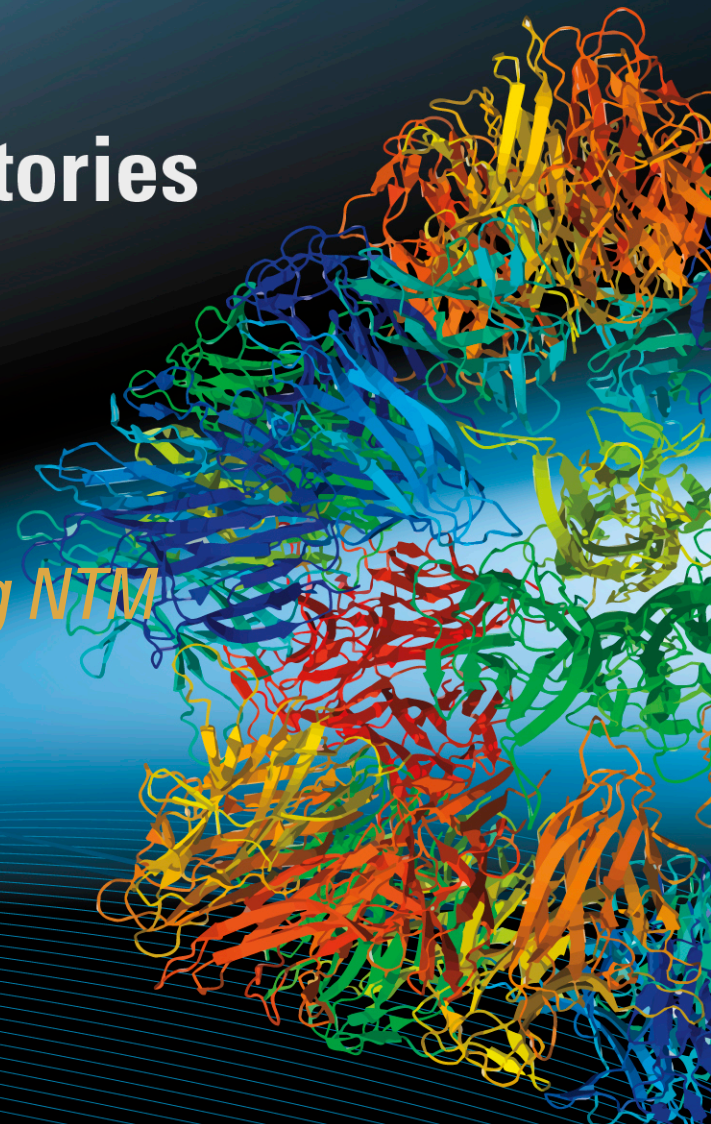


Advanced Diagnostic Laboratories

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Building a Better Algorithm: Identifying NTM

San Diego – August 20, 2013





Outline

- **Taxonomy**
- **What's in a name**
- **Clinical significance – ATS/IDSA**
- **Changing Epidemiology**
- **APHL/CDC Survey**
- **CDC Service**
- **Algorithm**



