Cliff Notes of Recently Published Recommendations and Guidelines

Max Salfinger, MD
Professor of Public Health & Co-Lead Laboratory Concentration DrPH Program
University of South Florida College of Public Health
Our practice is our passion.
Laboratory’s charge

To provide the clinician with accurate results in a timely fashion
New/updated guidelines

- **ASM Clin Microbiol Review January 2018**
  Practice Guidelines for Clinical Microbiology Laboratories: Mycobacteria

- **ASM Clin Microbiol Review May 2018**
  Implementing a Quality Management System in the Medical Microbiology Laboratory

- **CLSI M48 2nd ed, September 2018**
  Laboratory Detection and Identification of Mycobacteria

- **CLSI M24 3rd ed, November 2018**
  Susceptibility Testing of Mycobacteria, *Nocardia* spp. and Other Aerobic Actinomycetes

- **CLSI M64 1st ed, November 2018**
  Performance Standards for Susceptibility Testing of Mycobacteria, *Nocardia* spp. and Other Aerobic Actinomycetes
Manual of Clinical Microbiology, 2019

- 31 *Mycobacterium*: General Characteristics, Laboratory Detection, and Staining Procedures / 558

- 32 *Mycobacterium* tuberculosis Complex / 576

- 33 *Mycobacterium*: Laboratory Characteristics of Slowly Growing Mycobacteria Other than *Mycobacterium tuberculosis* / 595

- 34 *Mycobacterium*: Clinical and Laboratory Characteristics of Rapidly Growing Mycobacteria / 612

- 78 Susceptibility Test Methods: *Mycobacteria*, *Nocardia*, and Other Actinomycetes / 1398
Practice Guidelines for Clinical Microbiology Laboratories: Mycobacteria

Betty A. Forbes, late Geraldine S. Hall, Melissa B. Miller, Susan M. Novak, Marie-Claire Rowlinson, Max Salfinger, Akos Somoskövi, David M. Warshauer, Michael L. Wilson
Practice Guidelines for Clinical Microbiology Laboratories: Mycobacteria

- INTRODUCTION – Taxonomy
- REGULATORY REQUIREMENTS AND GUIDELINES FOR TESTING MYCOBACTERIA.
- IDEAL ALGORITHM/ALTERNATIVE ALGORITHMS FOR TESTING SPECIMENS FOR MYCOBACTERIAL DISEASES - Frequently Asked Questions
- BIOSAFETY
- WORK-UP OF SPECIMENS
- NUCLEIC ACID AMPLIFICATION TESTS
- SMEAR MICROSCOPY AND GROWTH DETECTION OF ACID-FAST BACILLI
Practice Guidelines for Clinical Microbiology Laboratories: Mycobacteria

- IDENTIFICATION
- ANTIMICROBIAL SUSCEPTIBILITY TESTING
- QUALITY ASSURANCE
- USE OF INTERFERON GAMMA RELEASE ASSAYS FOR DIAGNOSIS OF MYCOBACTERIUM TUBERCULOSIS INFECTION
- USING A REFERENCE LABORATORY - When To Refer? How To Assess?
- PUBLIC HEALTH REQUIREMENTS
- RESOURCE-LIMITED SETTINGS
- CONCLUSION
- REFERENCES - 346
### Fast Track program & algorithm

- **Mid-80s/early 90s:** If patient care and public health are always considered paramount, regardless of admission time or hospital type, etc., the concept of services at that time had **several shortcomings**.

- **In 1993,** New York State created a **model Fast Track program** for TB testing to form a network of laboratories to expedite testing for highly infectious TB suspects.

- With the establishment of such a network, when new assays are validated and implemented in the central laboratory, the **entire network** of enrolled submitting entities **immediately benefits**.

