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Nontuberculous Mycobacteria Infections in Immunosuppressed Hosts

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Synopsis

Diseases and therapies that reduce cell-mediated immunity increase the risk of nontuberculous mycobacterial (NTM) disease. Historically acquired immunodeficiency virus (AIDS), cancer, and hematologic and solid organ transplants have been associated with NTM disease. More recently, immunosuppressive drugs including anti-tumor necrosis factor (anti-TNF) biologics have been associated with NTM disease in population-based studies. Extrapulmonary NTM disease, including disseminated and skin and catheter-related disease, is more common in immunosuppressed compared to immunocompetent patients. *Mycobacterium avium* complex remains the most common cause of NTM infection of all sites, but rapid growers including *M. abscessus*, *M. chelonae*, and *M. fortuitum* play an important role in skin and catheter-related infections. With the exception of prophylaxis for AIDS patients with very low CD4+ counts, the prevention of NTM remains difficult. Management is complicated and involves restoring immune function and removing catheters in addition to treatment with species-specific antibiotic treatment per current ATS/IDSA guidelines.

Introduction

Nontuberculous mycobacteria (NTM) are important causes of pulmonary and extrapulmonary disease in immunosuppressed hosts. Early descriptions of NTM in immunosuppressed hosts come from the cancer literature: in 1976 an institutional report described 30 NTM infections, comprising half of 59 mycobacterial infections in cancer patients over a 5-year period.¹ Then, in the 1980s, disseminated *M. avium* complex (MAC) disease was identified as an important pathogen in the setting of acquired immunodeficiency syndrome (AIDS) highlighting the risk of these environmental organisms within severely

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immunocompromised host.^{2,3} Simultaneously NTM cases were reported in reviews of mycobacterial disease in renal transplant patients, though tuberculosis was the focus with poorer patient outcomes.^{4,5} Other case reports focusing on NTM disease appeared in the cancer literature.⁶⁻⁸ Since that time, tuberculosis has declined significantly in the U.S. and formal population-based epidemiologic studies have demonstrated the burden and increasing incidence of NTM infections and further described the clinical and epidemiologic risk factors for these infections.⁹⁻¹³ While MAC continues to cause the majority of NTM disease in the setting of immunosuppression, it is likely that changes within laboratory diagnostics, the host, and the environment have contributed to an increasingly diverse array of NTM species now being recognized as associated with immunosuppressive states. This includes greater recognition of rapidly growing NTM (*M. abscessus*, *M. chelonae*, *M. fortuitum*), as well as species that are difficult to grow in culture whereby molecular techniques might increase their identification (e.g. *M. haemophilum*). Further, changes in the prevalence of immunosuppression have likely contributed to these changing trends in NTM disease as well. The introduction of highly active antiretroviral therapy (HAART) diminished the importance of MAC in the HIV setting, while increasing use of organ transplantation, particularly stem cell transplants, as well as the widespread use of new biologic and other immunosuppressive therapies for patients with immune-mediated inflammatory disease has increased the number of patients susceptible to NTM infection. This review discusses the changing landscape of NTM in the immunosuppressed setting, as well as highlighting the particular challenges of NTM prevention and management for immunosuppressed patients.

Disease description

NTM disease is increasing in the U.S. Prevots et al used data from several large health maintenance organizations in the western U.S. and found an increase of 2.6% per year from 1994-2006.¹¹ The first incidence estimate of NTM disease is 5.7/100,000 in Oregon in 2012, with rates 3-4 times higher in individuals over 70.¹⁴ Most of this is pulmonary disease in which a large proportion occurs outside of recognized settings of immunosuppression. For others, however, immunosuppression contributes to the risk of acquisition or progression and death. This has been described in institutional-based cohorts of patients with cancer or undergoing solid organ transplants or stem cell transplants. More recent population-based studies have confirmed that NTM disease is associated with oral and inhaled corticosteroids associated with chronic obstructive pulmonary disease or biologic therapies for immune-mediated inflammatory diseases.^{13,15} A recent study of comorbid factors associated with 2990 NTM-related deaths from 1999-2010 using death certificate data found that 2% were associated with primary immune deficiency, 1.1% with lymphoma and hematologic malignancies, and 0.5% with human immunodeficiency virus (HIV).¹⁶

