



Nontuberculous Mycobacteria (NTM) Newly Reportable to MDH

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Objectives for this webinar

- Discuss NTM background
- Describe knowledge of NTM within the U.S. and MN
- Review results of the MDH NTM laboratory survey
- Introduce the MDH lab-based NTM surveillance protocol
- Discuss MDH-PHL NTM identification methods



NTM background

- NTM encompass all species of *Mycobacterium* aside from *M. tuberculosis* complex and *M. leprae*.
- NTM are also known as **atypical mycobacteria**.
- There are almost 200 species of NTM.

Where are the bacteria found?



- NTM are isolated from a wide range of environmental sources
- NTM form biofilms and are often resistant to disinfectants

Healthcare-associated infections



- Health care devices and equipment can be contaminated with NTM, leading to NTM infection.

- Disease onset can be weeks, months, or years after NTM exposure.
- Diagnosis of NTM is often delayed.

Treatment of NTM



- Treatment of NTM infection involves multiple antibiotics for long durations and may require surgical debridement.
- Antimicrobial resistance can occur in many clinically important NTM species.

- NTM can cause different infections depending on the involved body site(s).
 - Pulmonary NTM
 - Extrapulmonary NTM (ENTM)

- Pulmonary NTM infection is more common than extrapulmonary NTM.
- Pulmonary infections occur in the lungs and are the result of the inhalation of airborne particles containing the bacterium.
- Positive pulmonary NTM is diagnosed from identification from specimens of:



- Lung tissue
- Broncho alveolar wash
- Sputum
- Endotracheal secretions

Who is at risk for pulmonary NTM?

- Pulmonary NTM infections primarily occur in individuals with underlying lung disease:
 - Bronchiectasis (enlargement of the airways)
 - COPD
 - Cystic fibrosis
 - Alpha-1 antitrypsin deficiency
 - Prior infection with tuberculosis

Symptoms of pulmonary NTM

Symptoms of pulmonary NTM are similar to those of tuberculosis and include:

- Cough with sputum production
- Shortness of breath
- Tiredness or fatigue
- Fever
- Unplanned weight loss
- Lack of appetite
- Night sweats
- Coughing up blood



Outbreaks of pulmonary NTM

- Current data suggest that the frequency of healthcare-associated outbreaks of pulmonary NTM may be increasing.
- Reported healthcare-associated outbreaks of pulmonary NTM have been caused by numerous factors.

Extrapulmonary NTM (ENTM)

- ENTM is much less common than pulmonary NTM.
- Positive ENTM is diagnosed from any specimen outside of the lungs and excluding BAL and endotracheal secretions.

- There are three main disease syndromes of ENTM infection.
 - Cervical lymphadenitis
 - Disseminated infections
 - Opportunistic infections

National and global outbreaks of ENTM

- Outbreaks in a variety of health care settings of ENTM have occurred in the United States and globally, causing serious morbidity and mortality.
 - Novel species, Arkansas 2018
 - *M. abscessus/chelonae*, California 2016
 - *M. abscessus*, Georgia 2015
 - *M. chelonae*, Florida 2015
 - *M. abscessus*, multistate 2014
 - *M. chimera*, 2011-current