Aerobic Actinomycetes Genera

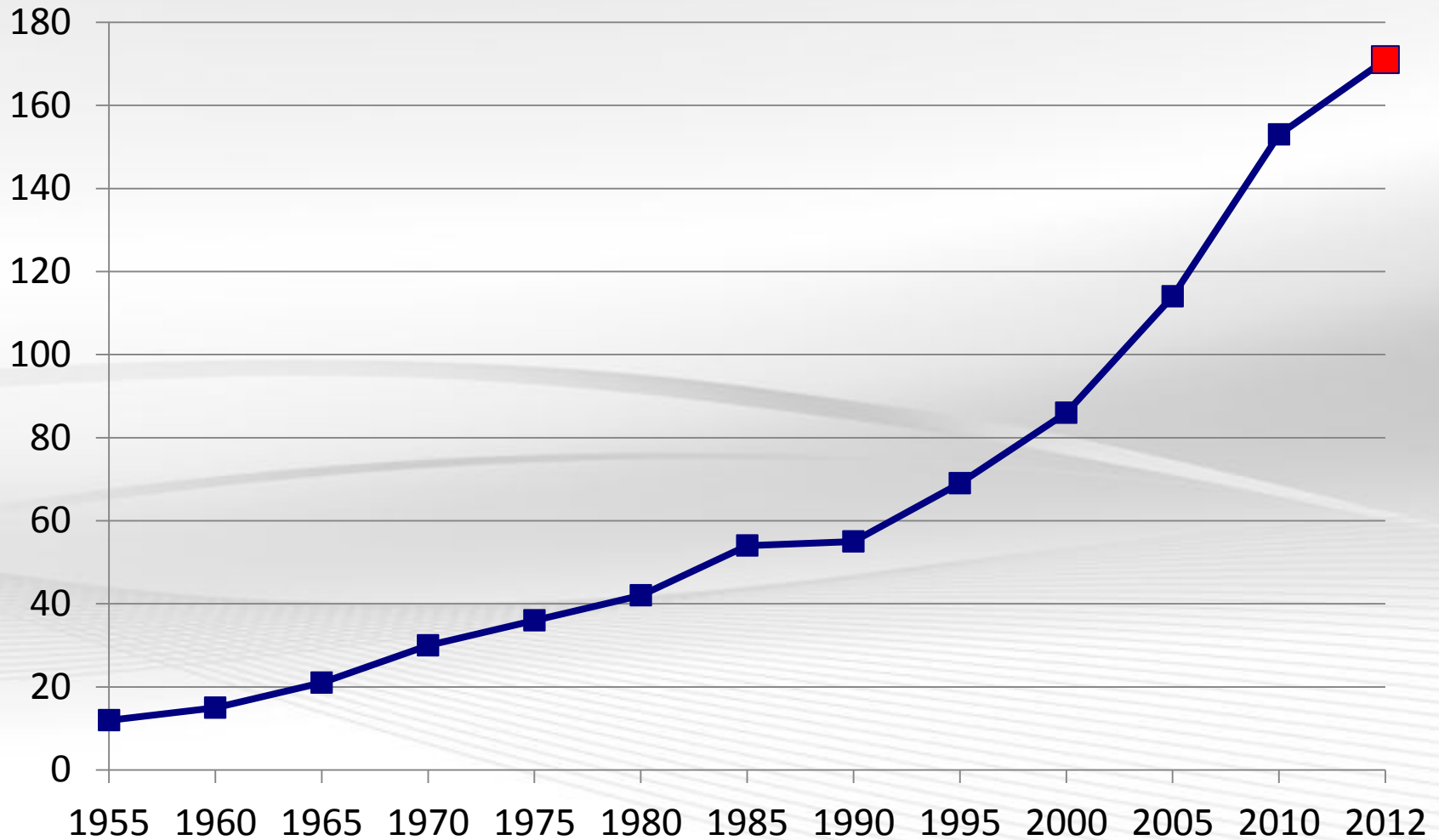
- **Nocardia**
- **Rhodococcus**
- **Mycobacterium**
- **Corynebacterium**
- **Gordonia**
- **Tsukamurella**



Mycobacterium sp.

- **>170** Species in genus *Mycobacterium* (2012)
- ***M. tuberculosis* complex**
M. tuberculosis; M. bovis; M. bovis BCG; M. africanum;
M. caprae; M. microti; M. canettii; M. pinnipedii; M. mungi; M. orygis
- ***M. leprae* – Leprosy or Hansen’s Disease**
- ***M. ulcerans* – Buruli Ulcer**

Published New Mycobacterial Species (N=171)





NTM or what?

- **Anonymous**
- **Unclassified**
- **Unknown**
- **Tuberculoid**
- **Environmental**
- **Opportunistic**
- **Nyrocin**
- **MOTT-Mycobacteria other than tubercle bacilli**
- **Nontuberculous mycobacteria (NTM)**

Debrunner et al Clin Infect Dis. 1992 Aug;15(2):330-45

Pathogenic Potential of NTM

Non-HIV Patients

Table 4. Pathogenic potential of nontuberculous mycobacterial isolates ($n = 513$).