In general, the underlying mechanism that increases the risk of NTM disease in immunosuppressed patients is disruption or depletion of cell-mediated immunity, a critical component of host defense against mycobacteria. Mycobacteria infect macrophages and stimulates the CD4+ T-helper 1 (TH1) pathway which involves interleukin-12 (IL-12) and interferon gamma (IFN- γ). IFN- γ then activates infected macrophages which control infection. Another key mechanism of control is via tumor necrosis factor alpha (TNF- α), a pro-inflammatory cytokine that is required for formation and maintenance of granulomas

that effectively inhibit bacterial growth.¹⁷ Most of the research into the mechanisms of infection and immunological control has been conducted on *M. tuberculosis*, *M. bovis*, and *M. avium*. However, it is clear that there are differences in virulence and immune response to different species, evidenced by species variations in the predominant site of infection and the fact that several species, including *M. haemophilum* and *M. genavense*, cause infection almost exclusively in immunocompromised patients.¹⁸⁻²⁰ The various settings of immunosuppression that are related to NTM infection are summarized in Table 1 and described in more detail in their respective sections.

In immunocompetent patients about 77% of NTM disease is pulmonary.⁹ In immunosuppressed patients that proportion ranges from less than 5% in AIDS patients to 67% in patients on biologic therapies for immune-mediated inflammatory diseases, with a corresponding increase in disseminated and skin (including surgical site or catheter-related) infection (Table 1).^{21,22} MAC is the most common species for pulmonary and disseminated NTM infection, followed by *M. abscessus*, *M. kansasii* (found in the Southern and Midwestern U.S. and internationally) and *M. xenopi* (Northern U.S. and Canada).²³ Rapid growing NTM including *M. fortuitum*, *M. abscessus*, *M. chelonae*, *M. mucogenicum*, and *M. neoaurum*, are causes of skin and catheter-related infection and bacteremia.^{24,25} NTM species and typical sites of infection are listed in Table 2.

NTM infection by underlying disease or treatment

HIV/AIDS

Epidemiology—The epidemic of disseminated MAC infection began in 1982 with a sharp increase in the number of cases associated with the AIDS epidemic.³ Up to 24% of AIDS patients had disseminated MAC by 1989-90.² Distinguishing it from other opportunistic infections that occurred earlier in the course of HIV infection, disseminated MAC was associated with very low CD4+ counts, generally below 50 cells/mm³.^{2,3} The introduction of highly active antiretroviral therapy (HAART) in 1997 led to a sharp decline in the number of disseminated MAC cases.^{26,27} *M. kansasii* also causes disseminated NTM infection, but causes pulmonary disease in over half of AIDS patients.^{21,23} Post-HAART population data on disseminated NTM has been reported in Oregon, with a published rate of 0.3/100,000 in 2005-2006 remaining stable at 0.2/100,000 in 2012 (data unpublished).⁹ This suggests the rate of disseminated NTM in the setting of HIV is quite low, at least in Oregon. It is unknown what proportion of the 9 cases in 2012 had coexistent HIV/AIDS. However, if all of these were assumed to be AIDS-related, using the state-wide 2012 estimate of 5500 people living in Oregon with HIV as a denominator the proportion of HIV/AIDS patients with disseminated NTM in Oregon was less than 0.2% in 2012.²⁸

HIV related pulmonary disease is still poorly understood. Even in TB endemic countries, NTM may cause significant disease in HIV-infected patients. In Thailand and Vietnam, NTM disease prevalence was 2% among HIV-infected patients enrolled and screened for mycobacterial infections.²⁹ Half of these infections were classified as pulmonary and half as disseminated. The cases with pulmonary disease and negative blood cultures generally had typical NTM imaging, including nodules, cavity disease, or infiltrate, suggesting that disease

might be related to other underlying lung diseases similar to what is seen in the non-HIV setting.