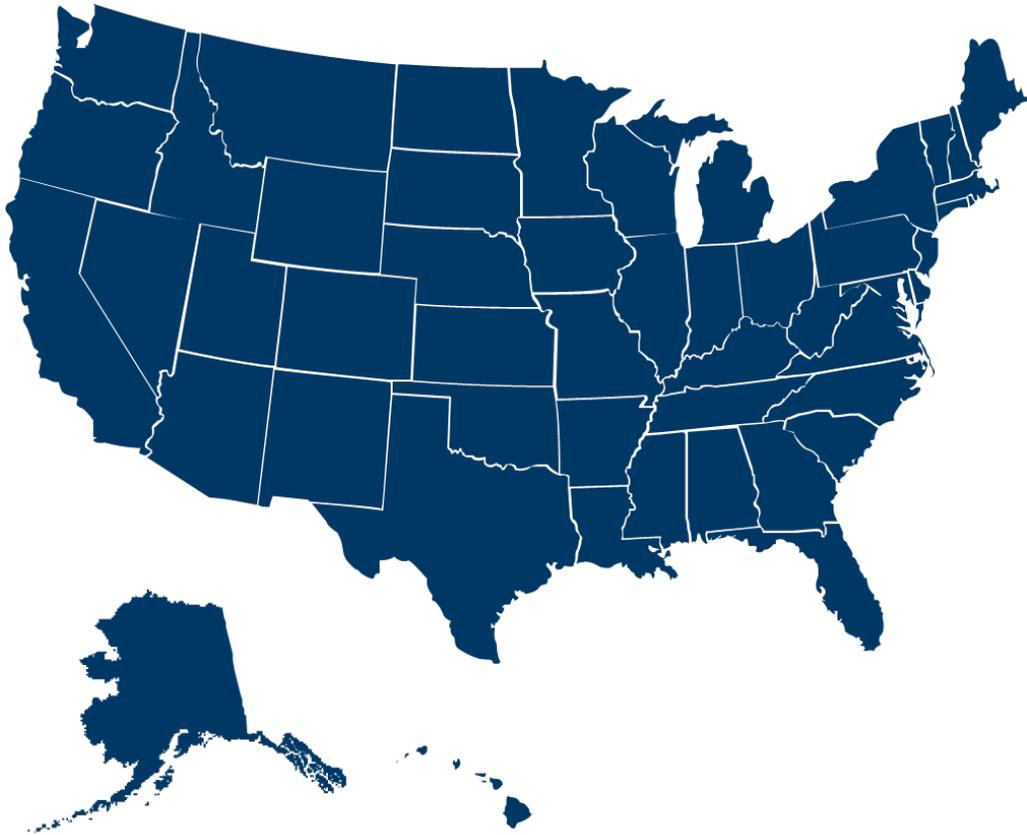
Outbreaks of ENTM in Minnesota

- Global *M. chimaera* outbreak affected MN residents
- 2016 outbreak of *M. chelonae* in Minnesota

Increasing NTM infections?

- The global prevalence of human disease caused by NTM (both pulmonary and ENTM), and the deaths associated with NTM infections, are believed to have increased over the last two decades.

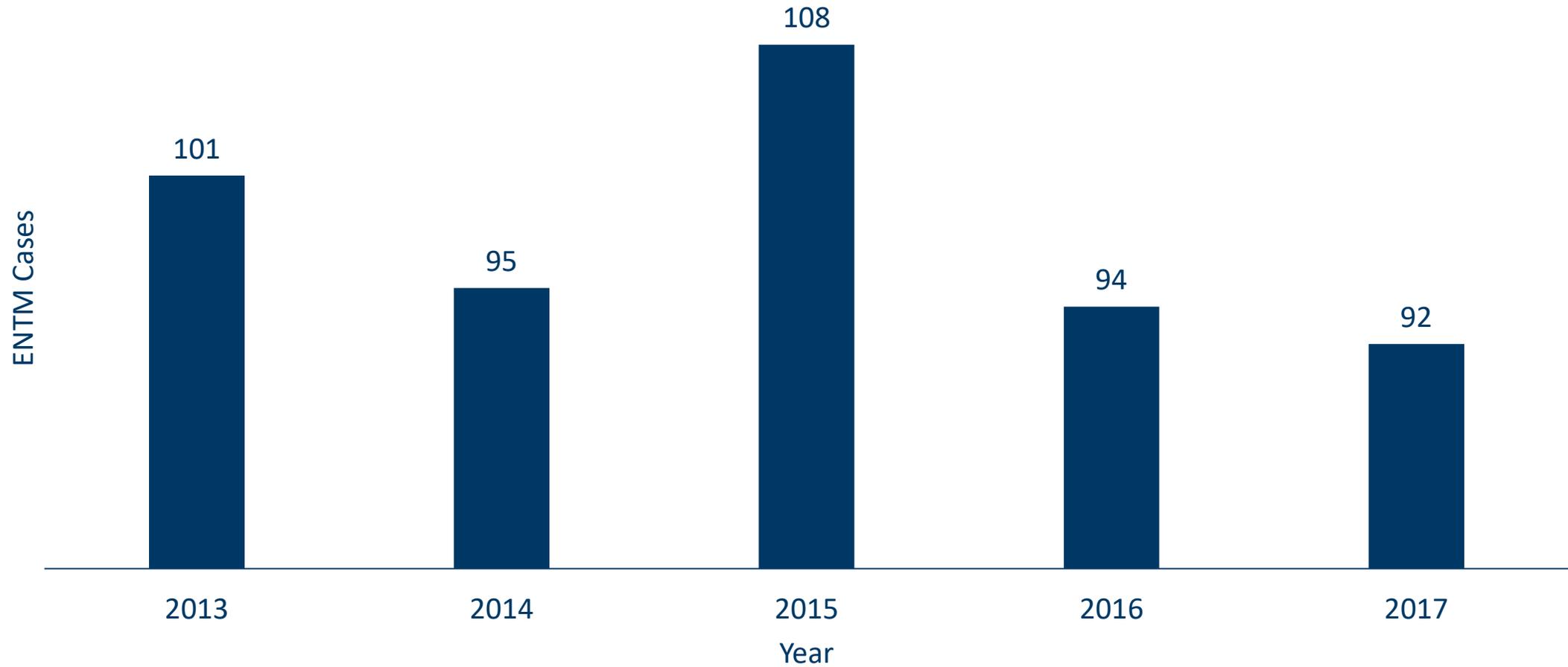
Current knowledge of NTM in the U.S. and MN