- There was a growing realization that no single method by itself is sufficient to address the entire spectrum of diagnostic challenges. To streamline the best choice for laboratory diagnosis and patient management, **a centerpiece of this practice guideline is the ideal algorithm and alternative algorithms** for testing specimens for mycobacterial diseases by utilizing this concept.
“In the past 25 years, a tremendous change in the epidemiology of drug-resistant TB and pulmonary NTM has occurred, thus warranting even further shortening of turnaround times. By the same token, molecular diagnostic assays are becoming the standard of care. With the plethora of tests available, ongoing communication between the health care provider and the laboratory is essential. In this review, we provide an in-depth discussion of the latest developments in mycobacteriology testing as well as a holistic approach to sample collection, reporting of laboratory results, and interpretation of results for the health care provider.”
CLSI M48 2nd ed, September 2018
Laboratory Detection and Identification of Mycobacteria

- Betty A. Forbes
- Melissa B. Miller
- Niaz Banaei
- Barbara A. Brown-Elliott
- Sanchita Das
- Max Salfinger
- Meenu K. Sharma
- Akos Somoskovi
- Julie Tans-Kersten
- Fred C. Tenover
- David Warshauer
- Adrian M. Zelazny
Susceptibility Testing of Mycobacteria, Nocardia spp. and Other Aerobic Actinomycetes

“This standard includes recommendations for testing Mycobacterium tuberculosis complex (MTBC), certain nontuberculous mycobacteria (NTM), Nocardia spp., and other aerobic actinomycetes. Currently, sufficient data exist to support recommendations for antimicrobial susceptibility testing (AST) of MTBC, Mycobacterium avium complex (MAC), M. kansasii, M. marinum, the rapidly growing mycobacteria (RGM), Nocardia spp., and certain other aerobic actinomycetes.”
Expanded the description of molecular testing for both MTBC and NTM to determine antimicrobial susceptibility or resistance.

For MTBC, Table 3 (Considerations for Molecular or Repeat Testing After Initial Testing on MTBC Using a Commercial Short-Incubation Broth System) and text are included to describe the integration of molecular and culture-based test results for the best possible prediction of the expected drug efficacy.

For NTM, text is included to describe integration of molecular techniques to assist in determining efficacy of macrolides and amikacin in the treatment of infections caused by MAC and various RGM.
Added a description of challenges to MTBC AST accuracy with use of rapid broth systems and/or the agar proportion method, particularly limited sensitivity in detection of low-level resistance to rifampin and ethambutol.

Added information in Appendix A regarding the relationship of pharmacokinetics and pharmacodynamics in determining breakpoints and interpretive criteria.

Updated all breakpoint and quality control tables and moved them to a newly created informational supplement, CLSI document M62.
TB NAAT

- FDA approved for respiratory specimens
  - Smear-positive (Dec. ‘95)
  - Smear-negative (Sept. ‘99)
- MMWR, January 16, 2009 [Universal]

- In July 2013, the FDA granted Market Authorization to a cartridge-based assay. This NAA test can simultaneously identify *Mycobacterium tuberculosis* complex (TBC) and genetic mutations associated with resistance to rifampin from raw sputum and concentrated sputum sediments.
TB NAAT Recommendations - 2009

“NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities.”

MMWR Jan 16, 2009
San Francisco study

- In a prospective cohort study with a pragmatic, before-and-after implementation design, the authors analyzed 621 consecutive hospitalized patients undergoing sputum examination for evaluation of active pulmonary TB from January 2014 to January 2016 at the Zuckerberg San Francisco General Hospital and Trauma Center.

JAMA Intern Med. 2018; 178(10):1380-1388
San Francisco study

- The mean hospital costs per molecular TB test-negative patient decreased from $46,921 to $33,574 after implementation of the algorithm, providing an average savings of $13,347 per patient.
- The authors estimated utilization and costs for approximately 250 patients completing TB evaluation each year and projected a total annual savings to the hospital of $3.3 million.

JAMA Intern Med. 2018; 178(10):1380-1388
Florida NAAT 2009-2017
Sputum – 3-year interval: 75%, 84%, 87%

Rungtip Bootseeta et al. NAA Testing for TB and NTM in Florida [2019 NTCA Poster session]
Thank you!

max@health.usf.edu