



Nontuberculous Mycobacteria in Normal and Abnormal Hosts

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8/5/2026



Disclosures of Financial Relationships with Relevant Commercial Interests

- Research Grant---Insmed, AN2,
- Consultant--- Insmed, AN2

Nontuberculous Mycobacterium (NTM)

- “MOTT” or “Atypical”
- Environmental organisms
 - Soil, lakes, rivers, municipal water systems
 - Resistant to chlorine and most disinfectants
- Biofilm
 - Live within amoeba, legionella, others

Laboratory Growth Characteristics

- “Slow” growers (>2 weeks in AFB media, liquid media more quickly)
 - *M. avium* complex (MAC), *M. kansasii*, *M. marinum*, *M. xenopi*
- “Rapid” growers (4-7 days in routine blood agar)
 - *M. abscessus*, *M. chelonae*, *M. fortuitum*
- “Need help” growing
 - *M. marinum*, *M. haemophilum*, *M. ulcerans*
 - *M. genavense* (often molecular ID)

NTM Disease Clinical Manifestations

- Pulmonary (75%)
 - MAC
 - *M. kansasii*
 - *M. xenopi*
 - *M. abscessus*
 - *M. malmoense*

Important Bug-Setting Associations

- Corneal Disease
 - *M. chelonae*
- Healthcare/hygiene associated outbreaks
 - *M. chelonae*, *M. fortuitum*, *M. abscessus*, *M. chimaera*
- Line-associated
 - *M. mucogenicum*
- HIV setting
 - MAC, *M. kansasii*, *M. genavense*, *M. haemophilum*
- Tropical setting
 - *M. ulcerans* (buruli ulcer)

Other Pearls Based on Species

- | | |
|---|---|
| • <i>M. gordonae</i> <ul style="list-style-type: none">• Contaminant | • <i>M. szulgai</i> , <i>M. kansasii</i> , and <i>M. marinum</i> <ul style="list-style-type: none">• Cross-react with IGRAs |
| • NTM are not communicable <ul style="list-style-type: none">• CF? | • <i>M. fortuitum</i> lung disease <ul style="list-style-type: none">• Aspiration |
| • <i>M. immunogenum</i> , <i>M. simiae</i> <ul style="list-style-type: none">• Pseudo-outbreaks | • <i>M. marinum</i> <ul style="list-style-type: none">• Fish and fishtanks |

Question #1

- 72-year-old female with chronic cough, normal CXR, and 1/3 sputums grow MAC.

Which one of the following do you recommend?

- A. CT scan of chest AND Additional sputum AFB cultures
- B. Empiric therapy with azithromycin, ethambutol, and rifampin
- C. Additional sputum AFB cultures
- D. Wait for in vitro susceptibility data and then treat

Pulmonary NTM

- 2007 ATS/IDSA diagnostic criteria:
- Patient has both radiographic evidence of disease and pulmonary symptoms
- **AND**
- At least 2 sputum cultures positive, or
- One BAL or tissue specimen with positive culture
- **OR**
- Tissue with granulomatous histopathology in conjunction with positive culture (BAL or sputum)