Isolate	No. of strains associated with disease/ total no. of strains (%)
<i>M. avium</i> complex	13/61 (21)
<i>M. kansasii</i>	9/35 (26)
<i>M. xenopi</i>	4/25 (16)
<i>M. malmoense</i>	3/3 (100)
<i>M. fortuitum</i>	2/36 (6)
<i>M. simiae</i>	1/1 (100)
<i>M. marinum</i>	1/3 (33)
<i>M. terrae</i>	1/31 (3)
<i>M. gordonae</i>	0/229
<i>M. scrofulaceum</i>	0/22
<i>M. nonchromogenicum</i>	0/16
<i>M. chelonae</i>	0/14
<i>M. flavescens</i>	0/13
<i>M. triviale</i>	0/8
<i>M. gastri</i>	0/6
<i>M. thermoresistibile</i>	0/2
<i>M. vaccae</i>	0/2
Others*	0/6

* Three rapidly growing, two scotochromogenic, and one nonphotochromogenic species.



Clinical Significance

Microbiologic (in addition to clinical & radiographic) criteria:

NTM isolated from one BAL specimen or at least two separate sputum specimens

or,

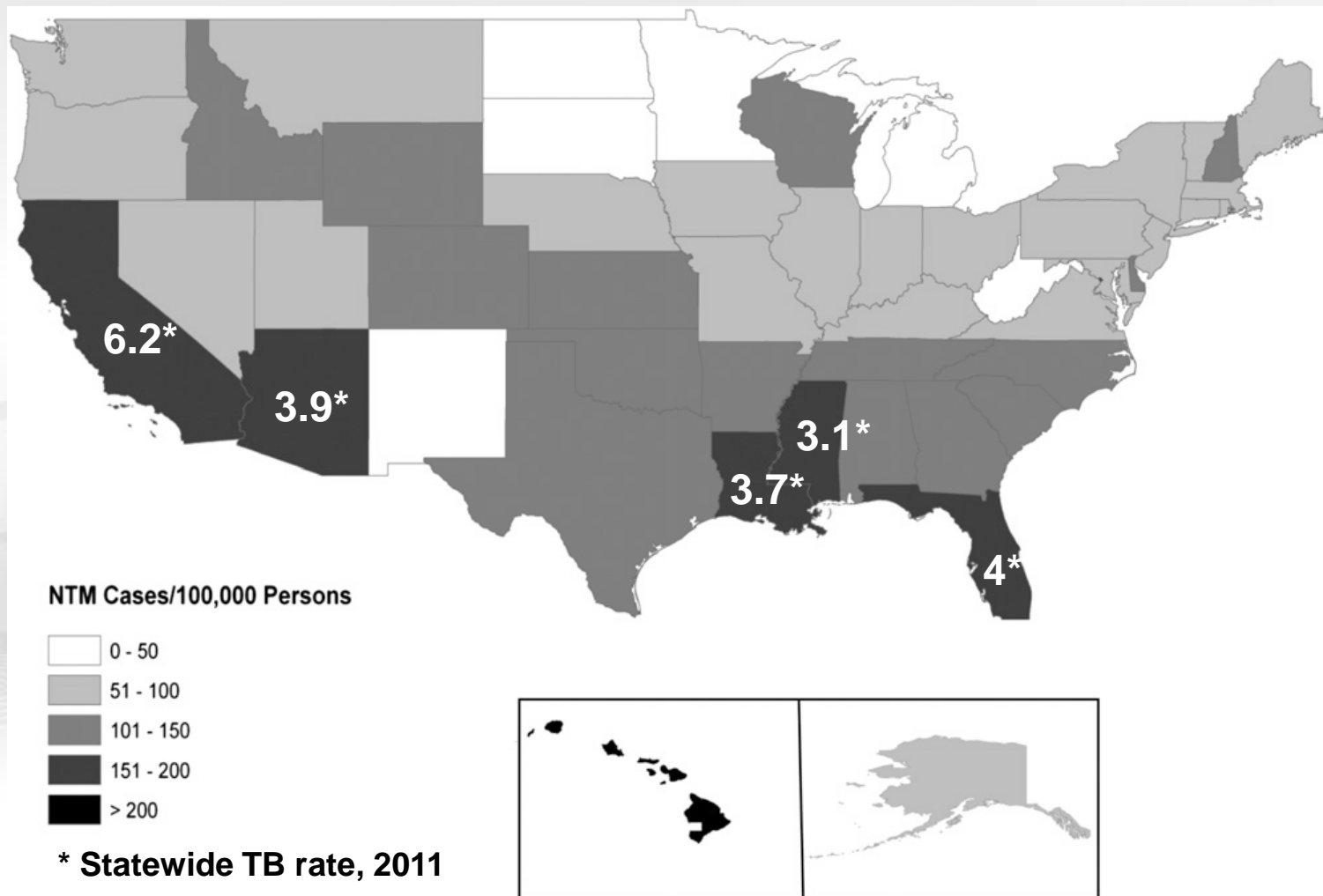
Lung tissue with granulomatous histopathology in combination with an NTM culture positive respiratory specimens or tissue biopsy