Diagnosis, Prevention, and Treatment—Initially, rifabutin prophylaxis was recommended if CD4+ counts dropped below 50 cells/mm³, but changed to azithromycin or clarithromycin after clinical trials showed their effectiveness.³⁰ In 2002, after the introduction of HAART, the recommendation was made to discontinue prophylactic antibiotics if HIV disease was well controlled.²⁷ Currently, prophylactic treatment with once weekly 1,200 mg of azithromycin is recommended for HIV-infected patients with CD4+ counts below 50 cells/mm³.²³

Treatment for disseminated MAC includes antivirals to control the underlying immunosuppression in addition to therapy for the NTM infection. The optimal regimen against disseminated MAC is clarithromycin, ethambutol, +/- rifabutin (see Table 3), based on randomized clinical trials.²³ Rifabutin is often added as the third antibiotic although the additional benefit of this drug is less established. Untreated disseminated MAC was shown to shorten the time to death in AIDS patients, but treated patients had a similar survival compared to non-MAC matched controls.³¹ A study of HIV-infected patients hospitalized at a single hospital showed a 10% mortality rate among 19 patients hospitalized for disseminated NTM infection.³²

Immunosuppressive therapies for immune-mediated inflammatory diseases

Corticosteroids

Oral and inhaled corticosteroids are routinely prescribed to suppress inflammation in a number of chronic conditions, including COPD, asthma, and rheumatoid arthritis. Corticosteroids are known to increase the risk of pneumonia in COPD patients and tuberculosis as much as 5-fold,³³ while the relative risks of NTM are likely even greater. Oral prednisone use was 8 times higher among NTM cases than controls in a case-control study in Oregon and Washington.³⁴ Inhaled corticosteroids were associated with a significantly increased NTM risk of 24.3 in a study of COPD patients in Denmark.¹³ Asthmatic NTM cases had a longer duration and higher dose of ICS compared to controls in a Japanese case-control study.³⁵ In all three studies there was a clear dose response, with higher risks of NTM with oral prednisone doses >15 mg and >800 mg fluticasone equivalent.

Biologic therapy

Tumor necrosis factor alpha (TNF-alpha) is a pro-inflammatory cytokine that is integral to host defense against granulomatous mycobacterial and fungal infections.³⁶⁻³⁸ Medications that target the TNF pathway are the cornerstone of treatment for autoimmune inflammatory conditions including rheumatoid arthritis, psoriasis, and Crohn's Disease. Five TNF-alpha inhibitors are currently approved: infliximab, adalimumab, golimumab, and certolizumab are anti-TNF alpha monoclonal antibodies, and etanercept is a soluble receptor fusion protein.³⁹ In a U.S. study in new users of infliximab, etanercept, or adalimumab anti-TNF therapy, the overall rates of NTM disease were five to tenfold higher than disease rates seen

in the unexposed background RA and general populations and more common than TB.¹⁵ The drug-specific incidence rates per 100,000 patient-years and 95% confidence intervals were 35 (1-69) for etanercept, 116 (30-203) for infliximab, and 122 (3-241) for adalimumab. In South Korea a higher incidence of NTM disease of 230 per 100,000 patients was reported in two separate hospital-based reviews of 509 and 1165 patients treated with TNF antagonists.^{40,41} In a review of U.S. Food and Drug Administration MedWatch reports, just over half (55%) of NTM cases were pulmonary.²⁵ In the U.S. and South Korea, 70% to 100% of NTM infections were in patients with rheumatoid arthritis who frequently have associated underlying lung disease including bronchiectasis and interstitial lung disease.^{15,25,41,42}

Other biologic agents used in this setting include rituximab (anti-CD20 monoclonal antibody), abatacept (T-cell costimulator modulator), tocilizumab (anti-IL-6 monoclonal antibody), and ustekinumab (anti-IL-12 monoclonal antibody). There is a theoretical increased risk of NTM infection with these agents, but very little safety data exists and further study is required.³⁹ At the present time, the evidence of NTM risk is limited to small case series of NTM disease in patients treated with rituximab (2 cases) and tocilizumab (4 cases, 3 were also taking prednisolone +/- tacrolimus and 2 had prior NTM infection).^{43,44} It should be noted that rituximab has been used as an adjunct to successfully treat otherwise recalcitrant chronic NTM infections in patients with auto-antibody states involving IFN-gamma.^{45,46}

Diagnosis, Prevention, and Treatment

Prospective screening is not recommended for any of immunosuppressed groups, unlike tuberculosis where there are clear benefits to screening for latent infection prior to the initiation of biologics and immunosuppressive therapy.²³ However, some groups should be considered for further clinical work-up prior to initiation of biologic therapy. Patients with chronic cough that cannot be explained by usual causes should be considered for further workup for pulmonary NTM, including CT imaging and respiratory sampling.