Griffith D et al. AJRCCM 2007

Pulmonary NTM

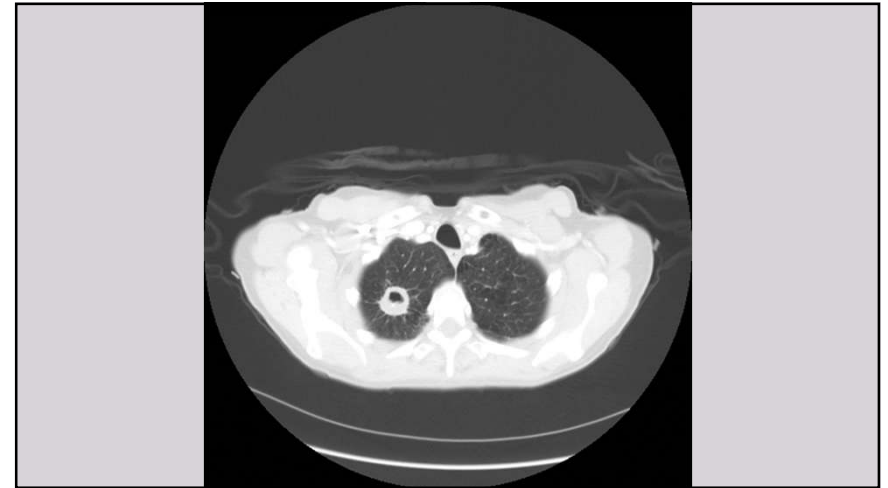
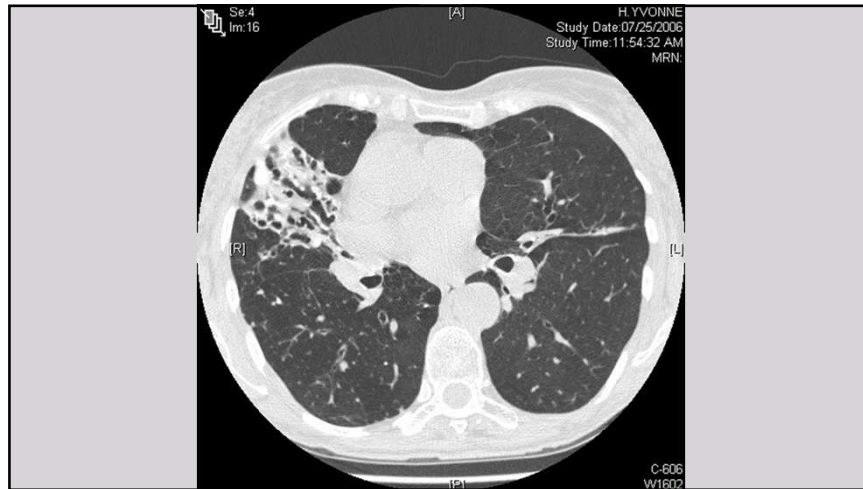
- MAC is most common etiology (60-90%)
- *M. kansasii* and *M. abscessus*
 - *M. kansasii* primarily in the South
 - Recent *M. abscessus* increase in CF
- Other organisms of importance
 - *M. xenopi* (northern US/ Canada, Europe)
 - *M. malmoense* (Europe)

Two Types of MAC Pulmonary Diseases

- **Older male, smoker, COPD**
 - Apical cavitary or fibronodular disease
 - More rapidly progressive
- **Older female (“Lady-Windermere”)**
 - Scoliosis, thin, pectus deformities*, hypomastia
 - Nodular and interstitial nodular infiltrate
 - Bronchiectasis right middle lobe / lingula
 - Bronchiolitis (“tree and bud”) on HRCT
 - Slowly progressive

*Isleman MD et al. Am Rev Respir Dis. 1991





Pulmonary NTM Risk Factors

- Underlying lung architectural abnormalities
 - Bronchiectasis, CF, α -1, emphysema
 - Prior TB, GERD/aspiration
- Exposure/transmission
 - Gardening/soil, Hot tubs
- Immunosuppressives
 - Prednisone, inhaled corticosteroids, biologics

NTM Pulmonary Disease Diagnosis

- **Diagnosis $\neq$ decision to treat**
 - Observation vs. suppression vs. cure

MAC Therapeutic Options

- Treatment best defined for MAC
 - Start [Macrolide, rifampin, ethambutol](#)
 - Amikacin first 1-2 months for cavitory disease
 - Treatment duration 18-24 months (12-month culture negative)
 - Macrolide monotherapy is contraindicated
 - Recommended to test susceptibility for macrolide
 - TIW okay if non-cavitory or not re-infection

MAC Therapeutic Caveats

- Non-cavitory mild/moderate MAC
 - 2 drugs (AZI/EMB) nearly equivalent to 3 drugs (AZI/EMB/RIF)
 - Encore data show arykace/AZI/EMB is superior to AZI/EMB in treatment naive

Pulmonary *M. kansasii* Therapy

- *M. kansasii* clinically more like TB
 - Thin-walled cavities, upper lobes
 - Treatment with INH, RIF, EMB
 - TIW therapy ok
 - Treatment duration: 12 months culture negativity
 - High treatment success rates (90%+)
 - RIF is key drug
 - FQ or Macrolide useful in RIF resistant disease

