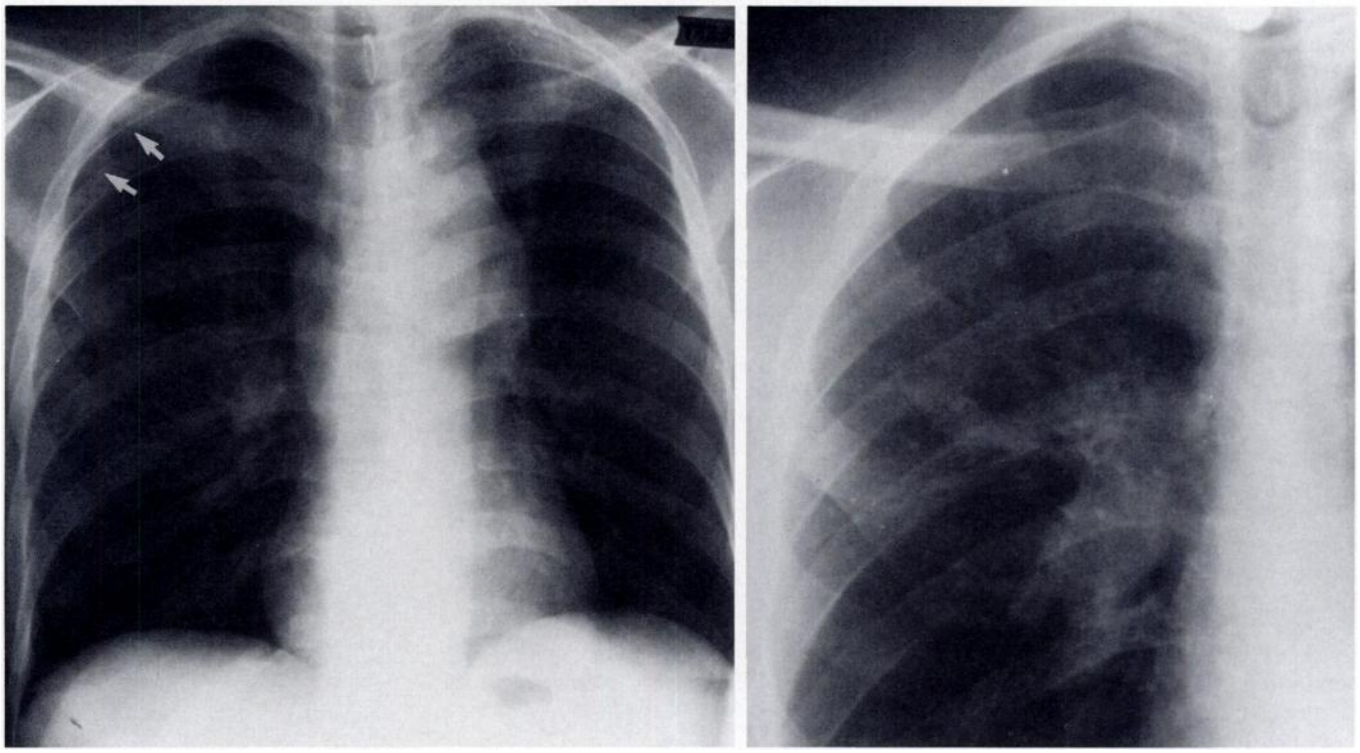


Figure 13. Disseminated MAC infection after renal transplantation in a man who developed a skin infection due to MAC on the dorsum of his foot. Chest radiograph obtained a week later shows a nodular opacity (arrows). Concurrently, he developed multiple cutaneous foci of disseminated infection. Although pathologically unproved, these foci probably represent disseminated infection to the lung.

due to macroscopic granulomas that are often in a peribronchial location. Occasionally, they may represent mucous plugs in small airways. Small patchy areas of consolidation or ground-glass attenuation and linear scarring may also be seen. Pleural thickening may be seen adjacent to areas of bronchiectasis. Volume loss and mediastinal adenopathy are also occasionally found. Moore (30) recently demonstrated that as the disease progresses, there is an increase in bronchiectasis on serial CT examinations. This indicates that although bronchiectasis may be a predisposing condition for NTMB infection, it is also caused by the infection.

Asymptomatic Nodules

As with other granulomatous infections, pulmonary infection with NTMB may result in solitary or multiple macroscopic granulomas. These are most often asymptomatic and gain medical attention because of a concern for malignancy. Surgical resection with histologic evaluation proves their benign nature. The true prevalence of such NTMB granulomas is unknown, since many granulomas are not resected because of known stability on serial radiographs or demonstration of calcium with CT phantom studies. Also, many of the



14. 15.

