



NTM Clinical: Who's Your Suspect?

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Diagnostics and care:NTM

- Current diagnostic techniques and future techniques in diagnostics
- Importance of strain typing and drug sensitivity testing
- Current standards of care and guidelines update
- Conflict of Interest
 - None
- Non FDA Approved Drugs
 - None

Susceptibility to NTM Pulmonary Disease

Impaired local defenses Bronchiectasis, emphysema, pneumoconiosis, previous cavitory tuberculosis, silicosis, COPD	Clinical history, chest imaging, pulmonary function tests
Alpha-1 antitrypsin deficiency	A1AT phenotype, level, genotyping
Cystic fibrosis	Sweat chloride test, CFTR genotyping
Primary ciliary dyskinesia	Cardinal clinical features, measurement of nasal nitric oxide, ciliary beat frequency, EM structure, genotyping (40+ genes)
Impaired systemic immunity STAT3 deficiency	Total IgE, cardinal clinical features & family history, STAT3 genotyping
Immunosuppressant use Tumor necrosis factor- α blockers, steroids, tacrolimus	Drug history, post-transplant
Lady Windermere syndrome	Clinical history with exclusion of the above susceptible factors, special body morphotypes

ATS/IDSA Pulmonary Dx Criteria

- **Clinical (all 3)**
 - Symptoms – cough most common
 - Radiographic – cavities, bronchiectasis, nodules
 - Exclusion of other diagnoses
 - *And...*
- **Microbiologic (any of these)**
 - 2 positive sputum specimens
 - 1 bronchial wash/lavage
 - Appropriate biopsy histopath & (+) resp culture

The Voice of the Patient

- 3 symptoms with most impact on daily life
 - **Coughing** (including coughing up blood, phlegm or mucus)
 - Triggers
 - Changes in weather Talking Sprays and fumes Eating Sleeping position (e.g., lying down flat) Laughing Physical exertion Dust Air conditioning Mold
 - **Fatigue**
 - From feeling “tired to your core,” to “walking through molasses”
 - Often had to “allocate” their energy to manage fatigue
 - “My day is based on personal energy. I plan out what I am going to do based on how I feel.”
 - **Shortness of breath**
 - Often requires pacing themselves to avoid feeling winded
 - Triggers: scents, walking, talking, physical activity that causes exertion

“Classic” NTM Lung Disease

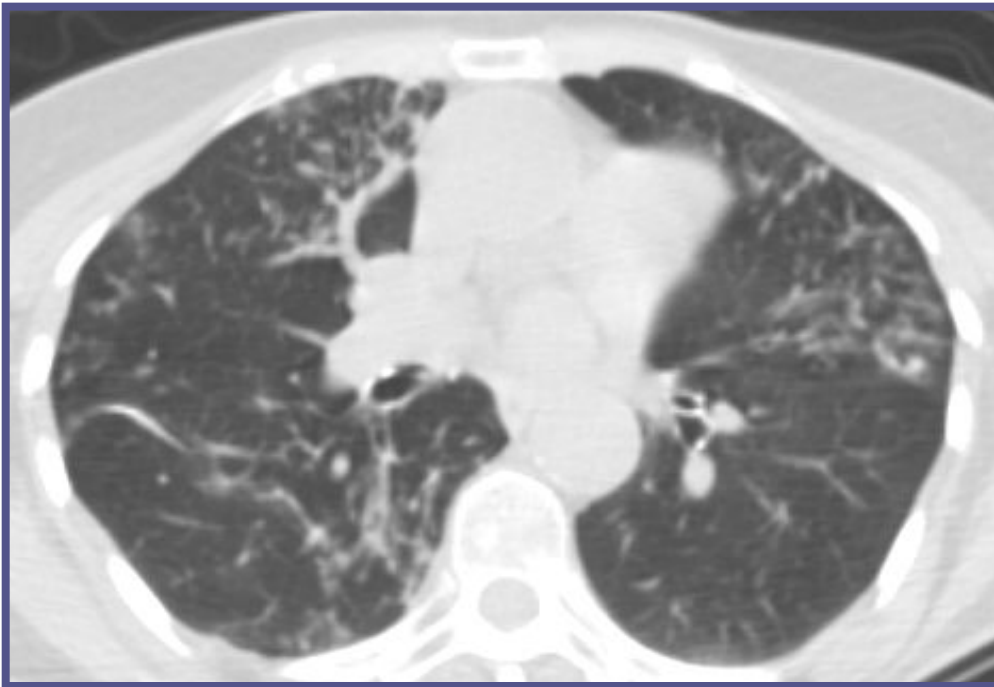
- Male smoker
- Cavitory, lots of bugs
- Difficult to treat
- Pathogenesis
 - Structural disease
 - Disrupted barriers
 - Poor clearance
 - Opportunistic