Pulmonary *M. abscessus ssp.* Therapy

- *M. boletti*, *M. massiliense*, *M. abscessus*
 - [Inducible macrolide resistance--erm \(41\) gene](#)
- “Cure” = rare
- Can be more rapidly progressive than MAC
- 3-4 drugs for 18-24 months
 - 4-6 months “induction” phase
 - “suppressive strategy” thereafter

***M. abscessus* Therapy**

- Parenteral agents
 - Omadacycline 100mg QD, Tigecycline 50mg QD, Cefoxitin 2gm TID, Imipenem 1000mg BID, Amikacin 10mg/kg TIW
- Oral agents
 - Clofazimine 50-100mg QD, Linezolid 600mg QD, moxifloxacin 400mg QD (rarely suscep), Azithromycin 250mg QD (if suscep), Omadacycline 300mg QD
 - Surgical resection

Extrapulmonary NTM

1. Immunocompetent settings
2. Immunocompromised settings

Question #2

A 40-year-old construction worker who grew up in central Mexico but is now living in Virginia has had multiple nodules of his left leg between the knee and ankle for at least 3 months.

- His leg is slightly tender and erythematous with nodules but no v fluctuance. There is no inguinal adenopathy.
- He has steroid dependent asthma for which he takes chronic prednisone.
- Otherwise, he feels well, has been working regularly, and has no fever or weight loss.
- He has been to urgent care several times.
- His white blood count and routine chemistries were normal on several occasions. Two weeks courses of doxycycline and cephalexin had no effect.

You obtain a chest x-ray which is normal and CT scan of his leg which shows no fluid collections or bone lesions.

A punch biopsy performed by a dermatologist 4 days ago is growing a mycobacteria

Question #2

Which Mycobacteria is this most likely to be?

- A. *Mycobacterium gordonae*
- B. *Mycobacterium tuberculosis*
- C. *Mycobacterium leprae*
- D. *Mycobacterium chelonae*
- E. *Mycobacterium kansasii*

Immunocompetent Settings

- Nail salon, trauma, surgical or injection procedures, fish tank, hot tubs
- Rapid or slow growing NTM
- Incubation period
- Infection usually occurs 2-8 weeks after contact with contaminated water source

Children Under 5 Years NTM > TB



- Usually MAC
 - Males > females, age 1-2 years old
- Surgical resection alone is best therapy
- Adjunctive ABX rarely needed

Post-plastic Surgery



- Usually Rapid Grower:
 - *M. chelonae*
- Remove foreign-bodies
- Therapy as per in-vitro susceptibility
- Length 4-6 months

M. Marinum - Fish Tank Granuloma



Treatment: Multiple Drugs

- Macrolides, sulfonamides, doxycycline, rifampin, ethambutol
- Treat with 2 agents X 3-4 months.
- Surgical debridement if necessary

Nail Salon Furunculosis

- Outbreaks and sporadic
- Rapid Growers most common (*M. fortuitum*)
- Oral antibiotics
 - 4 months fluoroquinolone and/or doxycycline
 - Can be self-limited



Tattoo-associated

- *M. chelonae*
- Tattoo-ink outbreaks
- 2-3 months oral therapy
 - Based on in-vitro susceptibility
 - 1-2 agents
 - Macrolides almost always



Immunosuppression Other than HIV

- Most frequently disseminated
 - Local inoculation versus GI route
- Risk factors and conditions
- ESRD, prednisone, biologic immunosuppressives
- Cancer, transplant, leukemia (hairy cell)
- Auto-antibody and cytokine/receptor deficiency states
 - INF-gamma, IL12-23 pathway, STAT-1
- Disease split between RGM and slow growers
 - RGM more common here than in pulmonary disease

M. chelonae in Cancer Patient



***M. chelonae* and *M. fortuitum* Treatment**

• ***M. chelonae***

- Macrolides, fluoroquinolone, linezolid
- IV drugs include aminoglycosides, imipenem, cefoxitin, tigecycline
- **Note: tobramycin is best for *M. chelonae***

• ***M. fortuitum***

- Macrolides, fluoroquinolone, bactrim, doxy (50%)
- IV drugs include aminoglycosides, imipenem, cefoxitin, tigecycline