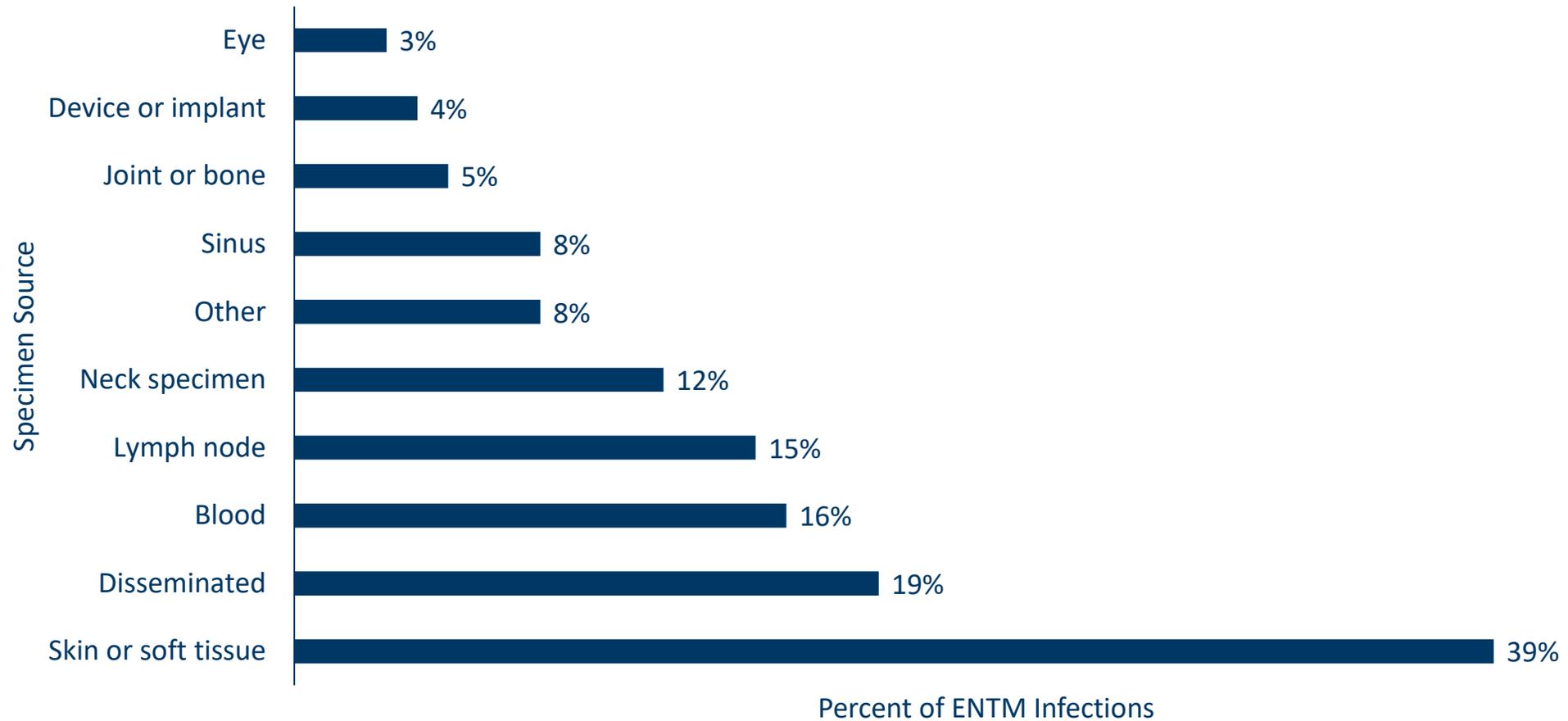
- NTM infections are reportable in seven states:
 - Oregon
 - Tennessee
 - Maryland
 - Missouri
 - Wisconsin
 - Mississippi (laboratory only)
 - Nebraska (laboratory only)

