Outbreak of Multidrug-Resistant Tuberculosis — Kansas, 2021–2022

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Abstract

An outbreak of multidrug-resistant (MDR) tuberculosis (TB) involved 13 persons in four households in a low-income, under-resourced urban Kansas community during November 2021–November 2022. A majority of the seven adults identified in the Kansas outbreak were born outside the United States in a country that had experienced an MDR TB outbreak with the same genotype during 2007–2009, whereas most of the six children in the Kansas outbreak were U.S.-born. Prompt identification, evaluation, and treatment of persons with MDR TB and their contacts is essential to limiting transmission.

Introduction

Tuberculosis (TB) incidence in Kansas is low; 37–43 TB cases were reported annually during 2019–2021. However, in 2022, the number of reported TB cases increased to 52 (*1*). Driving this increase was an outbreak of multidrug-resistant (MDR) TB involving 13 persons in four households in a low-income, underserved urban community. By definition, MDR TB is resistant to at least isoniazid and rifampin, two of the most effective anti-TB medications.* In 2021, MDR TB was present at initial diagnosis for only 77 (1.0%) of 7,882 TB cases reported in the United States (*2*).

Investigation and Results

The first person identified in this outbreak was an infant hospitalized in November 2021 with pulmonary and meningeal TB. Rifampin resistance was initially detected by DNA amplification of the *rpoB* gene mutation (*3*) and subsequently confirmed by DNA sequencing and growth-based drug susceptibility testing methods, which indicated additional resistance to isoniazid, pyrazinamide, and ethambutol (i.e., all four medications that constitute first-line therapy), but no resistance to second-line anti-TB medications. An investigation conducted by the local public health department (*4*) identified four additional members of the same household (household A) with MDR TB, including a severely ill adult with smear-positive pulmonary cavitary disease, who had been symptomatic since June 2021.

In January 2022, a young child from a second household (household B) was hospitalized with pulmonary TB and lymphadenitis. *Mycobacterium tuberculosis* was isolated from a culture of a cervical lymph node biopsy specimen. Culture-based testing demonstrated the same drug susceptibility pattern as that identified in the persons in household A. After observing a cough in the young child's mother, who was pregnant at the time, hospital personnel evaluated her, and she received a diagnosis of pulmonary MDR TB. During the contact investigation, local public health department staff members identified an additional four household members with MDR TB; one who was a severely ill young adult with pulmonary cavitary lesions who had been symptomatic since at least September 2021.

Further investigation led to the discovery that households A and B were in the same apartment complex, and that members of the two households socialized extensively. Adults from the two households also shared a car to commute to the same workplace. Two additional apartment households in a different neighborhood (households C and D) were also found to be connected to these families. A young teenager in household C who had spent time in both households A and B received a diagnosis of pulmonary MDR TB and extrapulmonary TB vasculitis. An extensive contact investigation involving other household contacts, a school, and a workplace was conducted. Contacts were tested when initially identified and were tested again with an interferon-gamma release assay blood test or tuberculin skin test 8 weeks after their most recent exposure to any household member with TB (*4*).

Initially, infections appeared to be limited to persons within the four households associated with this outbreak. However, an unexpected *M. tuberculosis* genotype match in a child with MDR TB in a neighboring state (household E) was identified in July 2022, bringing the total case count for this outbreak to 14. Additional investigation confirmed that the young adult from household B was also known to household E and had spent time in the home of household E while infectious.

In total, 13 persons with MDR TB disease were identified in Kansas, and one in a neighboring state, during November 2021–November 2022 (Table). Nine of the 13 were culture-confirmed, and five had clinically verified disease. The most recent person found to have extrapulmonary TB was in November 2022. In Kansas, nine household contacts received diagnoses of latent TB infection (LTBI), including four in household A, two in household C, and three in household D.

* https://www.cdc.gov/tb/publications/factsheets/drtb/mdrtb.htm

Within this Kansas outbreak, seven household members were tested and found to not have TB disease or LTBI (one in household B, one in household C, and five in household D).

The public health investigations suggested a common social network among associated households. Whole-genome sequencing was conducted through CDC's National TB Molecular Surveillance Center for persons with culture-confirmed TB in this outbreak. Whole-genome single nucleotide polymorphism (wgSNP) analysis demonstrated that the isolates differed by up to three single nucleotide polymorphisms, supporting the hypothesis that the outbreak represented transmission within this social network. In addition, wgSNP analysis indicated a close genetic relationship to *M. tuberculosis* isolates from previous outbreaks in the Federated States of Micronesia during 2007–2009 (*5*) and Guam during 2009–2016; some adults in the Kansas City outbreak also lived in the Federated States of Micronesia and Guam during these previous outbreaks. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[†]

Public Health Response

The immediate public health response focused on the identification, isolation, and treatment of persons with MDR TB. All household contacts were evaluated for TB disease and LTBI with an interferon-gamma release assay blood test or tuberculin skin test, chest imaging, and sputum testing. After expert consultation through the Heartland National Tuberculosis Center,[§] individualized treatment regimens were developed for each person with active TB disease and administered via daily, in-person directly observed therapy. Most adults (median age = 29 years) and an older teenager in household A received a 26-week regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) (*6*,*7*). The pregnant woman received bedaquiline, linezolid, moxifloxacin, and clofazimine, and then after delivery and cessation of breastfeeding, transitioned to the BPaLM regimen for an additional 6 months of therapy.