Treatment is described in Table 3, and is species specific requiring antimicrobial susceptibility for all except MAC, unless macrolide-resistant MAC is suspected.²³ When possible, decreasing or dropping immunosuppressive medications likely improves the likelihood of successful treatment.³⁸ Non-biologics such as methotrexate should be considered, or second-line therapies such as abatacept or tocilizumab which are currently considered lower risk.¹⁵ Outcomes of treatment for pulmonary disease are variable. Case fatality rates range from <10% to 15% in U.S. studies with short term follow up. Winthrop et al. reported a higher case fatality rate of 39% with a median of 569 days (range 21-2127) between diagnosis and death. Evidence from a small Japanese case series suggests that pulmonary NTM disease in rheumatoid arthritis patients who stop biologics have generally positive outcomes with NTM treatment, or stable NTM disease with no treatment, and deaths were related to underlying lung disease including pulmonary aspergillosis and interstitial lung disease.^{43,47}

Solid organ transplants

Solid organ transplant recipients take a variety of immunosuppressive medications after transplant. The most common maintenance drugs include calcineurin inhibitors (tacrolimus and cyclosporine), mammalian target of rapamycin (mTOR) inhibitor (sirolimus), prednisone, and others depending on the organ being transplanted. All data on NTM in transplants is found in case reports and institutional case series. To our knowledge there are no population-based prevalence or incidence estimates to track trends or differences between transplant centers. In a 2014 review of the literature including 293 solid organ transplant cases with NTM disease, lung transplant recipients had the most pulmonary NTM: 61% (61/100). Heart (11/45, 26%) and liver (5/16, 31%) transplant patients had similar amounts of pulmonary NTM, and kidney transplant patients had the lowest levels (22/132, 17%).⁴⁸ In a recent case control study from a single institution, after excluding patients with NTM detected prior to transplant, lung transplant was the most important risk factor for NTM infection, accounting for 55.9% of cases (19/34).⁴⁹ All four NTM cases in liver transplant patients, 15/19 (78.9%) lung transplant, and the pancreas-kidney transplant patient had pleuropulmonary infection. Among solid organ transplant patients recently reviewed at three institutions, MAC and *M. abscessus* each made up about 45% of the 49 total NTM infections.⁴⁹⁻⁵¹

Diagnosis, Prevention, and Treatment

Treatment in transplant patients is complicated by drug interactions between rifamycin, macrolide, and aminoglycoside and calcineurin inhibitors (cyclosporine, sirolimus) and tacrolimus used post-transplant, and should guide the selection of appropriate antibiotics.^{52,53} There are several case reports of organ graft versus host disease in patients who decreased immunosuppressive medications, which needs to be balanced against the need for improved immune function for effective clearance or control of NTM disease.^{48,53} Outcomes for renal transplant patients reported in a review of the literature are variable, with 41 (44%) of 94 cases considered resolved, 3 (3%) deaths (2 disseminated and 1 pulmonary), and 30 (32%) with complicated relapsed or long-term infection.⁵³ Outcomes for the 22 lung transplant patients were better and included 7(32%) who cleared NTM, 8 (36%) who showed improvement, 6 (27%) with no response or relapse and 1 (5%) death from disseminated *M. abscessus*.⁵³ More recent reports show very similar outcomes in 15 NTM cases in lung transplant patients at two institutions, with 9 (60%) clearing infection, 4 (27%) with persistent infection or recurring colonization, 1 (7%) unknown outcome, and 1 (7%) dead from disseminated *M. abscessus*.^{50,51} To our knowledge, there are no published reports of deaths due to NTM in heart transplant patients.

Lung transplant special considerations: Lung transplant patients are at higher risk of NTM infection pre-transplant, due to the underlying condition that makes them eligible for transplant. Most transplant centers do not treat colonized patients, but should treat all pulmonary NTM disease per ATS/IDSA guidelines.^{23,50} In the case of lung transplants in patients with cystic fibrosis, prior pulmonary *M. abscessus* infection in patients is associated with mycobacterium infection post-transplant. Based on evidence from one transplant center, *M. abscessus* should not be considered a contraindication to lung transplant and local

control and clearance is possible if disease recurs.⁵⁴ At another institution with culture results prior to transplantation of 145 patients, 2 had NTM disease.⁵¹ One was treated prior to and after single lung transplantation and continued to test positive until his death from *Aspergillus* pneumonia; the other was not treated and grew MAC 15 months after transplantation but not considered a case.

