The Clinical Impact of Rapid Nucleic Acid Amplification Tests for Detection of *M. tuberculosis*

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"TOWARDS ZERO TB"

GLOBAL BURDEN IS ENORMOUS

• *GLOBAL PANDEMIC
  ✓ 9 Million Cases Annually
  ✓ 2 Billion People Infected

• GLOBAL MORTALITY
  ✓ 2 Million Cases annually

• GLOBAL MDR DRUG RESISTANCE
  ✓ Hot Spots (60% of Cases)
    – India, China, Russian Federation
  ✓ MDR: 1 in 20 new cases
  ✓ XDR-TB: 84 countries
  ✓ Totally Drug Resistant Strains
    • Mumbai 2012

• TB ANYWHERE IS TB EVERYWHERE

TB IN THE BIG APPLE

“I’m in a NY State of mind”
# HISTORY OF TB IN NYC

**BREAKING THE CHAIN OF TRANSMISSION**

<table>
<thead>
<tr>
<th>1992</th>
<th>1997</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak Epidemic Yr</strong></td>
<td><strong>↓ 55% fewer cases (21/100,000)</strong></td>
<td><strong>Directly Observed Therapy</strong></td>
</tr>
<tr>
<td>~4,000 cases (52/100,000)</td>
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</tbody>
</table>
| 1 in 5 TB cases were MDR | ↓ 87% less MDR | **LAB MANDATES:**
| 61% of US MDR cases | | **DAILY TB LAB RESULTS**
| | | **AFB SMEARS, ID & DRUG SUSCEPTIBILITY**
| | | |
| Decline in Public health infrastructure | Downsizing large homeless shelters | |
| | Increased number of TB clinics | |
| The Emergence of Drug-Resistant TB in NYC, T. Frieden et al NEJM 328, 1993 | DOH budget ↑ from $4 million to >$40 million | |
| Tuberculosis in NYC – Turning the Tide, T. Frieden et al NEJM 333:229, 1995 | Improved screening, isolation (e.g. prisoners) | |
TB IN THE BIG APPLE

**PATIENTS**

- *NYC 2012
  - 8 cases/100,000
  - ~3 x US cases
- 84% Foreign Born
  - China most common followed by Mexico
- 6% TB cases were Healthcare workers
  - Occupational exposure confirmed in 2 of 39 cases

**TESTS**

- Culture “Gold Standard”
  - 24% case were culture neg
- AFB Smear Results
  - Of 499 cases with pulmonary disease
    - 52% were AFB smear negative
- Drug Resistance
  - MDR (18 cases)
  - XDR (2 cases)
    - 100% ↑ over 5 yrs

*NYC DOHMH 2012 Towards Zero TB
Bureau of Tuberculosis Control Annual Summary
FAST TRACKING TB DETECTION

*NYC DOH MANDATED REPORTING

- AFB smear positives from any anatomic site
  - Do not delay AFB positive smear result pending NAATs
- Nucleic Acid Amplification Test positives
- Culture positives for MTBC
  - Initial culture is sent for DNA analysis NYCDOH
- Susceptibility test results
- Clinical suspicion of TB such that clinician initiates isolation or anti-TB Treatment
- Extrapulmonary: Biopsy, pathology tissue consistent with TB (including necrotizing granulomas)

*Reporting: Through NYS electronic reporting system within 24 hr
### NYC TB CASES BY SITE 2012 (n=651)

<table>
<thead>
<tr>
<th>Pulmonary Disease Only 64%</th>
<th>Extrapulmonary Disease Only 23%</th>
<th>Both Pulmonary &amp; Extra Pulmonary 13%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Lymphatic</strong> n=93 39%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Pleural</strong> n=51 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Bone/joint</strong> n=26 11%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Meningeal</strong> n=13 6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Genitourinary</strong> n=12 5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Peritoneal</strong> n=10 4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Laryngeal</strong> n=1 &lt;1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Other</strong> n=30 13%</td>
<td></td>
</tr>
</tbody>
</table>
FAST TURNAROUND TIME TO RESULTS CRITICAL TO RAPID DETECTION OF MTB

