

# Non-tuberculous Mycobacteria (NTM) Infections

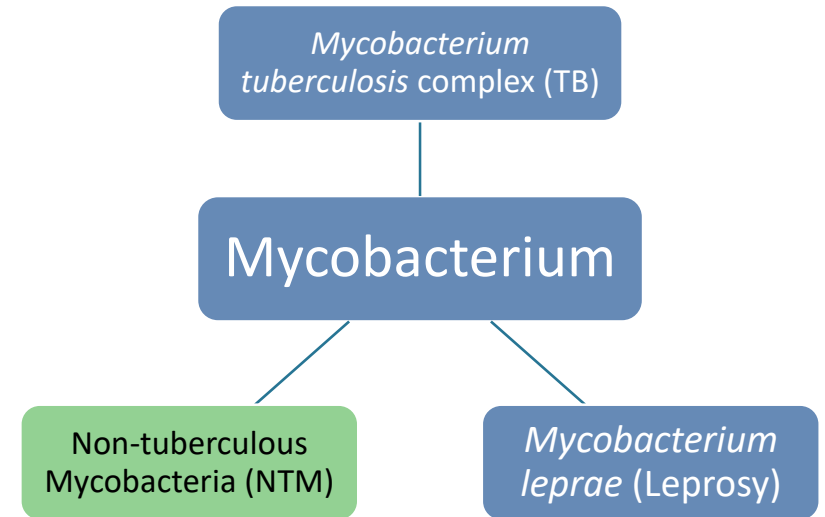
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*April 26, 2023*

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# What are NTM?

- Over 190 species!
- Different than “normal” bacteria
  - Acid fast bacilli
  - Variable growth times
    - “Rapid growing mycobacteria” take 7 days or less for identification
    - Others can take weeks or MONTHS for full identification/susceptibility
- Natural habitat
  - Soil, water, dust, animals
  - Community tap water is a major reservoir – organisms often isolated from biofilms in plumbing



- Transmission
  - Environmental
  - Generally NOT contagious person to person

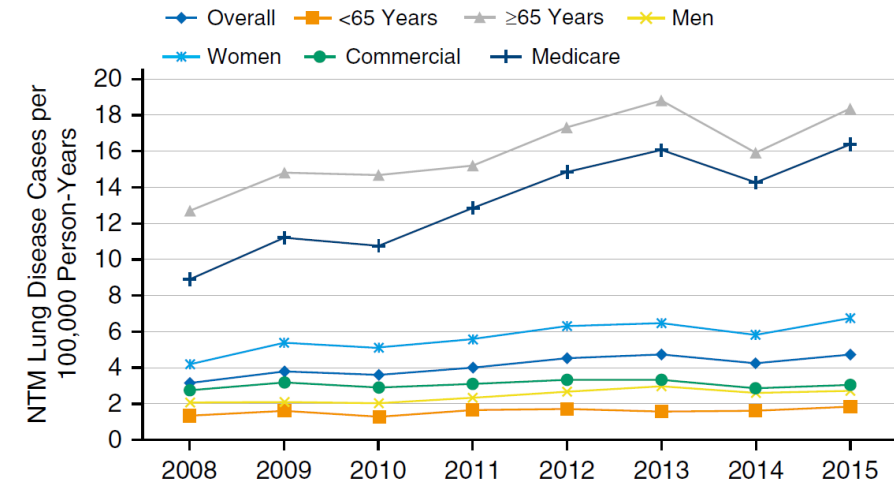
# Increasing clinical relevance

- NTM first recognized to cause human disease in 1930s
- AIDS patients – *Mycobacterium avium* complex (MAC)
- Non-immunocompromised patients
- Healthcare associated infections
- Low treatment success rates and lack of quality evidence to guide management
- Increasing incidence and prevalence

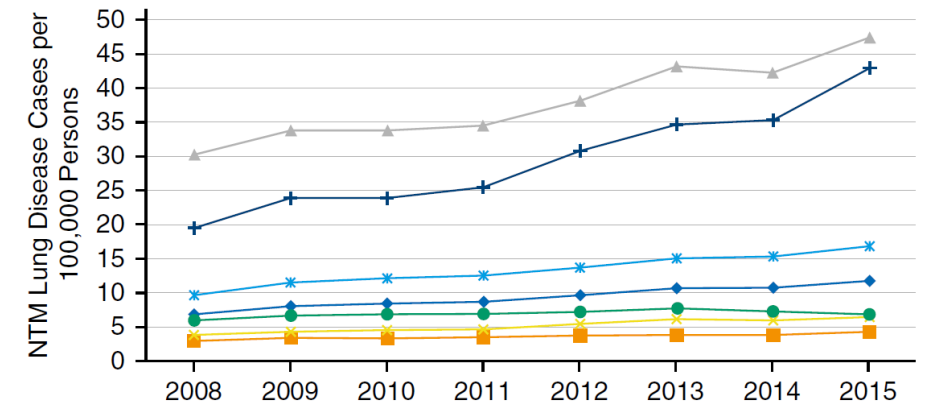
# Epidemiology

- Difficult to estimate burden of NTM disease
- Overall trend: NTM is on rise!
  - Worldwide
  - Especially in elderly women
- Reasons?
  - Improving identification techniques
  - Aging population
  - Medical advances