The infant, young child, other children, and young teenager presented a unique treatment challenge because BPaLM has not been studied in children aged <15 years (*6*). Three of these children (aged 9–13 years) received a 26-week regimen of bedaquiline, linezolid, moxifloxacin, and delamanid. Delamanid, an MDR TB medication used in Europe,[¶] was authorized for compassionate use by the Food and Drug Administration after review by the Kansas Department of Health and Environment's Institutional Review Board. The infant and young child's treatment regimens included bedaquiline, cycloserine, levofloxacin, and linezolid. The length of treatment was individualized and dependent on clinical improvement. Adherence was excellent among all persons who entered treatment, and as of September 2023, 13 of the 14 persons with MDR TB disease have completed treatment. One adult who received a clinical diagnosis of extrapulmonary TB disease declined treatment despite extensive measures on the part of public health and clinicians. Local public health staff members continue to maintain careful communication and relationship with this person, should they

TABLE. Persons with multidrug-resistant tuberculosis (N = 14) or latent tuberculosis infection (N = 9), by household — Kansas City, Kansas, 2021–2022

Location, household, patient	Diagnosis mo/yr	TB status or disease site
Kansas City, Kansas		
Household A		
Infant	Nov 2021	Pulmonary and meningeal disease
Older teenager	Nov 2021	Pulmonary and extrapulmonary disease
Adult*	Nov 2021	Pulmonary and extrapulmonary disease
Adult	Nov 2021	Latent infection
Adult	Nov 2021	Latent infection
Adult	Mar 2022	Latent infection
Adult	May 2022	Pulmonary and extrapulmonary disease
Adult	May 2022	Extrapulmonary disease
Adult	Aug 2022	Latent infection
Household B		
Young child	Jan 2022	Pulmonary and extrapulmonary disease
Pregnant woman	Feb 2022	Pulmonary disease
Young adult[†]	Mar 2022	Pulmonary and extrapulmonary disease
Adult	Mar 2022	Pulmonary and extrapulmonary disease
Child	Apr 2022	Pulmonary and extrapulmonary disease
Child	Apr 2022	Extrapulmonary disease
Household C		
Young teenager	Mar 2022	Pulmonary and extrapulmonary disease
Adult	Mar 2022	Latent infection
Adult	Mar 2022	Latent infection
Adult	Nov 2022	Extrapulmonary disease
Household D		
Adult	Apr 2022	Latent infection
Adult	Apr 2022	Latent infection
Adult	Apr 2022	Latent infection
Neighboring state		
Household E		
Child	Jul 2022	Pulmonary and extrapulmonary disease

Abbreviation: TB = tuberculosis.

* This adult's tuberculosis symptoms began in June 2021; this patient was thought to be the source of infection for the infant in the household.

† The young adult's tuberculosis symptoms began no later than September 2021; this patient was thought to be the source of infection for both the young child in the household and the child in a neighboring state.

† 45 C.F.R. part 46, 21C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501et seq.

§ https://www.cdc.gov/tb/education/tb_coe/default.htm

¶ https://www.who.int/publications/i/item/9789240063129

desire treatment, or should their disease progress further and pose a health risk to the community.

The nine household members identified with LTBI began a 6-month regimen of daily moxifloxacin (*8*), also administered via daily in-person directly observed therapy. Monitoring also included laboratory testing and chest imaging at the start and end of treatment. All nine persons completed treatment without developing disease or complications. All persons treated for both TB disease and LTBI will continue close monitoring by public health clinicians every 6 months for ≥ 2 years after treatment completion; monitoring will include a chest radiograph, review of signs and symptoms, and a physical exam.

Discussion

MDR TB outbreaks have been exceptionally rare in the United States since the 1990s (*9*). Typically, MDR TB in the United States occurs sporadically among non–U.S.-born persons (*2*). This outbreak involved multiple U.S.-born children who became infected while living in Kansas, contributing to a national increase in pediatric children with tuberculosis reported in 2022 (*1*). Compared with drug-susceptible TB, MDR TB is associated with increased morbidity and cost related to both disease and medication-associated factors (*10*). Treating the persons affected by this outbreak required careful monitoring of those persons receiving newer MDR TB drugs to ensure cure and reduce risk for further drug resistance.

Identifying one person as the single source for this outbreak is difficult. Both sentinel events of TB disease in the infant and young child included a plausible source within the household (i.e., a non–U.S.-born adult with a lengthy illness course and infectious period). At least one of these adults was likely infected overseas years earlier and then experienced progression to active TB disease after moving to Kansas. Unfortunately, neither of the plausible source persons received a diagnosis for many months, leading to further transmission.

Implications for Public Health Practice

This outbreak in an urban, at-risk community resulted in tremendous financial, staffing, and capacity strain on the local public health department, where capacity was already diminished after nearly 2 years of COVID-19 pandemic response; however, recent collaborations established during COVID-19 prevention activities led to many positive working relationships with community partners such as the schools and hospitals, which facilitated efficient coordination of the outbreak response. This outbreak is also a cautionary tale, reminding other low TB incidence jurisdictions that sustained declines in TB incidence are not assured. Successful TB treatment and prevention requires ongoing identification and treatment of LTBI and a swift multifaceted public health response for each person newly diagnosed with TB.

Summary

What is already known about this topic?

U.S. multidrug-resistant (MDR) tuberculosis (TB) is uncommon and usually occurs in non–U.S.-born persons who likely acquired infection years earlier while living in other countries.

What is added by this report?

An MDR TB outbreak involving 13 persons with active disease and nine with latent TB infections was identified within four Kansas households in 2021 and included multiple U.S.-born children who became infected in Kansas. One person in a neighboring state with an epidemiologic connection to the Kansas outbreak was identified. Controlling this outbreak required newer MDR TB drugs not often used in the United States.

What are the implications for public health practice?

This outbreak underscores the importance of prompt identification and appropriate treatment of TB disease and latent infection, especially MDR TB.

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