Mycobacterium avium* Complex Pulmonary Disease Presenting as an Isolated Lingular or Middle Lobe Pattern

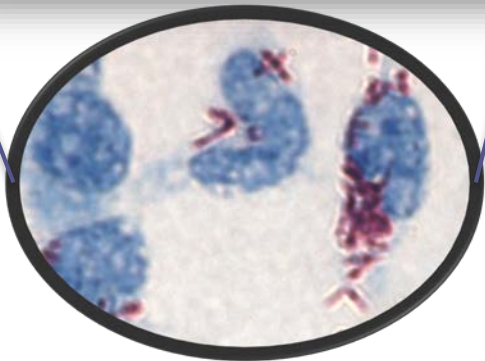
The Lady Windermere Syndrome

Jerome M. Reich, M.D.; Richard E. Johnson, Ph.D.†



- Nodular bronchiectasis
- No obvious predisposition
 - Postmenopausal women
 - Nonsmokers
 - Chronic cough

Nontuberculous Mycobacteria



- Ubiquitous environmental organisms
 - Water including potable, soil
- >180 species
 - *M. avium* complex
 - *M. abscessus* group
 - *M. kansasii*
 - *M. malmoense*
 - *M. xenopi*
- Clinical
 - Lung (85%)
 - Skin, soft tissues
 - Disseminated

Microbiology

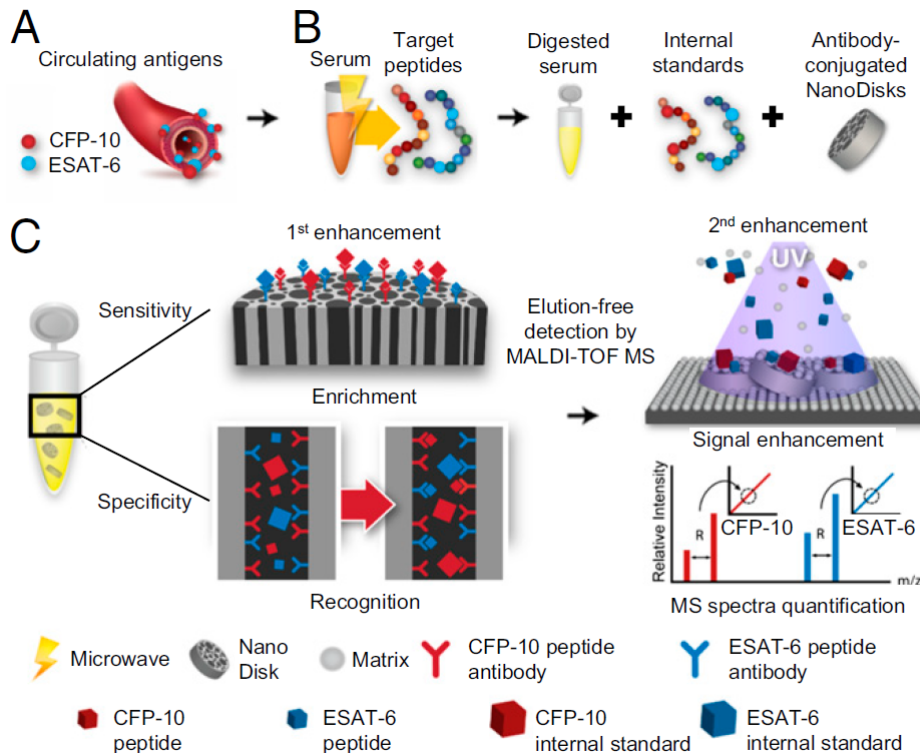
- **Expectorated sputum**
 - Generally preferable to bronchoscopy
 - Ideally, for diagnosis
 - 3 early morning specimens on different days
- **Induced sputum**
 - Can be done safely and effectively using same hypertonic saline and oscillatory devices we prescribe for management of bronchiectasis
- **Send-in sputum from home collection**
 - Can be refrigerated & sent by overnight courier without compromise in recovery of mycobacteria
 - Site logistics may not allow for this option