ATD/IDSA NTM statement Am J Respir Crit Care Med
175:367-416 (2007)

Questionnaires completed by 349 (60%) physicians on 915 PNTM patients, including 744 (81%) with MAC and 174 (19%) with *M. abscessus*; 3 patients were positive for both
Physician specialties included pulmonology (46%), ID (23%), internal medicine (21%), and family/general practice (10%)

*Using a nationally representative sample of physicians who manage the care of patients with MAC- and *M. abscessus*-associated lung disease, the authors found that fewer than 20% of patients who were actively treated by their physicians received an antibiotic regimen that adhered to evidence-based guidelines*

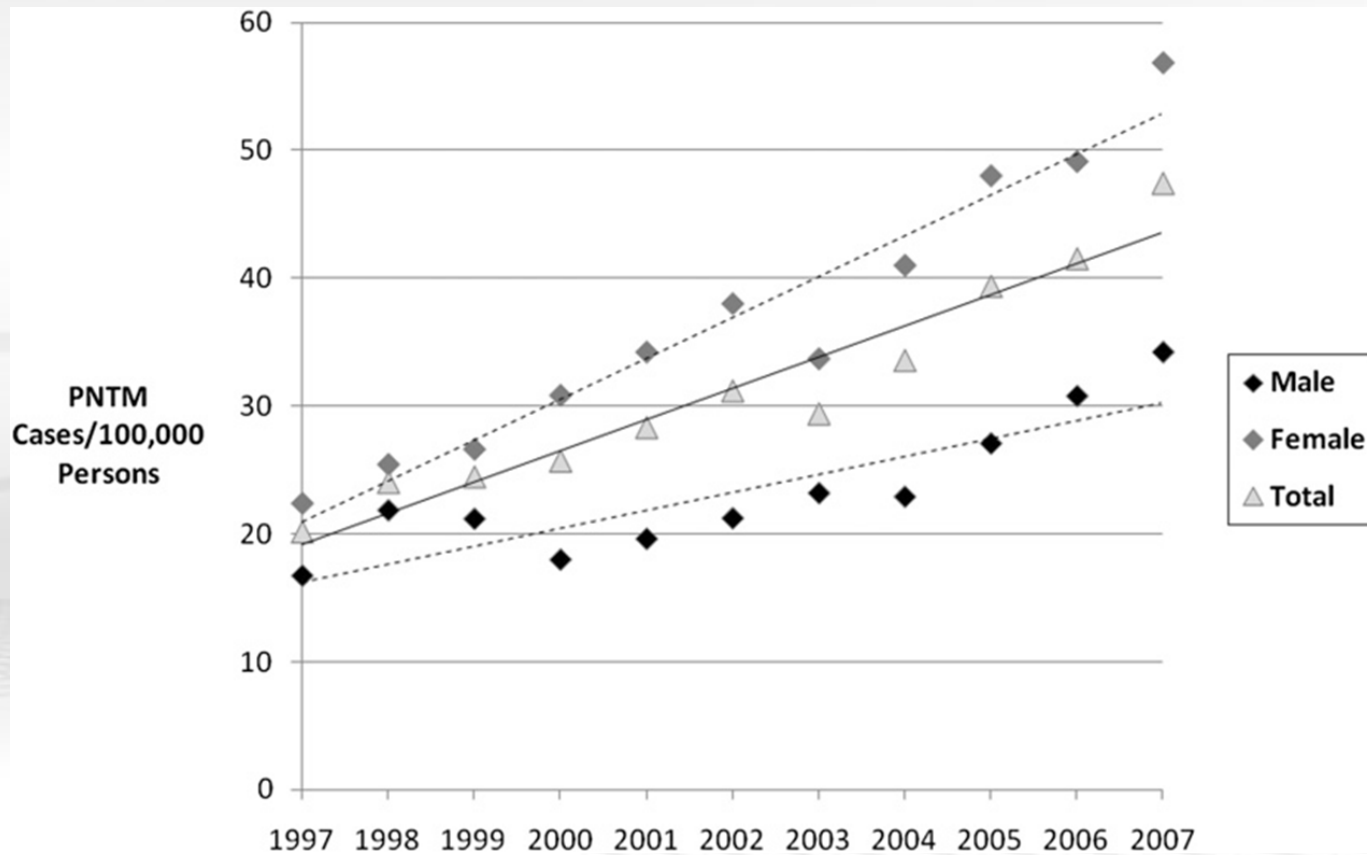
Prevalence of Nontuberculous Mycobacterial Lung Disease in U.S. Medicare Beneficiaries