CULTURE RESULTS

AFB STAIN + NAAT

SAME DAY < 1 hr

> 2 to 6 wks

EARLY MTB DETECTION
THE ESSENTIAL LINK TO BREAKING THE CHAIN OF TB TRANSMISSION
# Comparison of NAAT Tests

<table>
<thead>
<tr>
<th>FEATURES</th>
<th>MTD Gen-Probe</th>
<th>Xpert® MTB/RIF Cepheid</th>
</tr>
</thead>
<tbody>
<tr>
<td>TECHNOLOGY</td>
<td>Transcription Mediated Amplification</td>
<td>Nested real- time PCR</td>
</tr>
<tr>
<td>TARGET</td>
<td>16S rRNA</td>
<td><em>rpoB</em> gene</td>
</tr>
<tr>
<td>AMPLICON #</td>
<td>Relative Light Units (RLU) are measureable</td>
<td>No quantitative measure</td>
</tr>
<tr>
<td>ESTIMATED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SELF-CONTAINED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUTOMATION</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>INTERNAL CONTROL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRUG RESISTANCE</td>
<td>No</td>
<td>Rifampin (marker for MDR)</td>
</tr>
</tbody>
</table>
CEPHEID
GeneXpert MTB/RIF Assay

PROS

• VERY EASY TO USE
  ✓ TEST DAILY, ALL SHIFTS
• SINGLE USE DISPOSABLE CARTRIDGES
  ✓ NO AMPLICON CONTAMINATION
• SEDIMENT & DIRECT SPECIMEN
• DETECTS MTB Complex DNA
• DETECTS RIFAMPICIN RESISTANCE by rpo GENE MUTATIONS

NEEDS IMPROVEMENT

• RIFAMPIN RESISTANCE ONLY
  ✓ INH RESISTANCE SHOULD BE DETECTED
• SHOULD DIFFERENTIATE MTB FROM M. bovis
• ASSAY SHOULD BE QUANTITATIVE
  ✓ ?ELIMINATE AFB SMEARS?
FAST TRACKING TB DIAGNOSIS
CUMC-NYPH ALGORITHM

SPECIMEN

AFB SMEAR

+ -> Xpert

- -> CONSULTATION (≥ 3 sputa)

CULTURE

SUSCEPTIBILITY

CONSULTATION (≥ 3 sputa)

INDEX OF SUSPICION FOR TB
CUMC PARADIGM
OPTIMIZING NAAT SENSITIVITY SPECIMENS

• Freeze all sediments from patients prospectively
  ✓ When NAAT is tested, we also test previously collected samples
    – Increases assay sensitivity
    – Can identify concurrent pulmonary & extrapulmonary TB infections

• Multiple pulmonary specimens per patient
  ✓ 3 sputa in one day: Decreases Turnaround Time
  ✓ Increases sensitivity of paucibacillary specimens

• MTB NAAT Tests
  ✓ AFB smear-positives: Test routinely
  ✓ AFB smear-negatives: Restricted test
    – Consult with Micro and ID or pulmonary

• Pathology routinely notifies Microbiology of specimens that are AFB positive or show necrotizing granulomas
  ✓ Was specimen sent to Micro?
  ✓ Follow up with clinicians: Educate to THINK TB
CUMC TB Dx Fast Track

- **Patients with AFB Smear +/- Culture + Specimens (2012)**
  - **TB 50%** (18 patients)
  - **MAC 15%** (259 patients)
  - **Rapid Growers 41%** (33 patients)

- Optimize use of Xpert TB NAAT

<table>
<thead>
<tr>
<th>NAAT from Specimens 2011-2012</th>
<th>AFB Smear</th>
<th>Sens %</th>
<th>Spec %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary</strong> N=629</td>
<td><strong>Positive</strong></td>
<td>99</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td><strong>Negative</strong></td>
<td>90</td>
<td>100</td>
<td>100</td>
<td>99</td>
</tr>
<tr>
<td><strong>Extra Pulmonary</strong> N=106</td>
<td><strong>Positive</strong></td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td><strong>Negative</strong></td>
<td>80</td>
<td>100</td>
<td>100</td>
<td>98.6</td>
</tr>
</tbody>
</table>
### NAAT PERFORMANCE EXTRAPULMONARY SPECIMENS 2006-2014

