Emerging Infections Program Healthcare-Associated Infections–Community Interface Report: Extrapulmonary Nontuberculous Mycobacteria (ENTM), 2021

Surveillance Catchment Areas:

Colorado (5 county Denver area); Minnesota (statewide); New York (1 Rochester county); Oregon (statewide).

Population:

The surveillance area represents 13,545,779 persons.
Source: U.S. Census Bureau, Population Division, Vintage 2021 Special Tabulation

Case Definition:

An ENTM case was defined as the first identification during 2021 of an NTM species from a non-pulmonary body site (e.g., specimens other than sputum, tracheal aspirate, bronchoalveolar lavage, and lung), excluding stool and rectal swabs, in a resident of the surveillance area. Species excluded from surveillance were: *Mycobacterium tuberculosis* complex (causes tuberculosis); *Mycobacterium leprae* and *Mycobacterium lepromatosis* (cause leprosy); *Mycobacterium ulcerans* (causes Buruli ulcer); and *Mycobacterium gordonae* and *Mycobacterium paragordonae* (most often non-pathogenic).

Cases were considered prevalent if:

- medical records indicated ENTM disease was present in the 12 months prior to ENTM identification in 2021, or
- NTM was detected in at least one extrapulmonary specimen in 2020 within 12 months before the date of initial ENTM specimen collection in 2021.

Cases were otherwise considered incident.

Methods:

Case finding was active, laboratory-based, and population-based. Emerging Infections Program (EIP) site personnel routinely contacted microbiology laboratories serving residents of the surveillance area to identify cases.

A standardized case report form was completed for each case through review of medical records. Medical records were reviewed for information on demographic characteristics, clinical features and syndrome, and potentially relevant exposures. Exposures were captured if they occurred in the year before or on the date of index specimen collection. Those determined to be related to the diagnosis or management of ENTM disease were excluded. In addition, information about whether the exposure occurred at the site of the NTM infection was also captured.

A convenience sample of ENTM isolates were sent to CDC for characterization. Species identification was performed at CDC using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-ToF) mass spectrometry, Sanger DNA sequencing of the full-length 16S rRNA and partial *rpoB* (region V, ~720 bp) genes, and whole genome sequencing (WGS). WGS was also used to perform multi-locus sequence typing.

Rates of ENTM infection among all patients were calculated using special tabulation U.S. Census population estimates for 2021. Cases with unknown race were assigned a race based on distribution of known race among cases by age, ethnicity, sex, and EIP site; cases with unknown ethnicity were assigned ethnicity based on distribution of known ethnicity among cases by age, race, sex, and EIP site.

ENTM surveillance data undergo regular data cleaning to ensure accuracy and completeness. Cases from 2021 with complete case report form data as of November 28, 2023, were included in this analysis. Because data can be updated as needed, analyses of datasets generated on a different date may yield slightly different results.

Results:

Table 1. ENTM (N=196) Cases by Incident Status, Emerging Infections Program, 2021

Incident Status	**No.**	**Rate[a]**
Incident	180	1.3
Prevalent[b]	15	0.1
Unknown[b]	1	<0.01
TOTAL[c]	196	1.4

[a] Cases per 100,000 population for EIP areas (crude rates)
[b] Excluded from further analysis
[c] Total rate represents overall prevalence

Table 2. Incident ENTM (N=180) Case Rates by Race/Ethnicity and Sex, Emerging Infections Program, 2021

Race/Ethnicity[a]	**Rate[b]**
Hispanic, any race	1.2
Non-Hispanic - White	1.4
Non-Hispanic - Black or African American	1.6
Non-Hispanic - Asian	0.8
Non-Hispanic - Other or multiple races	1.3

Sex	**Rate[b]**
Male	1.3
Female	1.4

[a] Unknown race (n=19) was imputed using age, sex, ethnicity, and state of residence; unknown ethnicity (n=20) was imputed using age, sex, race, and state of residence.
[b] Cases per 100,000 population for EIP areas (crude rates)

Table 3. Incident ENTM (N=180) Case Counts by Race/Ethnicity and Sex, Emerging Infections Program, 2021

Race/Ethnicity	No.	%
Hispanic, any race	17	9.4
Not known to be Hispanic[a] - White[b]	127	70.6
Not known to be Hispanic[a] - Black or African American[c]	11	6.1
Not known to be Hispanic[a] - Asian[d]	5	2.8
Not known to be Hispanic[a] - Other or multiple races[e]	6	3.3
Not known to be Hispanic[a] - Unknown race[f]	14	7.8

Sex	No.	%
Male	87	48.3
Female	93	51.7

[a] Records either indicated ethnicity was non-Hispanic, or ethnicity was not known

