

**Clinical symptoms** 

Shortness of breath

• Chronic cough

Fever/chillsNight sweats

Weight loss

Hemoptysis

# Diagnosing and Managing Nontuberculous Mycobacteria

# - CLINICAL

- Cough, fatigue, weight loss

**Diagnostic criteria** 

- RADIOGRAPH
- Nodular or cavitary opacities on chest radiograph or
- High resolutation computed tomography showing multifocal bronchiectasis with multiple small nodules

### BACTERIOLOGY

- Positive culture results from at least two separate expectorated sputum samples
- Positive culture results from at least one bronchial wash or lavage
- Transbronchial biopsy or other lung biopsy with mycobacterial histopathologic features and positive culture for NTM or biopsy showing mycobacterial histopathologic features and one or more sputum or bronchial washings that are culture positive for NTM

# Clinical phenotypes



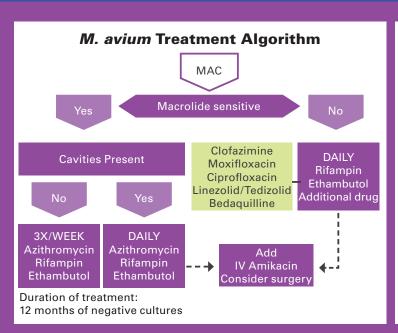




Bronchiectatic Nodular

Cavitary

Fibrocavitary



# **Treatment of MAC** Initial Therapy clarithromycin 1000 mg clarithromycin 500-1000 mg/day **or** azithromycin 250-500 mg/day Macrolide tiw or azithromycin 500-600 mg tiw Ethambutol 25 mg/kg tiw 15 mg/kg day rifampin 600 mg tiw Rifamycin rifampin 450-600 mg/day Aminoglycoside None strep or amikacin

# Change from intermittent to daily therapy Use of clofazimine 30% additional culture conversion 30% additional culture conversion 30% additional culture conversion

## Treatment of M. abscessus M. abscessus M. abscessus M. massiliense M. bolletti "Functional" erm 41 gene Imipenem (IV) Macrolide? Macrolide Cefoxitin (IV) Tigecycline (IV) IV Amikacin IV Amikacin Linezolid/Tedizolid Clofazimine Moxifloxacin 2+ mos 1-2+ mos Bedaquiline Consider surgery for focal disease. ≥2 other drugs ≥1 other drug Duration 12 mos culture negativity.

# Interpretation of extended clarithromycin susceptibility results for *M. abscessus*

M. abscessus subspecies	Clarithromycin susceptibility days 3–5	Clarithromycin susceptibility day 14	Macrolide susceptibility phenotype	Genetic implication	Macrolide Effect
M. massiliense M. abscessus*	Susceptible	Susceptible	Macrolide susceptible	dysfunctional erm(41) gene	anti-mycobacterial
M. abscessus M. bolletii	Susceptible	Resistant	Inducible macrolide resistance	functional erm(41) gene	immunomodulatory
Any	Resistant	Resistant	High-level constitutive macrolide resistance	23S ribosomal RNA point mutation	immunomodulatory

\*15-20% of  $\it M.~abscessus$  will have a dysfunctional ERM41 gene (c28 sequevar)

# **Surgical Treatment of Pulmonary NTM Disease**



# Indications to consider surgery

- Massive hemoptysis
- Failure of medical therapy
- Intolerance to medical therapy
- Macrolide resistant MAC infection
- Cavitary lesions
- Focal severe bronchiectasis
- Focal disease with *M. abscessus* infection

1 Am J Respir Crit Care Med Vol 175. pp 367–416, 2007. | 2 Antimicrob Agents Chemother. 2015;59(8):4994-4996. 3 CHEST 2016; 149(5):1285-1293. | 4 Am J Respir Crit Care Med 2017; 195(6): 814–823. | 5 Thorax 2017;72(Suppl 2):ii1