<table>
<thead>
<tr>
<th>SPECIMENS</th>
<th>Tested (Culture+)</th>
<th>Xpert TB +</th>
<th>Sens %</th>
<th>Spec %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNG TISSUE</td>
<td>89 (6)</td>
<td>5</td>
<td>83</td>
<td>100</td>
<td>100</td>
<td>98.8</td>
</tr>
<tr>
<td>TISSUE BX</td>
<td>97 (11)</td>
<td>9</td>
<td>81.8</td>
<td>100</td>
<td>100</td>
<td>97.7</td>
</tr>
<tr>
<td>(e.g. Bone, Pleural)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LYMPH NODE</td>
<td>42 (10)</td>
<td>6</td>
<td>60</td>
<td>100</td>
<td>100</td>
<td>88.9</td>
</tr>
<tr>
<td>WOUNDS</td>
<td>44 (9)</td>
<td>9</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td>127 (6)</td>
<td>6</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*CSF specimens received = 2087*
# NAAT Poor Sensitivity

## Pleural Fluids vs. Tissues

<table>
<thead>
<tr>
<th>PATIENT</th>
<th>SPECIMEN</th>
<th>MTB Culture Positive</th>
<th>NAA INHIB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AFB SMEAR</td>
<td>MTD *RLU</td>
</tr>
<tr>
<td>1</td>
<td>PLEURAL FLUID</td>
<td>neg</td>
<td>neg</td>
</tr>
<tr>
<td>2</td>
<td>PLEURAL FLUID</td>
<td>neg</td>
<td>neg</td>
</tr>
<tr>
<td>3</td>
<td>PLEURAL FLUID</td>
<td>neg</td>
<td>*77,295</td>
</tr>
<tr>
<td>3</td>
<td>PLEURAL TISSUE</td>
<td>neg</td>
<td>*&gt;3 million</td>
</tr>
</tbody>
</table>

*Cut off for negative = 30,000 RLU
Cut off for positive = 500,000 RLU
EXTRAPULMONARY SPECIMENS

INTRINSIC HURDLES

- PATIENTS HAVE ATYPICAL PRESENTATIONS
  - DIAGNOSIS & TREATMENT CAN BE MISSED OR DELAYED
  - INFECTION CONTROL PRECAUTIONS DELAYED
    - ? Airborne Isolation Precautions?
    - TB exposures during diagnostic procedures (e.g. draining abscesses, operating room procedures)
- PAUCIBACILLARY SPECIMENS
  - NAAT lower Sensitivity & lower Neg Predictive Values
  - Obtaining >1 extrapulmonary specimen will increase assay sensitivity but is difficult
- NO GUIDELINES FOR NAAT USE WITH EXTRAPULMONARY SPECIMENS
- NA AMPLIFICATION INHIBITORS MORE COMMON
  - Less inhibitors in tissue specimens than body fluids

THINK BEYOND THE LUNG
# NAAT EXPEDITING TB DIAGNOSIS

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>5 yo</td>
<td>51 yo</td>
<td>48 yo HIV+</td>
</tr>
<tr>
<td><strong>Specimen</strong></td>
<td>Brain Bx</td>
<td>Bone Tissue</td>
<td>3 Sputa</td>
</tr>
<tr>
<td><strong>Primary Dx</strong></td>
<td>Metastatic tumor</td>
<td>Osteomyelitis</td>
<td>PCP pneumonia</td>
</tr>
<tr>
<td><strong>Microbiology Tests</strong></td>
<td>AFB Smear neg/NAAT pos (2 hours)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Culture</strong></td>
<td></td>
<td>MTB Culture pos (21-26 days)</td>
<td></td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td>Lymphs, AFB neg, granuloma</td>
<td>Necrotizing granuloma</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Final Dx</strong></td>
<td>Tuberculoma</td>
<td>Skeletal TB &amp; lymphadenitis</td>
<td>Pulmonary TB</td>
</tr>
</tbody>
</table>
CUMC Isolation Practices

THINK TB

- High risk patients with pulmonary symptoms
  - Endemic areas, Prior Hx TB, HIV +, homeless, Immunosuppressed, IVDU, Prison, Organ Tx
- Patients with persistent cough, fever, unexplained weight loss, abnormal chest radiograph
- Tuberculin skin test or IGRA test positive coupled with Hx of exposure to TB or cough & fever
- Pediatric facilities: Generally young children are not considered infectious but transmission to healthcare workers during procedures causing aerosolization has been reported. (Int J Tuberc Lung Dis, 2005 9:589-692)

Promptly place suspect infectious TB pts on Airborne Isolation in a negative pressure room
# CUMC Infection Control Practices