- To explore the burden of NTM in Minnesota, we obtained line list data from three Minnesota laboratories along with the MDH-PHL from 2013 to 2017.
- Overall, 3,564 pulmonary infections and 490 ENTM infections were confirmed by *Mycobacterium* isolation and identification to species.

The number of ENTM isolates did not increase during 2013-2017



Most ENTM isolates were from skin and soft tissue infections



Why conduct NTM surveillance?

- Rationale for data collection and analysis of NTM infections in Minnesota:
 - NTM infections are not reportable or centrally documented in Minnesota.
 - We do not know the disease burden, epidemiology, or whether we are missing outbreaks.



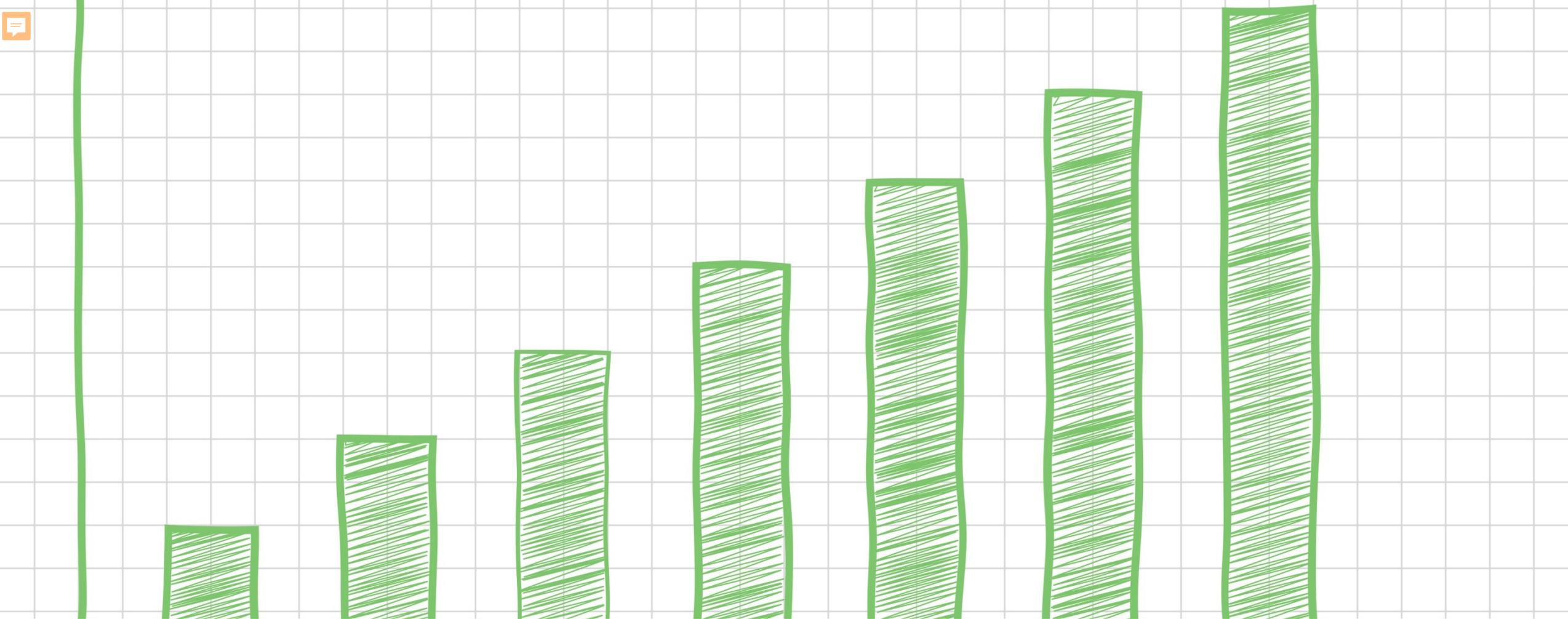
NTM laboratory survey

- The MDH-PHL sent out a REDCap lab survey to all MLS laboratories in September to learn more NTM identification in Minnesota.
- Thank you!

- The NTM lab survey asked a few short questions to determine which labs have the capability to identify NTM.
 - Does your lab specifically culture for pulmonary, extrapulmonary, or blood specimens?
 - Do you perform identification of nontuberculous mycobacterium in your lab?

Results of NTM laboratory survey

- MDH learned that only a few labs fully identify NTM to species:
 - The Minnesota Department of Health Public Health Lab (MDH-PHL)
 - Laboratory Corporation of America
 - Quest Diagnostics
 - Hennepin County Medical Center
 - Mayo Clinic
 - ARUP Lab



NTM surveillance protocol



Utilizing the laboratory survey data to conduct surveillance

- All laboratories that indicated they identify NTM to species are also currently able to report to MDH via electric laboratory reporting (ELR).

- Extrapulmonary NTM (ENTM): reportable statewide
- Pulmonary NTM: reportable only among residents of Hennepin and Ramsey counties

- ENTM infection is defined by a single specimen that is positive for any *Mycobacterium* species excluding *M. tuberculosis* complex, *M. leprae*, and *M. goodii* outside of the lungs or lung tissue.