Am J Respir Crit Care Med Vol 185, Iss. 8, pp 881–886, Apr 15, 2012

Pulmonary NTM Cases

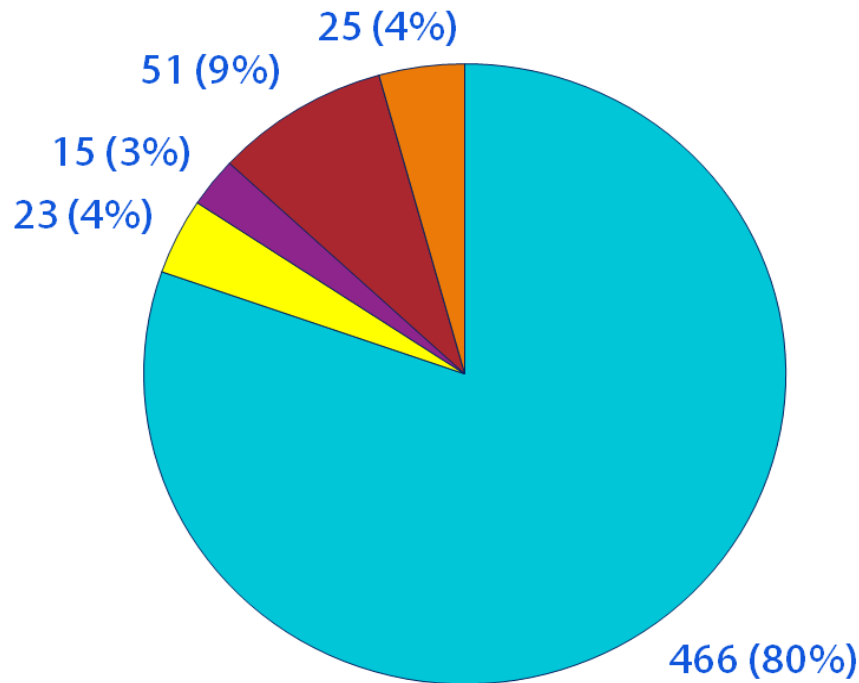
Annual prevalence of pulmonary nontuberculous mycobacteria cases among a sample of U.S. Medicare Part B enrollees by sex from 1997 to 2007