[b] 7 ENTM cases with unknown ethnicity

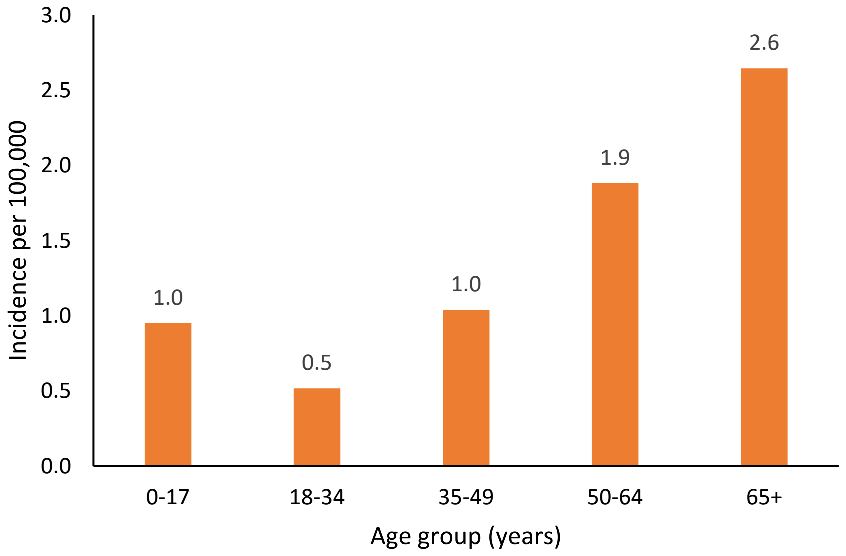
[c] 0 ENTM cases with unknown ethnicity

[d] 0 ENTM cases with unknown ethnicity

[e] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 0 cases had unknown ethnicity

[f] Of cases with unknown race, 13 cases had unknown ethnicity

Figure 1. Rate[a] of Incident ENTM (N=180) Cases by Age Group, Emerging Infections Program, 2021



[a] Incidence (no. per 100,000 population per year) calculated using 2021 special tabulation U.S. Census Data

Table 4. Incident ENTM (N=180) Cases by Species Identified from Index Specimen[a] at Clinical Laboratories, Emerging Infections Program, 2021

Slowly Growing NTM Species	**No.**	**%**
M. arupense	1	0.6
M. avium complex - *M. avium*	16	8.9
M. avium complex - *M. intracellulare* subsp. *chimaera*	1	0.6
M. avium complex - *M. intracellulare* subsp. *intracellulare*	7	3.9
M. avium complex - *M. marseillense*	1	0.6
M. avium complex, not otherwise specified	39	21.7
M. haemophilum	2	1.1
M. heckeshornense	1	0.6
M. heraklionense	1	0.6
M. interjectum	1	0.6
M. kansasii	4	2.2
M. mantenii	1	0.6
M. marinum	9	5.0
M. xenopi	1	0.6
Total	85	47.2

Rapidly Growing NTM Species	**No.**	**%**
M. abscessus[b]	28	15.6
M. chelonae complex[c]	31	17.2
M. cosmeticum	1	0.6
M. fortuitum complex[c]	19	10.6
M. goodii	1	0.6
M. llatzerense	1	0.6
M. mucogenicum complex[c]	1	0.6
M. mucogenicum	6	3.3
M. neoaurum	2	1.1
M. sediminis	1	0.6
M. smegmatis complex[c,d]	1	0.6
M. smegmatis	2	1.1
M. wolinskyi	1	0.6
Total	95	52.8

Other, Not Characterized NTM	**No.**	**%**
Not TB[e], not characterized further	1	0.6
Non-*M. avium* complex, not otherwise specified	1	0.6
Total	2	1.1

[a] Two had more than one species isolated: 1 *M. cosmeticum* and *M. smegmatis*, and 1 *M. chelonae* complex and *M. xenopi*

[b] Subspecies identification not reported to CDC

[c] Species identification not reported to CDC

[d] *M. smegmatis* complex includes *M. smegmatis*, *M. goodii*, and *M. wolinskyi*

[e] TB=*Mycobacterium tuberculosis* complex

Table 5. Incident ENTM (N=180) Cases by Source of Index Specimen, Emerging Infections Program, 2021

Index Specimen Source[a]	No.	%
Blood	25	13.9
Bone	6	3.3
Joint/Synovial fluid	17	9.4
Lymph node	29	16.1
Non-surgical wound	16	8.9
Pleural fluid	9	5.0
Sinus	9	5.0
Skin	17	9.4
Soft tissue	22	12.2
Surgical wound	10	5.6
Other	21	11.7

[a] 1 case had 2 index specimen sources

Table 6. Location of Incident ENTM (N=180) Cases at Time of Incident Specimen Collection, Emerging Infections Program, 2021

Location of Incident Specimen Collection	No.	%
Outpatient setting or emergency department	89	49.4
Acute care hospital	89	49.4
Long-term care facility	0	0.0
Long-term acute care hospital	0	0.0
Other	0	0.0
Unknown	2	1.1