- Pulmonary NTM is considered a case when:
 - NTM identified from microbiological testing of ≥ 1 BAL or bronchial wash specimen or lung tissue specimen
 - NTM identified from microbiological testing of ≥ 2 sputum specimens or tracheal aspirates
 - Lung biopsy specimen with histopathologic features plus NTM identified from microbiological testing of ≥ 1 sputum specimen

- To ensure all identified NTM cases are being reported via ELR, MDH would like to conduct quarterly audits of laboratories that can identify NTM.

Cases that cannot be reported through ELR

- If a case of NTM, either extrapulmonary or pulmonary, is identified at a facility that cannot be reported via ELR, cases may be reported using the [MDH Disease Report Card \(“Yellow Card”\)](https://www.health.state.mn.us/diseases/reportable/forms/reptcard.html) (<https://www.health.state.mn.us/diseases/reportable/forms/reptcard.html>)

Variables needed to conduct NTM surveillance

- The yellow card disease report card asks for data that is not needed for NTM surveillance.
- If filling out a yellow card to report NTM, the only variables that are needed include:
 - Medical record number
 - Patient name
 - County
 - Phone number
 - Date of birth
 - Disease
 - Lab findings
 - Source
 - Collection date
 - Person reporting
 - Institution/clinic
 - Phone number

Requesting patient charts



- MDH will need to conduct chart reviews of NTM cases that meet our surveillance definition to complete a CDC specified case report form.

- MDH will be collecting isolates of extrapulmonary infections to send to CDC.
 - MDH will utilize isolates that are routinely submitted to the MDH-PHL for shipment to CDC.
 - MDH may request specific isolates from laboratories if CDC requests additional isolates.
 - Additionally, if apparent clusters or outbreaks of NTM infection appear to be occurring, MDH may request those specific isolates.

Interviews of ENTM cases



- As many patient risk factors for ENTM may not be documented in a medical chart, MDH will be trying to interview ENTM cases.