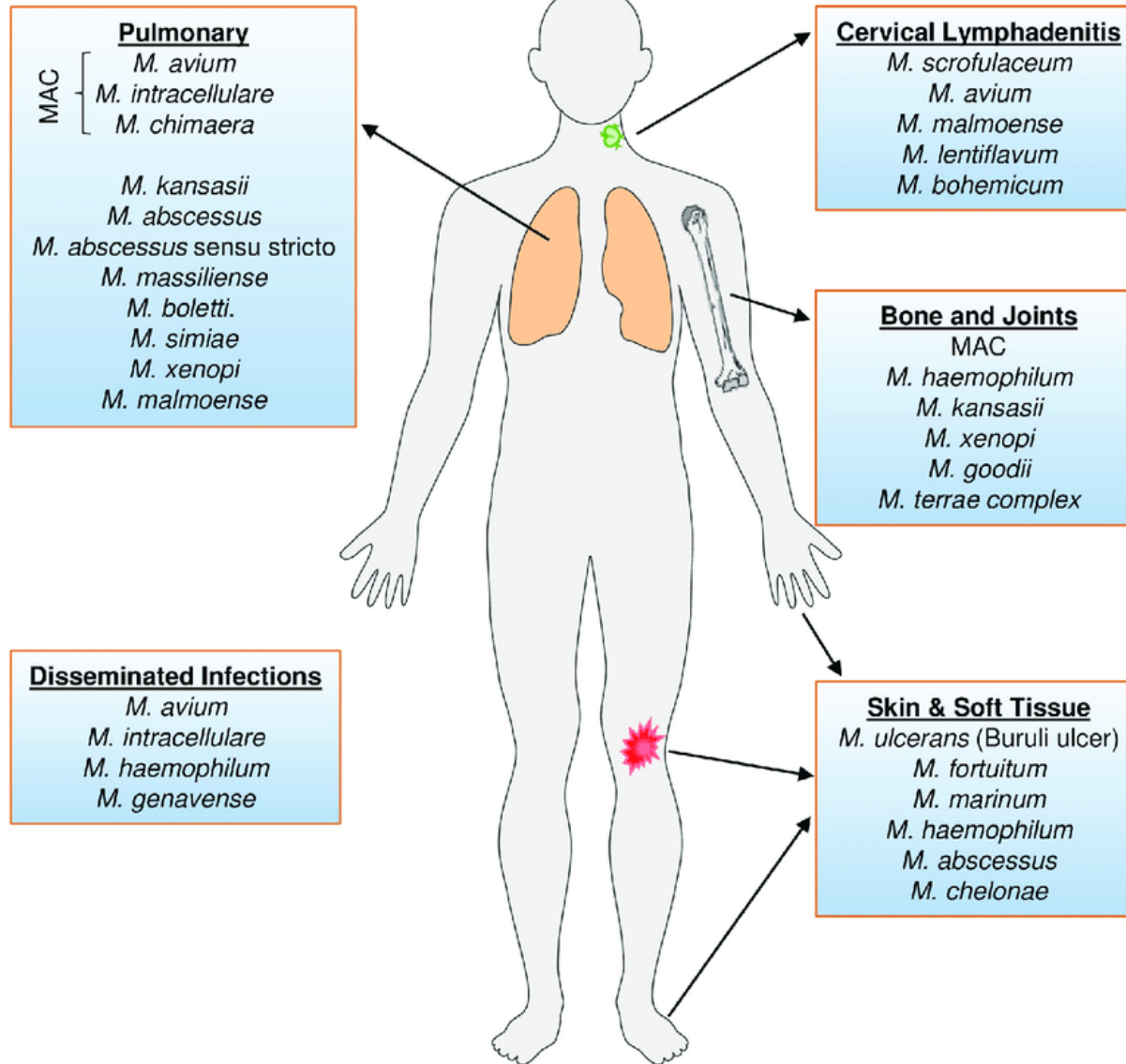
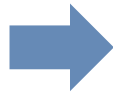
## Incidence



## Prevalence



Most common  
site of infection



# The perfect NTM storm



- Shower heads
- Hot tubs
- Gardening/soil
- Surgical/medical equipment
- Geographic location