Figures 14, 15. **(14)** NTMB infection in a young man with AIDS who presented with fever and acute pleuritic chest pain. Chest radiograph demonstrates extensive mediastinal adenopathy. A small pneumothorax is faintly seen in the right lung apex (arrows), revealing the cause of the chest pain. MAC, recovered from blood cultures, was the only demonstrated cause for mediastinal adenopathy. **(15)** NTMB infection in a young man with human immunodeficiency virus who presented with a fever. Characteristic of the disseminated infection in immunocompromised patients, both blood and sputum cultures were positive for MAC infection. Chest radiograph demonstrates right hilar adenopathy and an indistinct alveolar opacity in the right upper lobe.

smaller granulomas are undetected on chest radiographs. It was demonstrated in a recent study of the CT manifestations of NTMB infection (Miller WT Jr, unpublished data, 1992) that small nodular areas of high attenuation, probably representing granulomas, are frequently found at CT when they were not detected with chest radiography in patients with classical and nonclassical forms of disease. Given the high prevalence of asymptomatic patients with positive findings from skin tests, we suspect that many individuals may have small pulmonary granulomas resulting from NTMB infection that are undetected because of the asymptomatic status of the patients and the insensitivity of chest radiography.

On chest radiographs, these nodules may be single or multiple and vary in size (Fig 11). When the nodules are multiple, they are often clustered together. CT examination may demonstrate nearby nodules that are not seen on chest radiographs. This clustering of similar-sized nodules may be a clue to a nonneoplastic cause, since metastatic nodules are usually randomly distributed throughout the lung and primary carcinomas usually manifest as a dominant mass with smaller satellite nodules.

Achalasia and the Rapid Growers

Patients with achalasia seem to have a radiographic appearance of infection that is different from that of other patients with pulmonary NTMB infection. In a review of the literature, the majority of cases appear different from either the classical or nonclassical forms of disease. The majority of reports involved cases of patchy bilateral alveolar opacities that resembled aspiration pneumonia (14–17) (Fig 12). CT demonstrates nonspecific patchy air-space disease. This is not surprising because the mechanism of infection is thought to be chronic aspiration (15). Stasis of food in the esophagus and the presence of lipid material also appear to play a role in NTMB infection in patients with achalasia.

NTMB infection in achalasia is almost always associated with *M fortuitum–chelonei* complex rather than with other atypical mycobacteria. These organisms have also been shown to produce lung abscesses in other individuals, possibly also due to recurrent aspiration (32–34).

Pulmonary Manifestations of Disseminated Infection

Individuals with depressed immunity have an increased risk of developing hematogenously disseminated infection with NTMB. In some respects, patients with AIDS demonstrate features of NTMB infection that differ from those of other immunocompromised patients; therefore, these groups are discussed separately.

Immunocompromised hosts without AIDS.—A wide variety of patients with disorders of immunity have an increased risk of developing infections due to NTMB. Patients with AIDS are now the most common of these patients, but other risk groups include patients who undergo transplantation; patients with lymphoproliferative disorders, particularly those with hairy cell leukemia; and patients who undergo steroid and other immunosuppressive drug therapy (35–37).

The majority of these patients develop disseminated infection and have NTMB recoverable from the blood. In general, unlike normal hosts, NTMB infection is rarely isolated to the lung.

Most common symptoms include fever, weight loss, malaise and weakness, and nonspecific signs pointing to the systemic nature of the disease.

Radiographically, a wide variety of manifestations have been reported, including mediastinal and hilar adenopathy, focal infiltrates, nodules, cavities, and diffuse interstitial infiltrates (Fig 13).

Patients with AIDS.—NTMB infection in patients with AIDS has been extensively evaluated. Thirty percent of AIDS patients have NTMB infection, usually MAC, diagnosed during life and 50% at autopsy (19). This discrepancy between percentages acquired before and after the patient dies is probably due to the presence of superimposed debilitating or life-threatening illnesses, which obscure the diagnosis of NTMB during life. The organism is most often detected in blood cultures, reflecting the disseminated character of NTMB infection in patients with AIDS. Pulmonary symptoms are usually minimal. Frequently, organisms are recoverable from the lung in sputum or bronchoalveolar lavage fluid; however, parenchymal invasion of the lung is often absent. These patients are usually bacteremic, with MAC recoverable from blood cultures. The exact mechanism whereby organisms in the blood become recoverable from respiratory secretions is not known. However, it is clear that many patients with AIDS have respiratory and blood cultures that are positive for MAC and yet have no pulmonary symptoms and a normal chest radiograph.

Unlike normal hosts, the portal of entry in patients with AIDS is thought to be the gastrointestinal tract. This idea is reflected in the high prevalence of retroperitoneal adenopathy in this group of patients.

The chest radiograph is often normal. Adenopathy, mediastinal and hilar, is the most common chest radiographic finding (Figs 14, 15). At CT examination, adenopathy may be solid or have central necrosis. This feature is not exclusive to NTMB infection and can be seen with tuberculosis and fungal infections. Patchy alveolar infiltrates are less common but are occasionally demonstrated (35) (Fig 15).

CONCLUSION

NTMB infection causes wide-ranging pulmonary manifestations. These manifestations can be better understood as several clinical-radiographic syndromes, which have been called classical disease; nonclassical disease; asymptomatic nodules; achalasia-related nontuberculous infection; and disseminated disease of immunocompromised patients, including those who do and those who do not have AIDS. The majority of cases of pulmonary NTMB infection can be categorized into one of these subgroups. ■

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