Potential community and environmental exposures

- Nail salon (manicure, pedicure, waxing)
- Other beauty treatments (piercing, tattoo)
- Hot tub or spa
- Acupuncture
- Handled fish
- Fish tank
- Work with purchased soil products
- Trauma/wound
- Injection drug use



Potential health care exposures



- Immunocompromised condition
- Immunosuppressive therapy
- Injection or infusion
- Surgery
- Dental
- Dialysis

- MDH has created a NTM website with information regarding pulmonary NTM and extrapulmonary NTM.
- For more information about NTM and reporting please visit [Nontuberculous Mycobacteria \(NTM\)](https://www.health.state.mn.us/diseases/ntm/index.html) (<https://www.health.state.mn.us/diseases/ntm/index.html>)



MDH-PHL NTM identification methods

Paula Snippes Vagnone

credit to Jo Taylor (MDH EIS Officer)

- Discuss NTM background
- Describe knowledge of NTM within the U.S. and MN
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- Introduce MDH lab-based NTM surveillance protocol
- **Discuss MDH-PHL NTM identification methods**

Diagnostic Workflow at the Public Health Laboratory

1. Positive culture (broth or solid media)
2. Acid Fast Stain
3. Acid Fast Bacilli Present
 - a) If no previous positive *Mycobacteria* ID within the last 2 months:
 - **Subculture to solid media:** visually inspect growth weekly, report phenotypic observed growth, and correlate growth with LPA result
 - **Run Line Probe Assay (LPA)** from positive culture, MGIT broth, or solid media
 - If no species ID with LPA, reflexed to **16S sequencing**
 - b) If previous positive *Mycobacteria* ID within the last 2 months:
 - **Subculture to solid media:** check that morphology correlates to most recent LPA result and report – “morphology consistent with...”

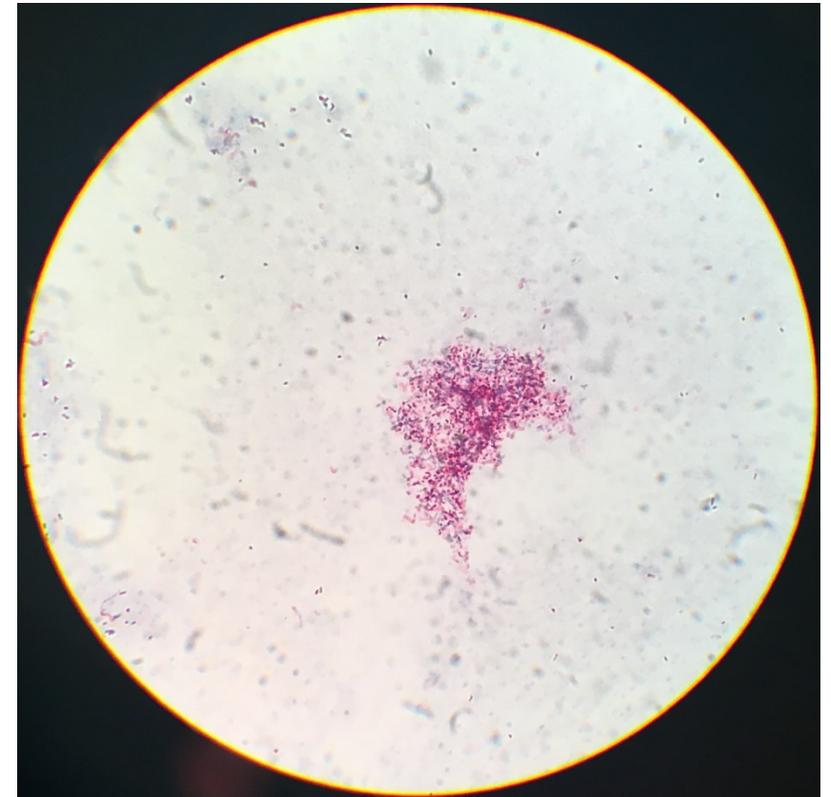
BD BACTEC™ MGIT™ Culture for Mycobacteria

- MGIT = Mycobacteria Growth Indicator Tube
 - Specimens are decontaminated before inoculation into MGIT (unless a sterile site such as CSF)
 - MGIT is incubated in the BD BACTEC™ instrument at 37°C (up to 42 days)
 - BD BACTEC™ MGIT™ detects increased fluorescence, indicating positive growth