<table>
<thead>
<tr>
<th>Disease</th>
<th>Isolation Category</th>
<th>Room Required</th>
<th>Protective Equipment for Room Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary TB Confirmed/Suspect</td>
<td>Airborne</td>
<td>Negative Pressure</td>
<td>N-95 Mask</td>
</tr>
<tr>
<td>Extrapulmonary TB with draining lesion</td>
<td>Airborne &amp; Contact</td>
<td>Negative Pressure</td>
<td>N-95 Mask, Gown &amp; Gloves</td>
</tr>
<tr>
<td>Extrapulmonary TB, no drainage, no pulmonary disease</td>
<td>None</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>TB Meningitis, no pulmonary disease</td>
<td>None</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>NTM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Impact of NAAT Results

## CUMC Infection Control Practices

<table>
<thead>
<tr>
<th>NAAT POSITIVE SPECIMENS - HIGH INDEX SUSPICION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AFB Smear pos or AFB Smear neg</strong></td>
<td><strong>Remain on Airborne Isolation precautions until</strong></td>
</tr>
<tr>
<td></td>
<td>• 2 wks Tx &amp; clinical improvement or</td>
</tr>
<tr>
<td></td>
<td>• Discharged on DOT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NAAT NEGATIVE SPECIMENS - LOW INDEX OF SUSPICION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AFB Smear pos</strong></td>
<td><strong>D/C Airborne Isolation if clinically cleared or has a history of NTM disease</strong></td>
</tr>
<tr>
<td><strong>AFB Smear neg</strong></td>
<td><strong>D/C Airborne Isolation if pt Dx with another disease (e.g. NTM) which responds to Tx or clinical history of NTM disease</strong></td>
</tr>
</tbody>
</table>
## What's New in Susceptibility Testing?

<table>
<thead>
<tr>
<th>METHODS</th>
<th>PRINCIPLE</th>
<th>PROS</th>
<th>CONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular</td>
<td>• Detect R mutants</td>
<td>• Same Day Results</td>
<td>• Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Can Miss Strains without Target Mutation</td>
</tr>
<tr>
<td>XpertMTB/RIF</td>
<td>• Nested Real Time PCR</td>
<td>• Single Use Cartridges with</td>
<td>• Detects only Rif Resistance – Marker for MDR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCR</td>
<td>• INH needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Quick &amp; Easy</td>
<td></td>
</tr>
</tbody>
</table>
**AUTGENOMICS**

**INFINITI MDR - RIP ASSAY**

**FEATURES**

- Microarray Biochip technology for detection of MTB resistance to Rifampin & INH
- Rapid TB ID & susceptibility to RIP from liquid or solid culture (3 h)
- Differentiates *M. bovis* from MTBC by detecting *pncA*\(^{57}\) mutation in the PZA gene

**INFINITI INSTRUMENT**

- Culture Heat Killed
- PCR Amplification
- Load amplified products
- Load consumables & chips
- Line listing – presence/absence specific mutations (R) & wild type (S) sequences
- Predict S/R RIF + INH, MTB vs *M.bovis*
AUTOGENOMICS CUMC STUDY

STUDY STRAINS
- 103 CUMC MTBC ISOLATES
  - 92% MTB
  - 7% M. bovis/BCG
  - 1% M. africanum
- RESISTANCE
  - 3% Rifampin mono-resistant
  - 19% INH mono-resistant
  - 13% MDR (RIF/INH resistant)

THE RAPID INFINITI SYSTEM WAS COMPARED AGAINST 2 CURRENT GOLD STANDARDS
- PHENOTYPIC STANDARD BROTH SUSCEPTIBILITY TESTS (MGIT & BACTEC)
- SEQUENCING

THE RAPID INFINITI SYSTEM DETECTS RESISTANCE BY TARGETING SPECIFIC GENE MUTATIONS
- 7 RESISTANT MUTATIONS FOR RIF$^R$ ($rpoB$)
- 3 FOR INH$^R$
  - 2 ($katG$) & 1 ($inhA$ promoter)
- PZA$^R$ DETECTION OF M. BOVIS ($pncA$)

THE RAPID INFINITI SYSTEM ALSO PROBES FOR WILD TYPE SEQUENCES to detect presence rare SNPs
**AUTOGENOMICS RESULTS**

**RIFAMPIN**
- **INFINITI compared to SEQUENCING rpoB**
  - ✓ 95% Sensitivity
  - ✓ 100% Specificity
  - ✓ 100% PPV
  - ✓ 99% NPV
- **INFINITI compared to PHENOTYPE**
  - ✓ 94% Sensitivity
  - ✓ 98% Specificity
  - ✓ 89% PPV
  - ✓ 99% NPV