Solid tumors and hematologic malignancies

Patients with cancer are at higher risk for NTM disease. Underlying cellular immunity impairment and immunosuppression from anti-neoplastic chemotherapy also contribute to the increased risk.^{1,8,55} Patients with lung tumors are at increased risk of pulmonary NTM infection probably due to localized airway destruction or damage, and hematologic malignancies put patients at higher risk of both localized infections near the site of catheter placement and disseminated infections. Hairy cell leukemia is particularly associated with disseminated NTM disease, documented in the literature starting in the early 1980s.^{6,7} A large institutional case series reported an incidence of 5% (9/186).⁵⁶ One estimate from Taiwan suggested 1.2% of patients with hematologic malignancy developed NTM infections.⁵⁵

Hematopoietic stem cell transplants (HSCTs)

HSCTs are used to treat a number of hematologic malignancies, including leukemia, multiple myeloma, and others. The number of HSCTs has increased dramatically from 200 in 1980 to 20,000 in 2010.⁵⁷ The risks of NTM are higher prior to the transplant due to underlying immune cell abnormalities and during the phase of immune reconstitution that follow induction immunosuppression and the HSCT. HSCTs are most frequently associated with catheter and blood infections, but 18% (17/97) were associated with pulmonary NTM in a 2014 review NTM-infected HSCT patients.⁵³ Graft versus host disease was an important risk factor, present in 46% of NTM infections and corresponding with an increase in immunosuppressive medications.⁵³ Overall, 26/93 (28%) were MAC/MAI, 23 (25%) were *M. abscessus*/*M. chelonae* and 22 (24%) were *M. haemophilum*. Most *M. haemophilum* infections were associated with skin and catheter infection, but at least 5 pulmonary cases were reported among 19 cases in bone marrow transplant patients.⁵⁸⁻⁶¹ In a review of 571 allogeneic hematopoietic stem cell transplant, 16 NTM infections were identified and 3 (19%) of these patients died from their NTM disease, one of the few studies to identify a high case fatality rate in immunosuppressed patients with NTM disease.⁶² Nine of these infections were *M. haemophilum*, 6 of which were associated with skin or catheter-related infections. In general, HSCT patients have a high rate of resolving infection after treatment and removal of catheters. However, death related to NTM occurred in 7/94 (7.5%) of HSCT patients with pulmonary and disseminated NTM disease reported in the literature.⁵³ Treatment for *M. haemophilum* and other rapid growing mycobacterial disease should include prolonged therapy (Table 3) and surgical removal of tissue as needed following catheter removal.²³

Primary immunodeficiency diseases

Primary immunodeficiency diseases (PIDs) include a large number of conditions associated with defects in antibody responses, and cellular and innate immunity.⁶³ A subset of these is associated with a documented or theoretical risk, and most are associated with the IL-12/IFN gamma axis.^{63,64} Other conditions pre-disposing to NTM include chronic granulomatous disease, common variable immune deficiency, and hypogammaglobulinemia are associated with NTM disease.⁶³ A recent study of conditions associated with NTM death found that primary immunodeficiency was a comorbid cause of death in 2% of NTM deaths, more than hematological malignancies or HIV/AIDS.¹⁶

Summary

Diseases and therapies that reduce cell-mediated immunity increase the risk of NTM disease. The increasing use of immunosuppressive drugs including anti-TNF biologics and patients undergoing stem cell and solid organ transplants means an increasing number of patients at risk for NTM disease in the U.S.³⁸ With the exception of population-based studies of anti-TNF biologics and corticosteroids that place the risk of NTM at 8-50 times the general population, we do not have a good understanding of the incidence of NTM disease in immunosuppressed populations.

