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Characteristics of clinical extrapulmonary nontuberculous mycobacteria isolates in Minnesota, 2013–2017

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Abstract

Approximately 80 species of nontuberculous mycobacteria (NTM) that cause disease are found environmentally and in animal reservoirs. Typically, pulmonary NTM infections are sporadic; extrapulmonary NTM (ENTM) infections are commonly outbreak associated. Recent sources of ENTM outbreaks in Minnesota include contaminated heater-cooler units used during cardiac surgery and contaminated hormone injections. We examined patient demographics and characteristics of ENTM isolates characterized by four Minnesota reference laboratories during 2013–2017 to assess potential value of systematic laboratory-based ENTM surveillance in Minnesota.

Laboratories characterized 490 ENTM isolates, representing an estimated burden of 1.8/100,000 people/year in Minnesota. Thirty-one species or complexes were identified; most common were *M. avium complex* (31%), *M. chelonae* (22%), *M. fortuitum* (11%), and *M. abscessus* (4%). Most

common specimen collection sites included skin and soft tissue (38%), blood (15%), neck lymph node or tissue (12%), sinus (8%), joint or bone (5%), device or implant (4%), and eye (3%). Median age of patients was 55 years (range: 2–98 years); 18% were from patients aged <18 years, 20% aged 18–44 years, 28% aged 45–64 years and 34% aged >65 years. Sex was documented for 238 (49%) patients; 127 (53%) were males. County information was available for 313 patients (64%); approximately half (49%) resided in metropolitan Minneapolis-Saint Paul.

Laboratory data can be used for ENTM surveillance in Minnesota. Implementing laboratory-based surveillance can detect ENTM cases, provide a mechanism for obtaining clinical and epidemiological information, and enable earlier identification of potential health care transmission or community clusters.

Introduction

Approximately 80 species of nontuberculous mycobacteria (NTM) that cause disease are found environmentally and in animal reservoirs. Extrapulmonary nontuberculous mycobacteria (ENTM) infections are associated with high morbidity, complex treatment regimens, and potential for community and health care-associated outbreaks. A widely publicized outbreak attributable to disseminated infections caused by *Mycobacterium chimaera* occurred worldwide during 2011–2016.¹ The outbreak was traced to contaminated water heater-cooler devices used during open-heart surgery. In the United States, approximately half a million patients were exposed, with 51–80 infections known to be associated with the contaminated devices.² Other examples include 14 cases of *M. abscessus* lymphadenitis in children in Georgia as a result of contaminated dental water lines³ and an outbreak of 38 *M. fortuitum* infections associated with a tattoo parlor.⁴

ENTM infection is reportable in seven states, including from health care providers in Oregon, Maryland, Missouri, Tennessee, and Wisconsin and from laboratories in Nebraska and Mississippi. Oregon and Nebraska have published summaries of their reported extrapulmonary cases.^{5,6,7,8} However, information about the burden of ENTM in the United States is limited, as is information about the relative contribution of risk factors for infection such as patient characteristics, health care exposures, environmental exposures, and contribution of specific *Mycobacterium* species to disease. Similarly, given the lack of surveillance or epidemiological data, knowledge regarding potential for effective public health interventions to reduce ENTM infections or outbreaks is limited.

As of October 1, 2019, laboratories are required to report isolates of ENTM from Minnesota patients to the Minnesota Department of Health (MDH). Before this reporting mandate, minimal information was available regarding ENTM disease in Minnesota. In 2016, during the global outbreak of disseminated *M. chimaera* caused by contaminated heart surgery water heater-cooler devices, three cases occurred in Minnesota.⁹ Also in 2016, an outbreak of *M. chelonae* infections associated with human gonadotropin injections occurred at a Minnesota weight loss clinic, with six cases reported.¹⁰

We collected data on ENTM isolates identified by four reference laboratories for diagnosis of mycobacteria in Minnesota to more fully understand the types and prevalence of ENTM

infections identified in Minnesota, to characterize the persons affected by ENTM infections and to help identify outbreaks.

