Final Identification of Nontuberculous Mycobacteria (NTM) Matters

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COI-I have no disclosures
● Toolbox 1 – specimen
● Toolbox 2 – positive culture
● Good news – bad news
● Pulmonary NTM
● National Jewish Health algorithm
● National Jewish Health laboratory data
● Beyond routine testing
● Patient centered approach
✓ Specimen – sputum, CSF, formalin-fixed tissue

- AFB microscopy
- Solid & broth-based media
- **NAAT-D** (TB complex)
- **NAAT-R** (RIF, INH and more)
- Direct AST

Molecular TB Testing 7 Days a Week
✓ AFB positive culture (broth-, solid-based media)

- TB Yes/No (final identification within TB complex)
- NAAT-R
- Broth-based AST
- Agar-based AST
- Minimal Inhibitory Concentration (MIC)
NTM Detected…

**Good news for TB Control** – No contact investigation, etc.

… and clinically significant…

**Bad news for the patient** – cure rates for *M. avium* complex or *M. abscessus* range from 50-75% but relapses are common and exogenous reinfection is a major challenge
PNTM = pulmonary nontuberculous mycobacteria
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<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>M. avium complex</td>
<td>18.0</td>
<td>26.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>M. xenopi</td>
<td>7.4</td>
<td>9.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>M. fortuitum</td>
<td>0.63</td>
<td>1.2</td>
<td>0.01</td>
</tr>
<tr>
<td>M. abscessus</td>
<td>0.63</td>
<td>1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other nontuberculous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycobacterium spp.</td>
<td>1.8</td>
<td>3.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All nontuberculous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycobacterium spp.</td>
<td>29.3</td>
<td>41.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
NTM in CF Patients

- AFB positive
- Rule out *M. tuberculosis* complex
- Sequence *rpoB* gene
  - if *M. abscessus* group, then
  - erm(41) and *hsp65*
> 8,800 isolates were analyzed using \textit{rpoB} gene sequencing

Seven \textit{Mycobacterium} species accounted for ~80% of all isolates tested

\begin{itemize}
\item 24.4\% \textit{M. abscessus} group
\item 19.9\% \textit{M. avium}
\item 16.4\% \textit{M. intracellulare}
\item 6.0\% \textit{M. chimaera}
\item 5.1\% \textit{M. fortuitum}
\item 3.8\% \textit{M. gordonae}
\item 3.7\% \textit{M. chelonae}
\end{itemize}
*M. abscessus/M. bolletii* isolates 491 bp *erm(41)* gene

*M. massiliense* isolates 218 bp *erm(41)* gene with deleted region

*M. massiliense* is positive for the *erm(41)* gene but contains a 273-bp deletion within the gene rendering the gene nonfunctional.
<table>
<thead>
<tr>
<th>Species</th>
<th>Number identified</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. abscessus</em></td>
<td>1,470</td>
<td>71.7%</td>
</tr>
<tr>
<td><em>M. massiliense</em></td>
<td>420</td>
<td>20.5%</td>
</tr>
<tr>
<td><em>M. bolletii</em></td>
<td>110</td>
<td>5.4%</td>
</tr>
<tr>
<td>other</td>
<td>58</td>
<td>2.4%</td>
</tr>
</tbody>
</table>
Treatment response rates to combination antibiotic therapy including clarithromycin were much higher in patients with *M. massiliense* lung disease than those with *M. abscessus* lung disease.

Koh et al Am J Respir Crit Care Med 183:405-410 (2011)
### Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>M. abscessus (n=24)</th>
<th>M. massiliense (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>18 (75%)</td>
<td>32 (97%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Unchanged</td>
<td>4 (17%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td>2 (8%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>HRCT Findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>10 (42%)</td>
<td>27 (82%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Unchanged</td>
<td>7 (29%)</td>
<td>5 (15%)</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td>7 (29%)</td>
<td>1 (3%)</td>
<td></td>
</tr>
<tr>
<td>Sputum conversion</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Converted</td>
<td>6 (25%)</td>
<td>29 (88%)</td>
<td></td>
</tr>
<tr>
<td>Relapsed</td>
<td>4 (17%)</td>
<td>3 (9%)</td>
<td></td>
</tr>
<tr>
<td>Failed</td>
<td>14 (58%)</td>
<td>1 (3%)</td>
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</table>

Koh WJ et al. AJRCCM. 2011;183:405-410
**Pulmonary NTM**

**Signs and Symptoms:**
Cough (chronic); Fatigue; Weight Loss; Hemoptysis; Dyspnea

**Radiology**
- Fibrocavitary – *M. avium* complex
- Nodular & interstitial nodular infiltrates – *M. avium* complex
- Fibrocavitary – *M. kansasii*
- Multi-lobar, reticulonodular or mixed reticulonodular-alveolar opacities – *M. abscessus* group

The NTM species is identified by the laboratory!

Daley CL: Nontuberculous mycobacterial infections *Eur Respir Mon* 2011 52:115-129
✓ Combination MIC
✓ Extended MIC concentrations for inhaled Amikacin
✓ Surgery
“Surgical evaluation in nontuberculous mycobacterial (NTM) infections plays an essential role as part of multidisciplinary management of this complex pulmonary process. Resection of damaged lung parenchyma combined with appropriate antimicrobial therapy may interrupt a cycle of disease progression and relapse in select patients.”

✓ Pulmonary/ID Expert
✓ Expert Laboratory
✓ Experienced Surgeon
Questions?

Mycobacteriology & Pharmacokinetics staff (5 not present)

Thank you!

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