Length of treatment for disseminated infection
3 drugs (including 1 IV) X 4-6 months
Depends on immunosuppression reversal

M. chimaera

- Slow growing. *M. avium* complex
 - Pulmonary disease
- Extrapulmonary disease
 - 150+ cases from open heart surgery: prosthetic valve, vascular graft, LVAD, heart transplant
- Aerosol from contaminated heater-cooler units used in operating room for cardiac by-pass.
- Time to diagnosis 1.7-3.6 years post-op, with cases reported up to 6 years postoperatively.
- Mycobacterial blood cultures
- Treatment: forever?



Question #3

A 27-year-old male with sickle cell disease presents with a chest syndrome crisis: he has his typical fever, chest pain, and leukocytosis. He is cultured and started on vancomycin and levofloxacin.

His initial chest radiograph shows bilateral infiltrates: an x-ray one week prior showed only some chronic scarring.

- Sputum Gram stain, acid-fast stain, and culture show only modest amounts of normal flora.
- His CBC and Chem 12 show a leukocytosis, hemolytic anemia, and mild LFT abnormalities.

Careful physical examination reveals no localizing physical findings: a tunneled double lumen subclavian line, in for 4 months, appears unremarkable.

After 96 hours, the laboratory reports that one blood culture is growing a non-branching beaded Gram-positive bacillus that is acid-fast stain positive.

- Three additional blood cultures are drawn (one through each lumen of the subclavian line) and one peripherally: at 48 hours they are all reported to be positive for an acid-fast non branching rod.

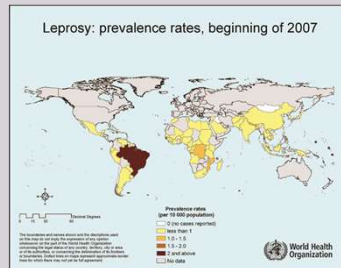
Question #3

Which of the following organisms would be most likely?

- A. *Nocardia asteroides*
- B. *Mycobacterium mucogenicum*
- C. *Rhodococcus equi*
- D. *Legionella micdadei*
- E. *Mycobacterium tuberculosis*

Hansen's Disease (Leprosy)

- Rare in US (100-200 cases per year)
 - Armadillos and gulf region
 - Rest imported
- Most humans resistant
 - Household contacts at risk (low risk)
 - Nasopharyngeal transmission?
 - *M. leprae* does not grow in culture



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Leprosy Disease Classification

- Paucibacillary (PB)
 - Most common form
 - “*Tuberculoid*”
 - Bacillary load < 1 million
 - Skin biopsy: AFB negative
 - <5 skin lesions
- Multibacillary (MB)
 - “*Lepromatous*”
 - Massive bacillary load
 - Skin biopsy: Floridly positive for AFB
 - >5 skin lesions





Leprosy Treatment

- PB (6-12 months)
 - Dapsone 100mg daily
 - Clofazimine 50mg daily
 - *Rifampin 600mg once monthly
- MB (12-24 months)
 - Dapsone 100mg daily
 - Clofazimine 50mg daily
 - Rifampin 600mg daily
- (US recommendations changed in 2025---now once monthly Moxi, RIF, Minocycline, 12-24 months)

Complications: (1) reversal reactions, treat with prednisone/MTX, (2) Erythema nodosum (EN), **treat with thalidomide**, clofaz, apremilast

Top 10 or 12 NTM Pearls for the Boards

- Footbaths = *M. fortuitum* or other RGM
- Plastic Surgery = *M. chelonae* or other RGM
- Equatorial Africa = *M. ulcerans*
- HIV disseminated MAC that doesn't grow = think of *M. genavense*
- *M. abscessus* usually has inducible macrolide resistance (erm gene)
- Macrolide, EMB, RIF for 18-24 months for pulmonary MAC
- *M. gordonae* is 99.9% a contaminant
- ATS/IDSA pulmonary case definition: need one BAL or two sputums or tissue
- Know NTM species that cross-react with TB IGRAs
- No clofazimine in HIV related MAC
- *M. kansasii* behaves like TB---responds to TB drugs (RIF, EMB, INH)
- PZA not useful for any NTM

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