Methods

We collected data on ENTM isolated during 2013–2017 from the Minnesota Department of Health Public Health Laboratory (PHL), Mayo Clinic, Hennepin County Medical Center, and University of Minnesota Medical Center.

Confirmed NTM infections included any isolates of *Mycobacterium* species that were not part of the *M. tuberculosis* complex or *M. leprae*. We excluded NTM specimen sources from stool, sputum, tracheal secretions, lung, or bronchoalveolar lavage, or if the specimen source or the body site was unknown.

Patients were only counted once. If more than one specimen was isolated from the same site in a patient, the first isolate collected was included. If more than one species was isolated from one patient, both species were noted as a coinfection. If a patient had isolates of the same *Mycobacterium* species from more than one infection site or the sites were blood, bone marrow, peritoneal, or pericardial, the infection was considered to be disseminated. Patients with a pulmonary isolate and extrapulmonary isolate were included. Isolates associated with a medical device or implant (e.g., catheter port, injection site, or heart graft) were separately classified to determine isolates potentially associated with health care exposure.

An estimated incidence of extrapulmonary nontuberculous mycobacteria infections in Minnesota was calculated based on the average state population 2013–2017 and the associated patient demographics; *Mycobacterium* species, time of specimen collection, and sites of infection were examined.

This project was reviewed by MDH and CDC and determined to be non-research because it was public health surveillance.

Results

Overall, 490 Minnesotan patients had NTM isolated from an extrapulmonary site, with 101 (2013), 95 (2014), 108 (2015), 94 (2016), and 92 (2017) patients identified each year during the study period. A majority of NTM isolates were characterized at PHL (n=256, 52.2%). Forty-three isolates did not have a known specimen source and were excluded. The number of clinical ENTM isolates identified by major reference laboratories in Minnesota was relatively stable each year 2013–2017. Confirmed cases represent approximately 98 cases annually in Minnesota, or an estimated rate of 1.8/100,000 people/year.

Patient ages were available for 457 isolates (93%); 18% were from patients aged <18 years, 20% from patients aged 18–44 years, 28% from patients aged 45–64 years, and 34% from patients aged ≥65 years. The median patient age was 55 years (Table 1). Patients aged <10 years most often had neck infections (n = 73, 64%). County information was available for 313 patients (64%); most resided in the seven-county Minneapolis-Saint Paul metropolitan

area (49%) or in Olmsted County (12%) (Figure 1). Sex of patient was available for 238 isolates (49%); 53% were from males.

The most common specimen collection sources of ENTM included skin and soft tissue (38%), and sources attributable to disseminated infections (19%), a majority of which were from blood specimens (15%) (Table 1). We also identified lymph node and related sources (15%) with most of these involving neck tissue, cervical lymph node, or parotid tissue (12%). Other sources included sinus (8%), joint or bone (5%), medical device or implant (4%) and eyes (3%) (Table 1).

M. avium complex, which are slowly growing mycobacteria, accounted for the greatest proportion of NTM isolates (153, 31%) and were isolated predominantly from lymph nodes and body sites indicative of disseminated disease. The rapidly growing mycobacteria (*M. chelonae*, *M. fortuitum*, *M. mucogenicum*, or *M. abscessus*) were commonly isolated from skin or soft tissue or nasal or sinus sites. Of note, these species accounted for 92% (12 of 13) eye specimens. Two thirds of the potential health care-associated infections in our data collection (classified as related to medical devices and implants) were due to *M. chelonae*, *M. mucogenicum*, *M. abscessus*, or *M. fortuitum* infection. Blood specimens accounted for 79% (26 of 33) of the rapidly growing *M. mucogenicum* isolates. *M. marinum* accounted for only 19 isolates, which were all recovered from skin and soft tissue sources, including 14 that were specified as hand or finger. Seven patients with disseminated ENTM infections also had a positive pulmonary specimen. A tattoo-associated infection with *M. neoaurum* was detected.