Microbiology

- **Possible indications for bronchoscopy**
 - Inability to collect adequate sputum specimens
 - To exclude other diagnoses
- **Bronchoscopic or surgical lung biopsy**
 - **Indications**
 - Exclude other diagnoses
 - Rarely to assess significance of positive culture
 - Very important that bronchoscopist/surgeon sends specimen (not in formalin) for culture

Future Diagnostics

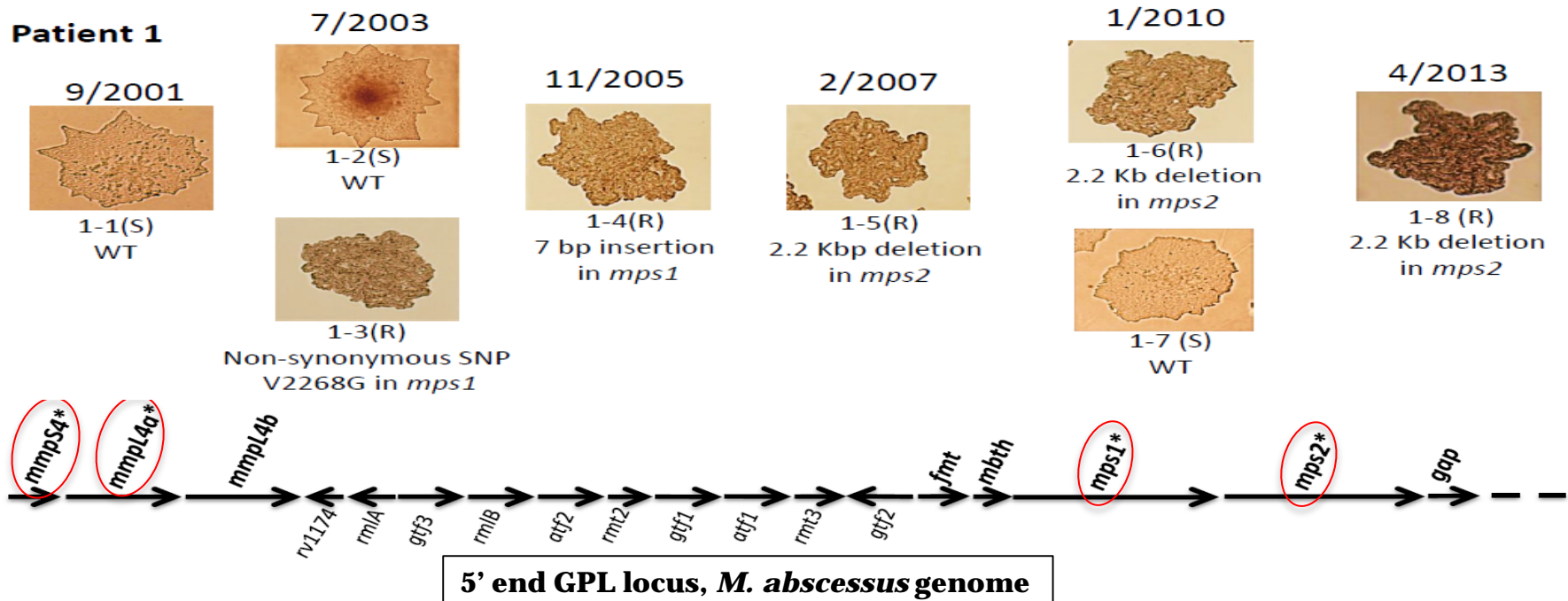
- Direct detection, rapid antimicrobial resistance tests
 - X-pert MTB/Rif – 2hr detection of MTB and rifampin resistance mutations



- Blood-based testing
 - Immune response indicators
 - Secreted mycobacterial antigens
- Limitations
 - Sensitivity/specificity
 - Ability to distinguish between mycobacterial species
 - Ability to inform on antimicrobial susceptibility

Importance of Strain Typing & AST

- Patients followed over time acquire multiple species, subspecies, strains of NTM
- Culture/current species ID may miss change in predominant species/strains



- Different species/strains may have different susceptibilities or strains may acquire mutations over time that change virulence, susceptibility
- Can affect determination of relapse vs reinfection
- Important in interpretation of clinical trial results

Park. J Clin Microbiol 2015
 Daniel-Wayman. (under review 2018)
 Boyle. Ann Am Thorac Soc 2016
 Olivier. Am J Resp Crit Care Med 2017

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