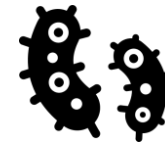
Host

Environment

Organism

## Risk factors for pulmonary NTM

- Structural lung damage/disease
- Post-menopausal women
- Elderly
- Immunocompromise (e.g. AIDS)
- Genetic predisposition



*M. mucogenicium*    *M. abscessus*  
*M. gordonae*                      *M. avium* complex                      *M. kansasii*



# Diagnosis of pulmonary NTM infection

Symptoms

Radiologic evidence



One of the following:

- CXR: nodules or cavitation
- CT: bronchiectasis, multiple small nodules

Exclusion of other diagnoses

Microbiologic evidence



One of the following:

- Sputum cx positive **x2**
- Bronchial wash cx positive x1
- Lung biopsy histopathology positive and any respiratory cx positive

NTM on culture  $\neq$  NTM infection

# Treatment of pulmonary MAC infection

Treatment selection is based on disease characteristics

## Nodular/bronchiectatic

3 drugs

Three times weekly

Azithromycin, rifampin, ethambutol

## Cavitary

≥3 drugs

Daily

Azithromycin, rifampin, ethambutol,  
IV amikacin (may be 3x/week)

## Refractory

≥4 drugs

Daily

Azithromycin, rifampin, ethambutol,  
IV amikacin (may be 3x/week) or  
inhaled amikacin

## Monitoring

Sputum cx every 1-2  
months

Chest imaging

Labs for antibiotic  
toxicity/levels

Symptoms

Antibiotic duration: at least 12 months from negative sputum cx



# Macrolides are KEY to success

Macrolide class includes:

- Azithromycin
- Clarithromycin

- Higher failure rate when omitted from regimen
  - Sputum conversion rates decrease from 80% to 5-36% in macrolide-resistant MAC
  - High mortality

## Inducible resistance

- *Erm* genes naturally present in some NTM
- *M. abscessus* subsp *abscessus*, *M. fortuitum*, *M. smegmatis*

## Acquired resistance

- Mutation occurs during treatment
- Must use adequate companion antibiotics
- 3 drugs minimum, 2-drug combinations are NOT recommended currently (but trial is underway)

# Treatment principles

Meeting diagnostic criteria for NTM pulmonary disease  
**DOES NOT** necessarily mean antibiotic treatment is required

Risk vs benefit  
evaluation  
must consider  
the following:

Symptoms

Pathogenicity  
of organism

Goals of  
therapy

Likelihood of  
success

Risks of  
therapy

Patient  
preference

# Treatment principles

- Definition of “success” matters
- Measuring success
  - Microbiologic
    - Negative sputum cx at 6 months
    - Durability?
  - Radiographic
  - Clinical/symptomatic
  - Quality of life
  - Mortality

## Risk vs benefit of treatment evaluation



Different success rates for pulmonary NTM	
MAC	<ul style="list-style-type: none"> <li>• 60-90% have sputum conversion</li> <li>• High relapse rates of ~50%</li> <li>• Pulmonary hygiene alone may be successful</li> </ul>
<i>M. kansasii</i>	<ul style="list-style-type: none"> <li>• 80-100% have sputum conversion</li> <li>• Low relapse rates of ~5%</li> </ul>
<i>M. abscessus</i> subsp <i>abscessus</i>	<ul style="list-style-type: none"> <li>• 33% have sputum conversion</li> </ul>

# Treatment principles

- Adverse drug reactions are very common and sometimes severe
  - >90% overall rate
  - Up to 40% will not complete treatment due to adverse drug reactions
- Different reactions possible
  - GI upset, liver impairment, kidney impairment, cardiac abnormalities (QTc prolongation), ocular toxicity, tinnitus, hearing loss, vertigo, neuropathy, phototoxicity, blood count abnormalities, hypersensitivities

## Risk vs benefit of treatment evaluation



## IV aminoglycosides for NTM

### **32% risk of permanent hearing loss**

Risk increased with age, duration of treatment, cumulative dose.

# To treat or not to treat?



45 year old male with history of smoking and COPD, frequent hospital readmissions, and new diagnosis of cavitary MAC disease.

80 year old female with late stage lung cancer and new diagnosis of *M. abscessus* subsp *abscessus* with *erm41* gene detected. Would require would require IV amikacin, IV imipenem, linezolid, and clofazimine.

# Infection Prevention

- Community and healthcare-associated outbreaks described
- Water systems
- Surgical contamination
  - May take months or YEARS to know infection was a surgery associated
- Instructions from CDC
  - Establish water management program
  - Follow state/local reporting requirements for NTM
  - Consider reporting or conducting surveillance for extrapulmonary NTM



Images obtained from: [waterandhealth.org](http://waterandhealth.org), [livanova.com](http://livanova.com), [uwa.edu.au](http://uwa.edu.au), [quesnelobserver.com](http://quesnelobserver.com)

# Thank You

Questions and Discussion

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