Table 7. Selected Clinical Characteristics of Incident ENTM (N=180) Cases, Emerging Infections Program, 2021

Charlson Comorbidity Index[a]	No.	%
0	68	38.6
1	28	15.9
≥2	80	45.5

Underlying Conditions[a]	No.	%
Connective tissue disease	13	7.4
Connective tissue disease: Rheumatoid arthritis	7	4.0
Diabetes mellitus	24	13.6
Immunocompromising condition/Immunosuppressive medication	70	39.8
Immunocompromising condition - HIV infection	12	6.8
Immunocompromising condition - AIDS/CD4 count <200	11	6.3
Immunocompromising condition - Other[b]	9	5.1
Immunosuppressive medication[c]	58	33.0
Injection drug use	6	3.4
Malignancy	30	17.0
Skin condition	22	12.5
Skin condition - Surgical wound	5	2.8

Syndrome[d]	No.	%
Abscess, not skin	23	12.8
Bacteremia	18	10.0
Catheter site infection	3	1.7
Disseminated infection	20	11.1
Empyema/Pneumonia	6	3.3
Internal surgical site infection	15	8.3
Lymphadenitis	26	14.4
Osteomyelitis	7	3.9
Septic arthritis	7	3.9
Sinusitis	3	1.7
Skin and soft tissue infection[e]	37	20.6
Tenosynovitis/Synovitis	8	4.4

Syndrome[d]	**No.**	**%**
Other	17	9.4
No infection[f]	56	31.1
Unknown	4	2.2

[a] Some case patients had more than one underlying condition. Excludes 4 cases with unknown underlying conditions

[b] Includes solid organ transplant, hematopoietic stem cell transplant, and primary immunodeficiency

[c] Includes abatacept, B cell depletion agents, corticosteroids (intravenous, intramuscular, or oral), and TNF-α inhibitors

[d] Some case patients had more than one syndrome

[e] Includes cellulitis, chronic ulcer/wound, decubitus/pressure ulcer, skin abscess, surgical incision infection, traumatic wound, and other skin/soft tissue infections.

[f] Patients may not have an infection associated with their NTM culture for several reasons, including that the patient had no infection diagnosed and the NTM identified was considered a contaminant; or if the patient's infection was attributed to another organism identified.

Table 8. Selected Exposures and Risk Factors in the Year Before Index Specimen Collection, Incident ENTM Cases with a Clinically Documented NTM Infection, Emerging Infections Program, 2021

	All Exposures		Exposure at Site of Infection[a]	
Exposures in the Past Year for Cases with Localized Infections[b] (n=93)	**No.**	**%**	**No.**	**%**
Dental procedure	2	2.2	0	0.0
Fish-related exposures[c]	10	10.8	--	--
Gardening or landscaping	10	10.8	--	--
Hot tub	6	6.5	--	--
Injection or infusion	40	43.0	20	21.5
Livestock/wildlife	3	3.2	--	--
Medical device	27	29.0	17	18.3
Nail salon	0	0.0	0	0.0
Neti pot	2	2.2	2	2.2
Surgical procedure	29	31.2	22	23.7
Swimming pool	2	2.2	--	--
Tattoo	0	0.0	0	0.0
Trauma	16	17.2	16	17.2
Other	10	10.8	1	1.1
None	16	17.2	35	37.6
Unknown	1	1.1	4	4.3

[a] Cells with "--" indicate fields where exposure at site of infection is not applicable

[b] Excludes incident cases with no infection type (n=56); unknown infection type (n=4); and cases either with bloodstream infection and no other infection types documented, or with disseminated infection (27)

[c] Fish-related exposures include fish tank, fishing, and fish bite

CDC Laboratory Characterization of ENTM Isolates

In 2021, four sites submitted 90 ENTM isolates to CDC. The total number of isolates received from each site ranged from 10 to 40. WGS was successfully performed for 89 of 90 isolates.

Table 9. Incident ENTM Species Identification, Isolates Tested at CDC (N=90[a]), Emerging Infections Program, 2021

Slowly Growing NTM Species	**No.**	**%**
M. avium complex – *M. avium*	26	28.9
M. avium complex – *M. intracellulare*	2	2.2
M. avium complex – *M. intracellulare* subsp. *chimaera*	1	1.1
M. avium complex – *M. intracellulare* subsp. *intracellulare*	2	2.2
M. kansasii	3	3.3
M. marinum	7	7.8
Total	41	45.6

Rapidly Growing NTM Species	**No.**	**%**
M. abscessus[b]	19	21.1
M. chelonae	13	14.4
M. fortuitum complex[c]	1	1.1
M. fortuitum	9	10.0
M. immunogenum	1	1.1
M. mucogenicum complex[d]	2	2.2
M. mucogenicum	1	1.1
M. porcinum	1	1.1
M. septicum	1	1.1
M. wolinskyi	1	1.1
Total	49	54.4