Acid-fast Staining of Positive Cultures

- Kinyoun Carbol Fuchsin Acid-fast stain
 - Determine the presence of Acid Fast Bacilli (AFB)
 - Observe and describe morphology:
 - Partially AF
 - Cording
 - Tight clumps
 - Branching
 - Short



INNO-LiPA Line Probe Assay (LPA)

- Primary ID method
- Used by MDH TB Lab since 2013
- Can detect 18 clinically relevant *Mycobacterium* sp.
- Based on a PCR and reversed hybridization principles

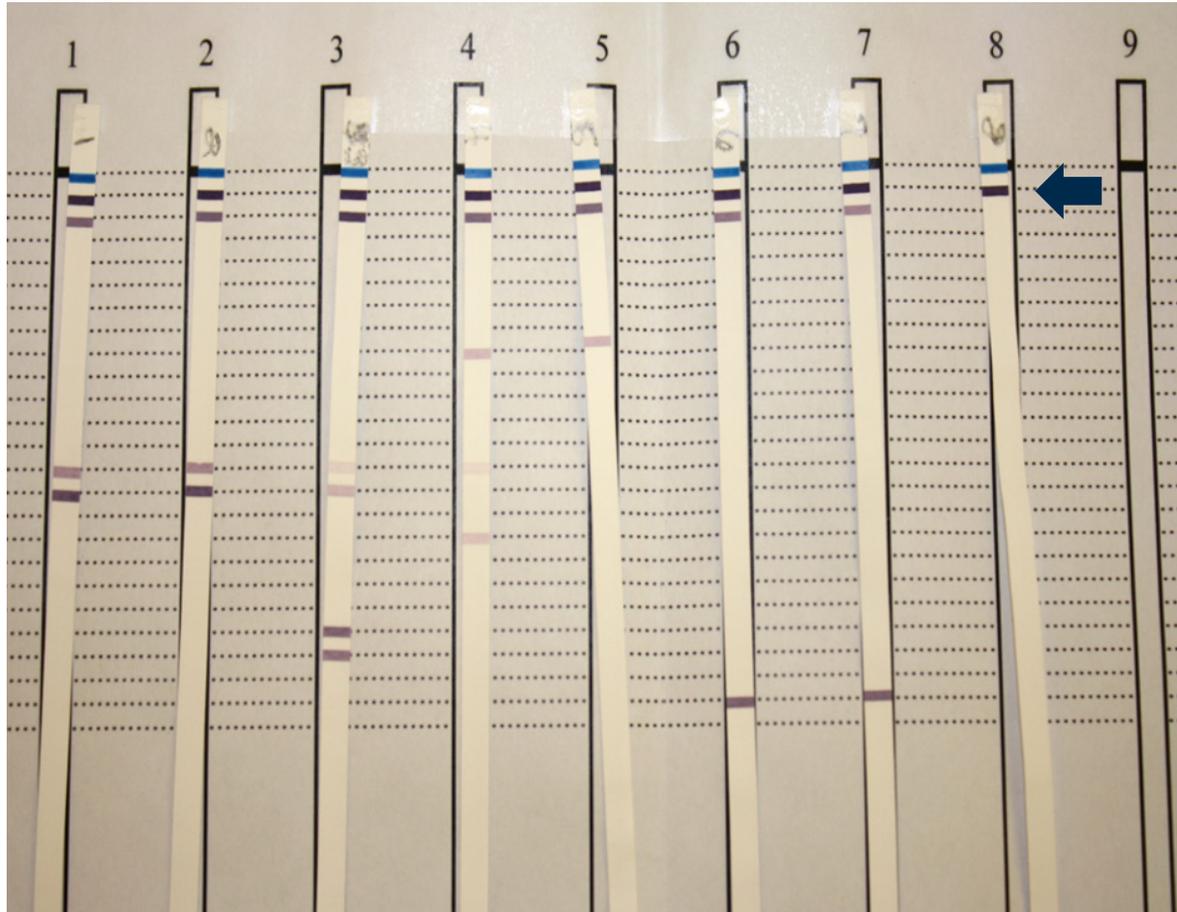
- MTBC
- *M. kansasii*
- *M. kansasii/gastri*
- *M. xenopi*
- *M. gordonae*
- *M. genavense*
- *M. simiae*
- *M. marinum/ulcerans*
- *M. celatum*
- *M. avium* complex
- *M. intracellulare*
- *M. scrofulaceum*
- *M. malmoense*
- *M. haemophilum*
- *M. chelonae*
- *M. abscessus*
- *M. fortuitum* complex
- *M. smegmatis*