Extrapulmonary NTM disease, including disseminated and skin and catheter-related disease, is more common in the immunosuppressed population. MAC remains the most common cause of NTM infection of all sites, but rapid growers including *M. abscessus*, *M. chelonae*, and *M. fortuitum* are important causes of skin and catheter-related infections. With the exception of prophylaxis for AIDS patients with very low CD4+ counts, the prevention of NTM remains elusive. Management can be prolonged and difficult, and restoring immune function and removing catheters are essential alongside appropriate antibiotic treatment per current ATS/IDSA guidelines.²³

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Key points

- Nontuberculous mycobacteria (NTM) disease is an important cause of disease in immunosuppressed hosts.
- *M. avium* complex is the leading cause of NTM disease in immunosuppressed patients, but rapid growers including *M. abscessus*, *M. chelonae*, and *M. fortuitum* and a variety of rare species are also important.
- In immunosuppressed patients about half of NTM disease is pulmonary and the remainder is split between skin/soft tissue and disseminated.
- Treatment is species specific and requires expert management with the ability to cure such infections related to the host's underlying immunosuppressive status.

Table 1

Immunosuppressive conditions and risks for NTM

Underlying disease or treatment	NTM cases in included references	Pulmonary	Disseminated	Skin/soft tissue/catheter	Overall Risk/Relative Risk (RR)	References
AIDS	972		(100%)		24%	2
Hairy cell leukemia	9		(100%)		5%	56
Hematopoietic stem cell transplant	97	18%	9%	70%	0.4-4.9	48,53,62
Hematologic malignancies	34	76%	24%		1.2%	55
Solid organ transplant	40	50%	15%	35%	0.02 (various organs) 1.1 (lung) per 100 person-years	51,49
Biologic therapy for immune-mediated inflammatory diseases	123	56-67%	8%	35%	74/100,000	25,15
Corticosteroid therapy for chronic respiratory disease	182	(100%)			RR oral: 8 inhaled: 24.3	34,13

Table 2

Nontuberculous mycobacterium species and common sites of infection in immunosuppressed hosts)

	Pulmonary	Disseminated	Skin/soft tissue/catheter-related
Slow growers	MAC [*] <i>M. kansasii</i> <i>M. xenopi</i> <i>M. malmoense</i>	MAC [*] <i>M. kansasii</i> <i>M. haemophilum</i> <i>M. marinum</i> <i>M. genavense</i> (R)	MAC [*] <i>M. marinum</i> <i>M. haemophilum</i> (R)
Rapid growers	<i>M. abscessus</i>	<i>M. chelonae</i> <i>M. abscessus</i> (R) <i>M. fortuitum</i> (R)	<i>M. abscessus</i> <i>M. chelonae</i> <i>M. fortuitum</i> <i>M. mucogenicum</i> (R)

ATS=American Thoracic Society, IDSA=Infectious Disease Society of America

(R)=rare

Adapted from 2007 ATS/IDSA guidelines; with permission.

* MAC: *M. avium*/intracellulare complex

Table 3Preferred nontuberculous mycobacteria treatment regimens, 2007 ATS/IDSA guidelines²³

Disease site/species	Drug combination ^{*,#}	Susceptibility testing
Pulmonary <i>M. avium</i> (nodular)	Macrolide + ethambutol + rifampin	Recommended for macrolides
Pulmonary <i>M. avium</i> (cavitary, severe, previously treated)	Above + iv/im streptomycin or amikacin	Recommended for macrolides
Disseminated <i>M. avium complex</i>	Clarithromycin + ethambutol + rifabutin	Recommended for macrolides
Pulmonary <i>M. kansasii</i>	Rifampin + ethambutol + isoniazid + pyridoxine	Recommended for rifampin
<i>M. abscessus</i>	Macrolide + one or more of iv amikacin, cefoxitin, or imipenem	Recommended for a panel of drugs
<i>M. chelonae</i>	Multidrug therapies including clarithromycin	Recommended for a panel of drugs
<i>M. fortuitum</i>	Multidrug therapies including clarithromycin [†]	Recommended for a panel of drugs
<i>M. haemophilum</i>	Multidrug from clarithromycin, rifabutin/rifampin, ciprofloxacin	Recommended (interpret with caution)

Data from Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. American journal of respiratory and critical care medicine 2007;175:367-416.

ATS=American Thoracic Society, IDSA=Infectious Disease Society of America

* oral unless noted; iv=intravenous; im=intramuscular

treatment length minimum 12 months culture negative (pulmonary), 4-6 months (skin/soft tissue)

[†] *M. abscessus* subspecies *abscessus* and *M. fortuitum* have an *erm* gene that can result in inducible macrolide resistance in the presence of a macrolide. Therefore, these drugs may not be effective in the treatment of infections caused by these organisms.