[a] 32 isolates were identified only to the complex level or lesser resolution by the submitter and testing at CDC was able to resolve all 32 to species or subspecies level; 1 isolate was identified by CDC to be a different species than the submitter although within the same complex

[b] Subspecies identification was not performed

[c] Due to discrepancies between WGS and *rpoB* sequencing results, this isolate was reported as *M. fortuitum* complex only and not resolved to the species level

[d] Due to discrepancies between WGS and *rpoB* sequencing results, we report this isolate as part of the *M. mucogenicum* complex only and not resolved to the species level

Table 10. Incident ENTM Sequence Types (ST[a]) by Species[b,c], Isolates Sequenced at CDC (N=89[d]), Emerging Infections Program, 2021

M. avium **(N=26)**	**No.**	**%**
ST11	7	26.9
ST175	3	11.5
ST990	3	11.5
ST14	2	7.7
ST183	2	7.7
ST4	2	7.7
ST993	2	7.7
Other STs	5	19.2

M. marinum **(N=7)**	**No.**	**%**
ST1028	2	28.6
ST22	2	28.6
Other STs	3	42.9

M. kansasii **(N=3)**	**No.**	**%**
ST38	2	66.7
Other STs	1	33.3

M. abscessus **(N=19)**	**No.**	**%**
ST80	4	21.1
ST422	3	15.8
ST173	2	10.5
ST5	2	10.5
Other STs	8	42.1

M. chelonae **(N=13)**	**No.**	**%**
ST37	6	46.2
ST440	3	23.1
Other STs	4	30.8

M. fortuitum **(N=9)**	**No.**	**%**
ST195	2	22.2
ST62	2	22.2
ST989	2	22.2
Other STs	3	33.3

[a] Multi-locus sequence types (STs) determined using the PubMLST *Mycobacteria* spp. scheme. Only STs found in more than one isolate are partitioned in the table; singleton STs are collapsed into Other STs

[b] STs were determined for a total of 13 species. Only species represented by at least 3 isolates in the dataset (6 species) are included in the table. The following 7 species were excluded from the table: *M. intracellulare*, *M. mucogenicum* complex, *M. septicum*, *M. immunogenum, M. wolinksyi*, *M. fortuitum* complex, and *M. porcinum*

[c] *M. avium*, *M. marinum*, and *M. kansasii* are slowly growing species; *M. abscessus*, *M. chelonae*, and *M. fortuitum* are rapidly growing species

[d] One isolate failed sequencing

Summary:

Surveillance data from 2021 represent the first full year of population-based surveillance for extrapulmonary nontuberculous mycobacteria (ENTM) infections through the Emerging Infections Program (a surveillance pilot was conducted for six months during 2019–2020)[1, 2]. The crude annual incidence rate of ENTM in 2021 was 1.3 per 100,000 persons. The incidence generally increased with increasing age and ranged from 0.8 among non-Hispanic Asian persons to 1.6 per 100,000 in non-Hispanic Black persons. *M. avium* complex was the most frequently isolated species group, followed by *M. chelonae* complex. Testing at CDC enabled greater species resolution for over a third of isolates (31/90; 34.4%). After further species identification, among isolates received at CDC, *M. avium* was the most common species followed by *M. abscessus*. Fifty-four distinct multi-locus sequence types (STs) were identified, of which the most common were *M. avium* ST11 and *M. chelonae* ST37. Skin and soft tissue infections were the most commonly reported infection type. Among patients with localized ENTM infections, medical record documentation indicated that the most common exposures at the infection site were surgery, injection/infusion, a medical device, or trauma.

References:

[1] Grigg C, Jackson KA, Barter D, et al. Epidemiology of Pulmonary and Extrapulmonary Nontuberculous Mycobacteria Infections Infections at 4 US Emerging Infections Program Sites: A 6-Month Pilot. Clin Infect Dis. 2023 Aug 22; 77(4):629-639. doi: 10.1093/cid/ciad214.

[2] Masters TL, Charles Toney N, Ewing TO, et al. Genomic Epidemiology of Extrapulmonary Nontuberculous Mycobacteria Isolates at Emerging Infections Program Sites – United States, 2019–2020. J Infect Dis. 2025 April 15; 231(4):902–912. doi: 10.1093/infdis/jiae488.

Citation:

Centers for Disease Control and Prevention. 2023. Emerging Infections Program, Healthcare-Associated Infections – Community Interface Surveillance Report, Extrapulmonary Nontuberculous Mycobacteria (ENTM), 2021. Available at: https://www.cdc.gov/healthcare-associated-infections/media/pdfs/2021-ENTM-Report-508.pdf

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