INNO-LiPA Line Probe Assay (LPA) Steps

- **Step 1:** amplification of 16s-23s rRNA spacer region - PCR
- **Step 2:** Hybridization of amplified 16s-23s spacer region with specific immobilized probes on a strip
- **Step 3:** Color development of membrane strips
- **Step 4:** Interpretation of colorization of specific lines on the strip



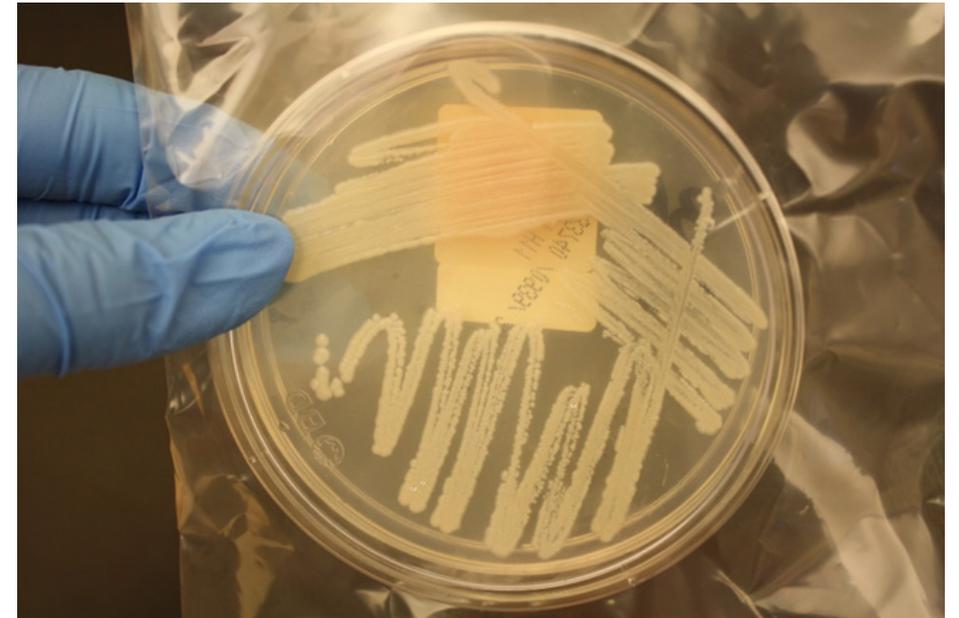
INNO-LiPA Line Probe Assay (LPA) Interpretation



1	Coni ctrl	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	MYC genus	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
3	MTB		3																				
4	MKA-1			4																			
5	MKA-2				5																		
6	MKA-3					6																	
7	MXE						7																
8	MGO							8															
9	MGV								9														
10	MSI									10													
11	MMU										11												
12	MCE											12											
13	MAIS												13	13	13	13	13	13	13	13*			
14	MAV													14									
15	MIN-1														15								
16	MIN-2															16							
17	MSC																17						
18	MML																	18					
19	MHP																		19				
20	MCH-1																			20	20	20	
21	MCH-2																				21		
22	MCH-3																					22	
23	MFO																						23
24	MSM																						24

NTM Species - Characteristics

- NTM species are categorized by speed of growth
 - Rapid growers (7 days)
 - *M. abscessus*
 - *M. fortuitum*
 - *M. chelonae*
 - *M. mucogenicum*
 - Slow growers (up to 6 weeks)
 - *M. avium* complex (MAC)
 - *M. marinum*
 - *M. ulcerans*
 - *M. kansasii*



- MDH-PHL will be sending NTM isolates meeting the NTM extrapulmonary case definition to send to CDC
 - Will utilize isolates that are routinely submitted to the MDH-PHL for identification (up to 40)
 - MDH may request specific isolates from laboratories if CDC requests additional isolates
 - If apparent clusters or outbreaks of NTM infection need investigation, MDH may request those specific isolates



Thank you!

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Questions?