Collection dates were available for 460 isolates (94%). A potential seasonal trend was noted, with the least number of ENTM specimens collected during summer months (Figure 2).

Discussion

Our report describes ENTM infections in Minnesota during 2013–2017, based on *Mycobacterium* diagnostic isolation reports from four Minnesota reference laboratories and demonstrates using laboratory data for ENTM surveillance in Minnesota. While case definitions and detection methods are different between states, the estimated burden of disease and NTM species detected in Minnesota appears to be higher than other states conducting surveillance: for example the rate in Minnesota is higher than the estimated rate in Oregon (1.1 cases/100,000 people/year) captured by their active surveillance system during 2014–2016.^{7,8}

The rapidly growing mycobacteria (*M. abscessus*, *M. chelonae*, and *M. fortuitum*) commonly isolated from skin and soft tissue are known to have caused health care-associated infections, including from cosmetic procedures,^{11,12} dental pulp-otomy,¹³ prosthetic joints,¹⁴ central venous catheters,^{15,16} and open-heart surgery.¹⁷ Twelve ocular infections were identified; ENTM keratitis commonly occurs after trauma, surgery, or as a result of contaminated contact lenses.¹⁸ We did not have information to determine whether trauma, procedures, or contaminated contact lenses were involved in many these cases. In terms of community exposures, only one skin tattoo infection was specified in the data

collection; however, other specimens submitted under the category “skin” or “swab” might have been related to tattoo or other cosmetic exposures.

Neck specimens, a majority of which are likely to be cervical lymphadenitis, generally occurred in young patients and involved *M. avium* complex, a common cause of NTM cervical lymphadenitis reported in children.^{19,20}

Slowly growing mycobacteria (*M. avium* complex and *M. marinum*) have been associated with environmental exposures, such as water.²¹ *M. marinum* in particular has been associated with exposure to aquariums, fish or shellfish, or injuries associated with saltwater and our data are consistent with this, with a majority of infections occurring in the hand in Minnesota patients.²²

The trend for fewer skin or soft tissue and neck specimens to be collected in summer is interesting and warrants further observation. One study from Australia reported that children with cervical lymphadenitis tended to present to health care during spring, although patients with skin and soft tissue infections frequently presented during summer.²³

Sixteen extrapulmonary *M. gordonae* isolates were identified; this species is a known contaminant of pulmonary specimens and has not always been associated with a pathogenic contribution to disease.²⁴ However, without clinical data we do not know its role in these 16 patients with extrapulmonary sites of involvement. Sites of infection included skin or soft tissue, gastric fluid, urine, pleura, lymph node, and eye. *M. gordonae* was one of the top three species isolated from hospital water in a study of NTM environmental contamination in health care settings.²⁵

Limitations of laboratory-based ENTM surveillance include that any patients who did not have their infection cultured would be missed. Second, the possibility exists that some health care providers sent specimens to a laboratory other than these four Minnesota reference laboratories. A majority of the ENTM specimens were from the Twin Cities or Rochester, Minnesota, where these laboratories are located. Third, some isolates without the body site of specimen collection specified might have been an ENTM infection. Finally, a substantial limitation of this description of ENTM in Minnesota is the minimal clinical information and exposure information available in laboratory reports. The requirement to make laboratory-confirmed ENTM reportable and include detailed specimen body site, clinical information, and patient interview data will improve understanding of ENTM and potentially enable recognition of common-source outbreaks. Importantly, obtaining more information pertaining to laboratory-confirmed ENTM infections in Minnesota could enable risk factor studies and suggest measures to prevent infection.