Adjemian et al AJRCCM 185:881-886(2012)

Respondents by Laboratory Type (n=580)

APHL-CDC Survey



Hospital-based Clinical

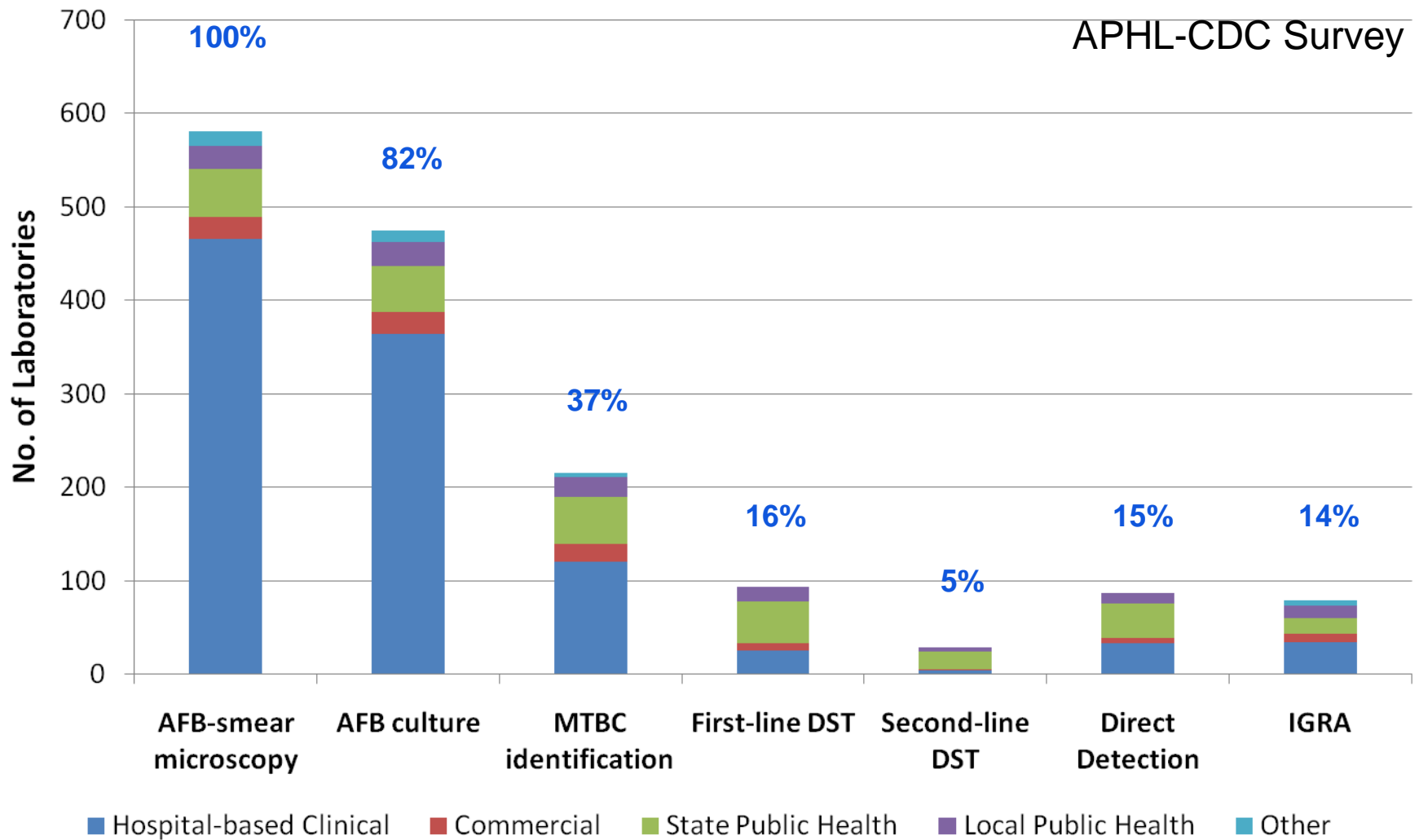
Other

Local Public Health Laboratory

Commercial Laboratory

State Public Health Laboratory

In-house Service Performed





CDC Service - NTM

Clinical and Environmental Microbiology Branch Division of Healthcare Quality Promotion:

- **NTM identification – mainly sequencing**
- **Pulsed-field gel electrophoresis (PFGE) to type isolates in support of outbreak investigations.**
- **No Antimicrobial Susceptibility Testing (AST)**

PS: A hospital or commercial laboratory would require written permission from the state health department in order to submit directly to CDC.

Identification Results of Clinical Isolates @ NJH Jan 2013 through April 2013

<i>rpoB</i> Identification	<i>erm</i> (41) deletion	<i>hsp65</i> Identification	No. of Isolates	%
<i>M. abscessus</i>	NO	<i>M. abscessus</i>	176	70.4%
<i>M. abscessus</i>	YES	<i>M. massiliense</i>	29	11.6%
<i>M. abscessus</i>	NO	<i>M. bolletii</i>	5	2.0%
<i>M. massiliense</i>	YES	<i>M. massiliense</i>	23	9.2%
<i>M. bolletii</i>	NO	<i>M. bolletii</i>	2	0.8%
TOTAL			235	94.0%

* 9 isolates did not amplify for the *erm* (41) target, 5 isolates did not amplify for the *hsp65* target

Totten et al – ASM poster 2013

NTM Identified at NJH 7-23 to 8-16 (2013)

	N	%
<i>M. abscessus</i>	60	21.3
<i>M. avium</i>	55	19.5
<i>M. chimaera</i>	65	23.1
<i>M. intracellulare</i>	46	16.3
<i>M. chelonae</i>	11	3.9
<i>M. fortuitum</i>	13	4.6
<i>M. gordonae</i>	11	3.9
Other	21	7.5
Total	282	100%




Treatment of *M. avium* complex (MAC)

- **MAC clinical isolates have a broad variability of their drug susceptibility/resistance pattern when tested quantitatively by MIC**
- **Individualization is key to success in the antimicrobial therapy of these infections**
- **Combination MICs – especially for rifampin and ethambutol, are aiding the clinician in designing the most appropriate drug regimen**

Heifets Sem Respir Infect **9**:84-103 (1994)

Heifets & Iseman N Engl J Med **323**:419-420 (1990)



Core TB Laboratory Services for Public Health Laboratories, APHL December 2009

This document does not address Nontuberculous mycobacteria (NTM). NTM disease presents challenges distinct from tuberculosis, so clarity requires a separate discussion of core tuberculosis laboratory functions. It should be noted, however, that **when the smear prepared from the specimen is acid-fast smear positive or when a culture is positive for AFB, it is essential that the laboratory determine as quickly as possible whether the AFB are TB complex or NTM.** This result should be reported as soon as it is available. Also note that, although NTM may not be as significant from a public health perspective, the public health laboratory may be the only available resource within a given jurisdiction for identification of these organisms, some of which are pathogenic.

M. abscessus [rough and smooth] &
M. avium [translucent]



Algorithm

**AFB pos.
smear**

**AFB pos.
culture**

**TB Control
is eager to get
results**

**TB
complex**

NTM, etc.

**MDR/XDR Screen,
Direct AST**

**Significance, Identification, MIC,
Combination MIC**

Speciation, Indirect AST, MIC

Therapeutic Drug Monitoring



“Doing more with less \$\$\$”

**You have your
own stories...**



In Conclusion

- **Ever growing number of NTM species**
- **CDC NTM Service - Division of Healthcare Quality Promotion**
- **NTM species matters**
- **NTM is a non-reportable entity – but TB Control has a need to know**
- **AST is important for clinically significant NTM**



Thank you!

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Pharmacokinetics

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1-800-550-6227, Option 3

1-800-550-6227, Option 4