Nontuberculous Mycobacteria in Normal and Abnormal Hosts

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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
- Skin and Soft tissue (15%)
  - MAC, M. marinum, M. abscessus, M. chelonae, M. fortuitum, M. kansasii, M. ulcerans
- Lymph node disease (5%)
  - MAC, (historically also M. scrofulaceum)
- Disseminated (5%)
  - MAC, M. kansasii, M. abscessus, M. chelonae, M. haemophilum
  - Hypersensitivity pneumonitis (0%)
  - MAC and hot-tubs

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### Important Bug-Setting Associations

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

### Other Pearls Based on Species

- ***M. gordonae***
  - Contaminant
- **NTM are not communicable**
  - *Except M. massilense in CF*
- ***M. immunogenum, M. simiae***
  - Pseudo-outbreaks
- ***M. szulgai, M. kansasii, and M. marinum***
  - Cross-react with IGRAs
- ***M. fortuitum lung disease***
  - Aspiration
- ***M. marinum***
  - Fish and fish tanks

### Question #1

72 year old female with chronic cough, normal CXR, and 1/3 sputums grow MAC. Which one of the following you do 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
- 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 cavity 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

*Taraske 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 ≠ 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 cavitary disease
  - Treatment duration 18-24 months (12 month culture negative)
  - Macrolide monotherapy is contraindicated
  - Recommended to test susceptibility for macrolide
  - TIW okay if non-cavitary or not re-infection
**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.

**M. abscessus Therapy**
- Parenteral agents
  - 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)**
  - Surgical resection

**Pulmonary M. abscessus Therapy**
- *M. boletii, M. massiliense, M. abscessus*
- Inducible macrolide resistance—erm (41) gene
- "Cure" = rare
- More rapidly progressive than MAC
- 3-4 drugs for 18-24 months
- 4-6 months “induction” phase
- “suppressive strategy” thereafter

**EXTRAPULMONARY NTM**
1. Immunocompetent settings
2. Immunocompromised settings

**Immunocompetent settings**
- Nail salon, trauma, surgical or injection procedures, fishtank, hot tubs
- Rapid or slow growing NTM
- Incubation period
  - Infection usually occurs 2-6 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
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Speaker: Kevin Winthrop, MD

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, thiamine
  - Trial 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

Question # 2


Question # 2

Based on the most likely diagnosis, which of the following do you recommend:

A. Start MAC therapy
B. Start HAART plus MAC prophylaxis
C. Start MAC therapy and HAART
D. Start HAART only

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NTM in HIV
- Disseminated MAC
- GI route of infection
- Less frequent in HAART era
- Related issues
  - Clofazimine increases mortality (do not use!)
  - Rifabutin dose adjustment with PI
  - Immune reconstitution inflammatory syndrome (IRIS)

Immunosuppression other than HIV
- Most frequently disseminated
  - Local inoculation versus GI route
- Risk factors and conditions
  - ESRO, 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 amphotericin B, imipenem, cefoxitin, tigecycline
  - Note: tobramycin is best for M. chelonae
- M. fortuitum
  - Macrolides, fluoroquinolone, bacitracin, doxy (50%)
  - IV drugs include amphotericin B, imipenem, cefoxitin, tigecycline

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

MYCOBACTERIUM CHIMAERA
- Slow growing. M. avium complex.
- Requires molecular identification
- Over 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: ???

Hansen’s Disease (Leprosy)
- Rare in US (40-50 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
# Leprosy Disease Classification

<table>
<thead>
<tr>
<th>Paucibacillary (PB)</th>
<th>Multibacillary (MB)</th>
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<tbody>
<tr>
<td>Most common form</td>
<td>&quot;Lepromatous&quot;</td>
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<tr>
<td>&quot;Tuberculoid&quot;</td>
<td>Massive bacillary load</td>
</tr>
<tr>
<td>Bacillary load &lt; 1 million</td>
<td>Skin biopsy: floridly positive for AFB</td>
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<tr>
<td>Skin biopsy: AFB negative</td>
<td>&gt;5 skin lesions.</td>
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<tr>
<td>≤ 5 skin lesions</td>
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## Leprosy Treatment

- **PB (6 months)**
  - Dapsone 100mg daily
  - Rifampin 600mg once monthly
  - Clofazamine 100mg daily

- **MB (12 months)**
  - Dapsone 100mg daily
  - Clofazamine 50mg daily
  - Rifampin 600mg once monthly OR
  - Clofazamine 300mg once monthly

Complications: reversal reactions, erythema nodosum
Treat with prednisone, thalidomide, other

## 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