Conclusions

Our report describes ENTM infections in Minnesota 2013–2017, based on *Mycobacterium* diagnostic isolation reports from four Minnesota reference laboratories. While the data are not directly comparable, the estimated burden of ENTM disease detected in Minnesota is higher than other states conducting surveillance. Our analysis supports using laboratory data to detect ENTM infections in Minnesota patients. Implementing laboratory-based

surveillance, as has been underway since October 1, 2019, might enhance ENTM case detection, provide a mechanism for obtaining clinical and epidemiological information, and enable earlier identification of potential health care transmission or community outbreaks.

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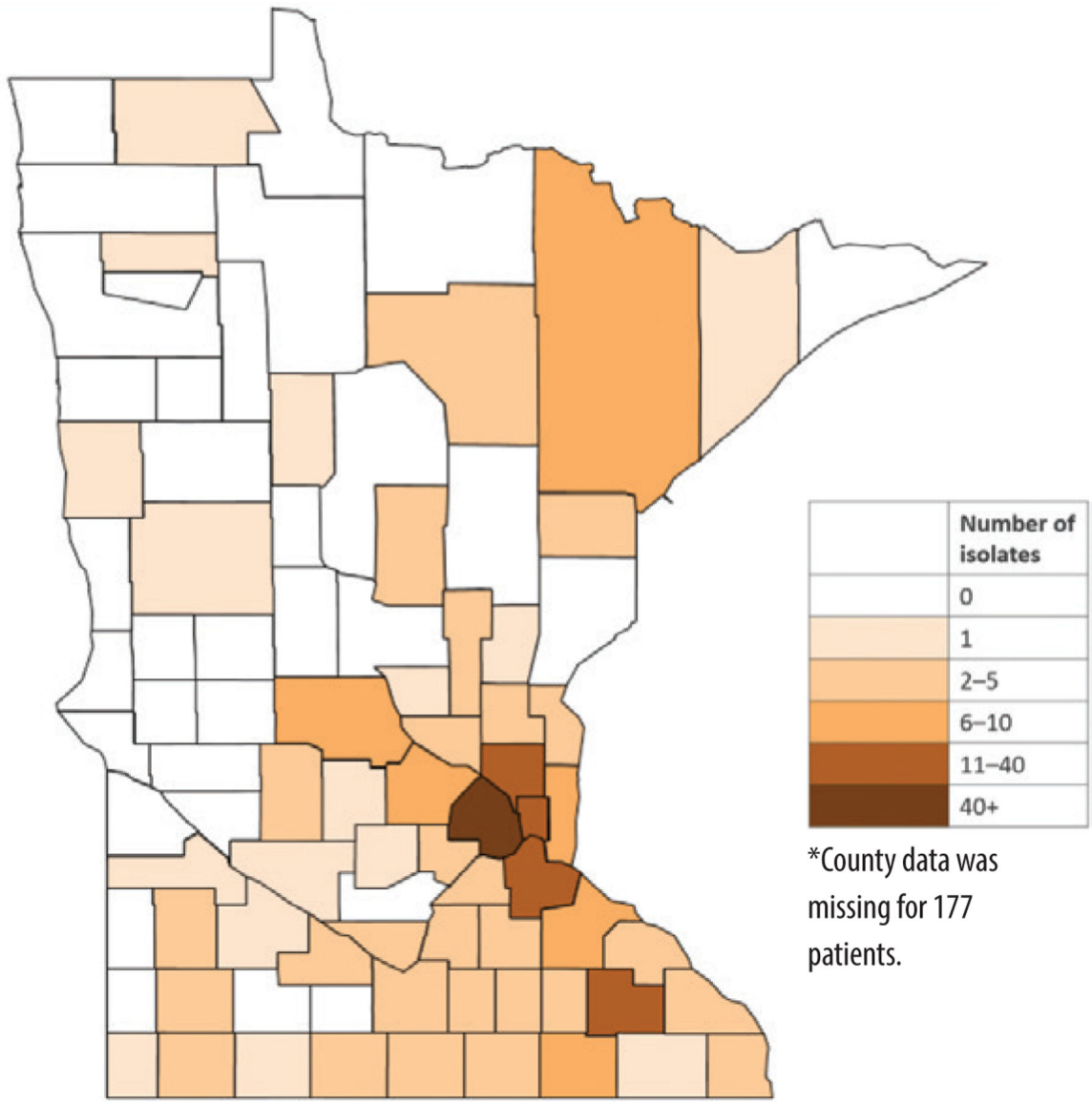


FIGURE 1. Extrapulmonary Nontuberculous Mycobacteria Infections by County — Minnesota, 2013–2017 (N = 313*).