**INH**
- **INFINITI compared to SEQUENCING & PHENOTYPE**
  - ✓ 95% Sensitivity
  - ✓ 100% Specificity
  - ✓ 100% PPV
  - ✓ 97% NPV

**COMING ATTRACTIONS**
- **MTBC ID & SUSCEPTIBILITY DIRECTLY FROM SPECIMEN**
- **NON TUBERCULOUS MYCOBACTERIA**
  - ✓ IDENTIFICATION

**IDENTIFICATION**
- 100% Detection of *M.bovis/BCG* by *pncA* for PZA Resistance
SAME DAY DIFFERENTIATION.... TB/NOT TB IS CRITICAL

- **CUMC:** 20% AFB SMEAR +/- NAAT NEG PULMONARY CASES ARE OFTEN MAC
  - ✓ RULE OUT TB ?
  - ✓ MAC DRUGS STARTED
- **CUMC:** 84% AFB SMEAR+/NAAT NEG IN COPD PTS MOST OFTEN INDICATE MAC DISEASE
  - ✓ IMPACTS PT TX & MANAGEMENT
  - ✓ WITH CLINICAL IMPRESSION CAN R/O TB
- RAPID DX & START OF APPROPRIATE THERAPY
  - ✓ TB, MAC OTHER NTM
- PT MANAGEMENT
  - ✓ HOSPITALIZATION? DISCHARGE? ISOLATION PRECAUTIONS?
- NO TEST IS 100%
  - ✓ “TB OR NOT TB” IS A CLINICAL CALL
NonTuberculous Mycobacteria

CLINICAL SIGNIFICANCE

- **SKIN & SOFT-TISSUE INFECTIONS**
  - Multiple Nodular Lesions
- **PULMONARY INFECTION**
  - Unilateral Noncavitary Lesion
- **ENDOCARDITIS - 9% MORTALITY**
- **FOREIGN MATERIAL**
  - Prosthetic Devices
- **POSTSURGICAL SITES**
  - e.g. sternal wounds

- NTM ARE NOT “ATYPICAL MYCOBACTERIA”!
- DISEASE, COLONIZATION, CONTAMINATION?

American Thoracic Society RECOMMENDATIONS FOR CLINICAL SIGNIFICANCE

- 3 CULTURE +/- AFB +/-
- 2 CULTURE +/- 1 AFB SMEAR +
- 1 BAL CULTURE +/- AFB SMEAR ≥ 2+
- ISOLATION FROM STERILE BODY SITE

THERE ARE NO NAATs FOR NTM IDENTIFICATION
MYCOBACTERIA

MTB complex (MTBC)
- *M. tuberculosis*
- *M. bovis, M. bovis BCG*
- *M. africanum, M. microti*
- *M. canettii*

Non Tuberculous Mycobacteria (NTM)
- *M. avium Complex (MAC)*
  - *M. avium*
  - *M. intracellulare*
- **Slow Growers**
  - *M. kansasii*
  - *M. xenopi*

RAPID GROWERS
- Grows 1 to 2 wks
## CUMC FACTS & FIGURES

PTS WITH POSITIVE CULTURES

<table>
<thead>
<tr>
<th>YEARS</th>
<th>MTBC % (n)</th>
<th>MAC % (n)</th>
<th>RAPIDS % (n)</th>
<th>OTHERS % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>11 (36)</td>
<td>68 (227)</td>
<td>10 (34)</td>
<td>11 (36)</td>
</tr>
<tr>
<td>2008</td>
<td>5 (21)</td>
<td>81 (314)</td>
<td>12 (47)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>2009</td>
<td>5 (17)</td>
<td>78 (278)</td>
<td>10 (37)</td>
<td>7 (25)</td>
</tr>
<tr>
<td>2010</td>
<td>5 (19)</td>
<td>76 (312)</td>
<td>9 (36)</td>
<td>10 (42)</td>
</tr>
<tr>
<td>2011</td>
<td>6 (16)</td>
<td>81 (210)</td>
<td>6 (17)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>2012</td>
<td>6 (18)</td>
<td>77 (259)</td>
<td>10 (33)</td>
<td>9 (32)</td>
</tr>
<tr>
<td>2013</td>
<td>4 (11)</td>
<td>80 (247)</td>
<td>13 (39)</td>
<td>4 (12)</td>
</tr>
</tbody>
</table>
COMMON CLINICALLY IMPORTANT NTM