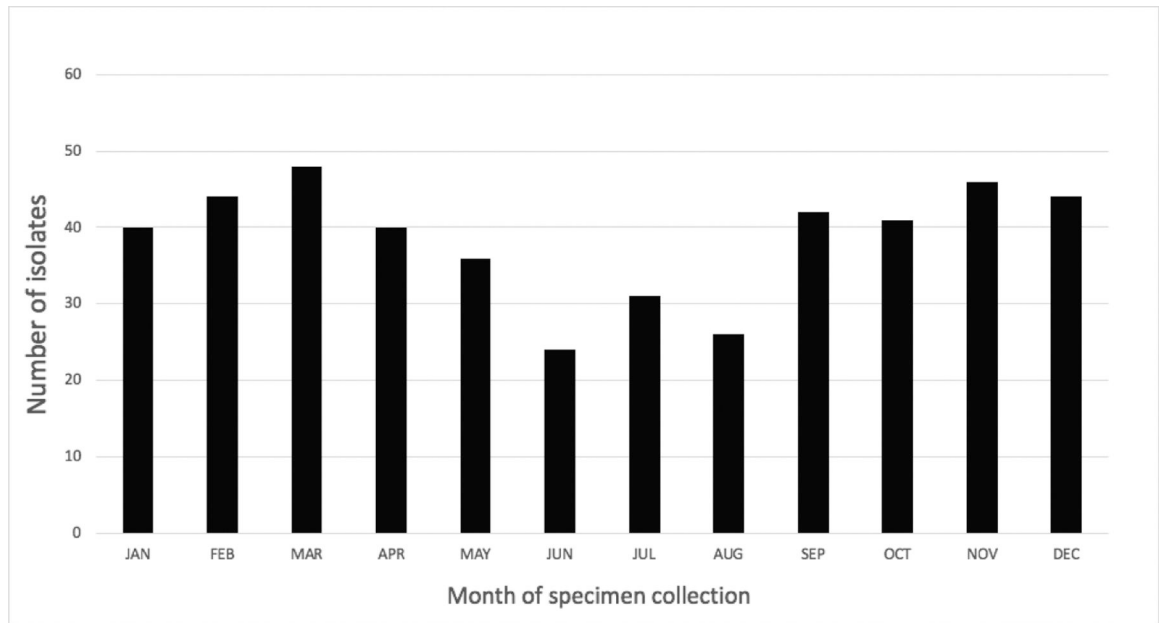


FIGURE 2. Average extrapulmonary nontuberculous mycobacteria infections by month — Minnesota, 2013–2017 (N=460*).

*Collection month information was missing for 30 patients

TABLE 1

Characteristics of Extrapulmonary Nontuberculous Isolates, by Collection Site — Minnesota, 2013–2017 (N = 490).

SPECIMEN COLLECTION SITE	MEDIAN AGE, YRS (RANGE)	MAC [§] NO. (%)	M. CHELONAE NO. (%)	M. FORTUITUM [¶] NO. (%)	M. ABSCESSUS NO. (%) [†]	M. MUCOGENICUM NO. (%)	OTHER [#] NO. (%)	TOTAL NO. (%)
Total	55 (2–98)	153	108	52	38	33	106	490
Skin or soft tissue (not neck) [*]	59 (5–96)	27 (17.7)	51 (47.2)	28 (53.9)	15 (39.5)	1 (3.0)	66 (62.3)	188 (38.4)
Disseminated (blood, peritoneal fluid, bone marrow, or pericardial fluid)	50 (11–88)	38 (24.8)	7 (6.5)	9 (17.3)	5 (13.2)	26 (78.8)	9 (8.5)	94 (19.2)
Blood	50 (21–88)	27 (17.7)	5 (4.6)	7 (13.5)	3 (7.9)	26 (78.8)	7 (6.6)	75 (15.3)
Multiple body sites	50 (2–70)	7 (4.6)	0	1 (1.9)	1 (2.6)	0	0	9 (1.8)
Peritoneal fluid	72 (11–75)	0	2 (1.9)	1 (1.9)	0	0	1 (0.9)	4 (0.8)
Bone marrow	42 (34–67)	4 (2.6)	0	0	0	0	0	4 (0.8)
Pericardial fluid	60 (46–75)	0	0	0	1 (2.6)	0	1 (0.9)	2 (0.4)
Lymph node	7 (3–92)	65 (42.5)	1 (0.9)	1 (1.9)	1 (2.6)	3 (9.1)	3 (2.8)	74 (15.1)
Neck specimens [‡]	7 (3–92)	53 (34.6)	1 (0.9)	1 (1.9)	1 (2.6)	1 (3.0)	1 (0.9)	58 (11.8)
Nasal or sinus	63 (5–86)	1 (0.7)	26 (24.1)	3 (5.8)	3 (7.9)	0	4 (3.8)	37 (7.6)
Joint or bone	70 (10–86)	8 (5.3)	7 (6.5)	3 (5.8)	2 (5.3)	0	5 (4.7)	25 (5.1)
Medical device or implant [‡]	49 (26–98)	0	2 (1.9)	2 (3.9)	6 (15.8)	2 (6.1)	6 (5.7)	18 (3.7)
Eye	66 (30–93)	0	8 (7.4)	1 (1.9)	3 (7.9)	0	1 (0.9)	13 (2.7)
Other	62 (2–91)	14 (9.2)	6 (5.6)	5 (9.6)	3 (7.9)	1 (3.0)	12 (11.3)	41 (8.4)

^{*} Includes infections in limbs (n=112, 59.6%), torso (n=23, 12.2%), face/mouth (n=12, 6.4%) and breast (n=9, 4.8%) as well as nail, axilla, ear, cervical, liver, perineal, scrotal, vaginal, skin tattoo

[‡] Includes neck mass, neck abscess or wound, cervical lymph node and parotid specimens

[†] Includes catheter or port sites, heart graft, implant in breast, injection site, pin track, gastric tube and jejunal tube sites

Other includes specimens from urine (n=9, 17.6%), aspirate/fluid unspecified, pleura, gastric fluid

[§] Mycobacterium avium complex; includes M. avium and M. intracellulare isolates.

[#] Includes Mycobacterium fortuitum complex, M. peregrinum and M. fortuitum ssp. acetamidolyticum.

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Includes *M. abscessus*, *M. abscessus* ssp *abscessus*, *M. abscessus* ssp *massiliense*, and *M. abscessus* ssp *bolletii* complex.

Includes *M. mucogenicum* and *M. mucogenicum/phocaicum*.

Other includes: *M. marinum* (n=19, 17.9%), *M. chelonae/abscessus* complex (n=19, 17.9%), *M. kansasii*, *M. neoaurum*, *M. immunogenum*, *M. haemophilum*, *M. arupense*, *M. chelonae* and *M. fortuitum* complex, *M. goodii*, *M. iranicum*, *M. obuense*, *M. smegmatis*, *M. avium* complex and *M. fortuitum* complex, *M. chlorophenolicum*, *M. conceptionense/houstonense/senegalense*, *M. fredericksbergense*, *M. lentiflavum*, *M. mageritense*, *M. malmhoense*, *M. mucogenicum/phocaicum*, *M. szulgai*, *M. heraklionense*, *M. wolinskyi*, *M. cosmeticum*.