- **MAC DISEASE**
  - HOT TUB SYNDROME (SPAS)
  - COPD
  - NODULAR BRONCHIECTASIS
  - DISSEMINATED DISEASE

- **RAPID GROWING MYCOBACTERIA (RGM)**
  - *M. abscessus, M. chelonae, M. fortuitum*
  - SKIN & SOFT TISSUE INFECTIONS
    - STERNAL WOUND INFECTIONS
  - Cystic Fibrosis pts, PROSTHETIC VALVES
  - COSMETIC SURGERY (DR)
    - “LIPOTOURISM”
2013 ALERT # 38

Outbreak on East Coast of Rapidly-growing Mycobacterium Infections following Cosmetic Surgery Performed in the Dominican Republic

One Case Reported in New York City

- An outbreak of *Mycobacterium abscessus* and *chelonae* infections associated with cosmetic surgery performed in the Dominican Republic has been identified, including one case in New York City and seven in other states.
- Please report to the Health Department any suspect cases of nontuberculous *Mycobacterium* skin and soft tissue infections in patients who report recent cosmetic procedures in the Dominican Republic.
<table>
<thead>
<tr>
<th>YEAR</th>
<th>#CASES</th>
<th>BODY SITE</th>
<th>NTM SPECIES</th>
<th>COUNTRY</th>
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<tbody>
<tr>
<td>2000</td>
<td>2</td>
<td>Breast, Buttocks</td>
<td><em>M. fortuitum</em></td>
<td>Unknown</td>
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<tr>
<td>2002</td>
<td>1</td>
<td>Breast</td>
<td><em>M. abscessus</em></td>
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<td>2003</td>
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<td>Buttocks</td>
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<td>2004</td>
<td>8</td>
<td>Abdomen</td>
<td>1- <em>M. fortuitum</em> 7- <em>M. abscessus</em></td>
<td>Dominican Republic (DR): Clinic in Santo Domingo</td>
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<td>2006</td>
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<td>2009</td>
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<td>4</td>
<td>Breast, buttocks</td>
<td><em>M. abscessus</em></td>
<td>Brazil</td>
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<td>4</td>
<td>Breast, Abdomen</td>
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<td>DR</td>
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</table>

* Subspecies *bolletii*
MOLECULAR RGM IDENTIFICATION

• Gene Sequencing
  ✓ 16S is no longer adequate
  ✓ Cannot differentiate subspecies within M. abscessus complex
  ✓ rpoB gene
  ✓ hsp65 needed

• Phenotypic Identification Insufficient
  – Time to identification > 1 week
  – Often inaccurate

RAPID IDENTIFICATION FROM CULTURE
Critical to appropriate administration of appropriate empirical antibiotics
IDEAL TEST TO FAST TRACK Dx & DETECT MTB

- BY-PASS NALC-NaOH DIGESTION & DECONTAMINATION
- ELIMINATE AFB SMEARS
  - QUANTITATIVE ASSAY
- MOLECULAR DETECTION RESISTANCE TO RIPE
- ULTRA SENSITIVE: PAUCIBACILLARY SPECIMENS
  - DETECTION IN SALIVA OR URINE
  - AVOID INVASIVE SPECIMENS
  - EXTRAPULMONARY SPECIMENS
    (body fluids, paraffin blocks)
- DISTINGUISH Viable FROM NON-VIABLE CELLS
  - GUIDE AIRBORNE PRECAUTIONS
  - MEASURE OF RESPONSE TO TB THERAPY

FOLLOW THE HELICAL ROAD TO THE FUTURE

High Sensitivity Rapid Dx, Rapid Dx
NAAT (Xpert) ALGORITHMS

• DISCONTINUE AFB SMEARS…..PROBLEMS
  ✓ Smear data improves NAAT interpretation/accuracy
  ✓ Smear positive specimens = quality specimen
  ✓ Smear conversion from positive to neg: Measures response to therapy

• 1-2 NEGATIVE NAAT (NO AFB SMEAR) vs 2-3 AFB SMEAR NEGATIVE SPECIMENS TO DISCONTINUE AIRBORNE ISOLATION….PROBLEMS
  ✓ Poor specimen Quality/Quantity = false negative results & false negative cultures
  ✓ Both NAAT and Smear optimize Infection Control decisions and diagnosis

• 1-2 AFB SMEAR POS SPECIMENS, NOT 3 SPECIMENS (WHO) RECOMMENDED

MUCHAS GRACIAS
Valencia

THANK YOU
New York City