A Tuberculosis Outbreak Fueled by Cross-Border Travel and Illicit Substances: Nevada and Arizona

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ABSTRACT

Objectives. From May 2006 to August 2008, the Southern Nevada Health District identified eight tuberculosis (TB) cases in six adults and two children in a Hispanic community. We conducted an outbreak investigation to determine the extent of TB transmission and prevent additional cases.

Methods. We investigated TB cases in Nevada and Arizona with the outbreak genotype or cases with suspected epidemiologic links to this cluster but without genotyping data. We reviewed medical records and interviewed patients and contacts. Subsequently, genotype surveillance was conducted for approximately four years to monitor additional outbreak-related cases.

Results. Eight outbreak cases were identified among six adults and two children. All patients were Hispanic and five were U.S.-born. The index patient was diagnosed while detained in Immigration and Customs Enforcement custody but deported before treatment completion. He was lost to follow-up for two years, during which time he served as the source for six secondary TB cases, including his own child. Along with the index patient, five patients reportedly engaged in the sale or use of methamphetamine. Follow-up surveillance in the two states identified eight additional cases with the outbreak genotype; three had epidemiologic links to the index case.

Conclusions. We found that incomplete TB treatment led to extensive TB transmission. We recommend thorough discharge planning and active measures to ensure continuity of care and TB treatment completion for people in custody at higher risk for loss to follow-up, which likely includes those engaged in the sale or use of illicit substances.

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Completion of treatment is a top priority of the tuberculosis (TB) control strategy in the United States.¹ People diagnosed with TB while incarcerated are recognized to be at high risk for failure to complete treatment related to loss to follow-up.²⁻⁴ A particularly challenging subgroup consists of people unauthorized to reside in the U.S. who are in U.S. Department of Homeland Security, Immigration, and Customs Enforcement (ICE) custody while undergoing administrative process for possible deportation. Based on immigration laws, once a federal immigration judge orders the deportation of an individual, ICE has limited time to carry out this order. Thus, when routine intake screening identifies detainees with TB disease, they begin treatment but can subsequently be deported (or released) once their TB is no longer considered contagious, even if treatment remains incomplete.⁵⁻⁷ Because these people are typically highly mobile, they are at risk for treatment interruption and loss to follow-up.⁵ Further, their likely return to the U.S. can lead to TB reimportation, including with drug-resistant strains, placing communities at risk for TB exposure.⁸ Therefore, ensuring treatment completion in such cases is of public health importance, requiring extensive multiagency collaboration among detention facilities, law enforcement agencies, and local, state, and national TB programs in both the U.S. and the receiving country.^{5,7,9}

From May 2006 to August 2008, the Southern Nevada Health District (SNHD) identified eight TB cases in six adults and two children in a Hispanic community with social ties to Mexico. All six adult patients (five residing in Nevada and one in Arizona) had drug-susceptible TB, with matching genotypes (i.e., spoligotype and 12-locus mycobacterial interspersed repetitive unit [MIRU]), suggestive of recent TB transmission.^{10,11} The two children had culture-negative TB. The suspected source, the index patient, was reportedly a methamphetamine distributor without legal residency in the U.S. who was diagnosed with TB while in ICE custody in 2006 but was deported and lost to follow-up before TB treatment completion. The detection of secondary cases, including two among children, raised concerns about ongoing TB transmission in a hard-to-reach population, prompting the SNHD to invite the Centers for Disease Control and Prevention (CDC) to assist with the outbreak investigation.

The purpose of the August 2008 investigation, which is described in this article, was to determine epidemiologic links among cases, the extent of TB transmission, and measures to prevent additional cases. Subsequently, from September 2008 through June 2012, we conducted surveillance of genotyped TB cases to monitor for additional cases with the outbreak genotype.

METHODS

Outbreak investigation

All Nevada and Arizona cases reported from May 2006 to August 2008 belonging to the genotype cluster or cases with a suspected epidemiologic link (based on similar demography and TB risk factors) to a patient belonging to the genotype cluster were included in the August 2008 outbreak investigation. An outbreak case was defined as either culture-confirmed TB with genotypic and epidemiologic links to another case in the cluster or clinically diagnosed TB (i.e., no isolate available for genotyping) with an epidemiologic link to a case in the cluster. Epidemiologic links were established based on known contact or shared location (e.g., house or jail cell) with a patient during the patient's infectious period.

The National Tuberculosis Surveillance System variables on demographics as well as clinical and social TB risk factors were abstracted from medical and public health records of cases included in the investigation.¹² Infectious periods were estimated only for adult patients, as transmission from people <10 years of age is unusual.¹³ In interviews with five available adult patients and parents of one pediatric patient, we verified abstracted data, ascertained information about locations frequented by patients, established epidemiologic links, and identified missed contacts. People who were reported as contacts by multiple patients or who spent any time with an outbreak patient were also interviewed to identify additional contacts. Because of difficulty in eliciting names of contacts, interviews with adult case patients, with their permission, included a review of their cell phone directories and recent usage for potential missed contacts.

Before the outbreak investigation, upon detection of each individual case, the SNHD had conducted a contact investigation to identify secondary cases or latent TB infection (LTBI) among exposed people.¹³ We compiled and analyzed the results of these investigations for each infectious outbreak case to assess the prevalence of LTBI, with the proportion of contacts having a tuberculin skin test result ≥ 5 millimeters (mm) as an indicator of possible recent TB transmission.¹³ To prevent further cases, exposed people with pending or incomplete TB evaluation and LTBI treatment were classified into high, medium, and low priority for follow-up based on the presence of TB risk factors, extent of exposure (i.e., intensity, duration, and frequency), and risk of developing TB disease.^{13,14} Additional contacts identified during the outbreak investigation interviews and chart reviews were added to the database and prioritized for evaluation.

Genotype surveillance

As of August 2008, the outbreak genotype (i.e., spoligotype 777776770000000 and MIRU 225325133324, nationally designated as PCR01556) was rare, representing 0.04% of all genotyped TB isolates in the U.S. Following the outbreak investigation in August 2008, the national distribution and epidemiology of the outbreak genotype continued to be monitored from September 2008 through June 2012 via the Tuberculosis Genotyping Information Management System.^{10,15} The purpose of this post-outbreak surveillance was to detect potential further outbreak-related cases in people not previously identified as contacts.¹⁶ Additional patients with TB isolates having the outbreak genotype in Nevada and Arizona were interviewed by local public health staff to determine whether they were epidemiologically linked to an outbreak patient.

RESULTS

Epidemiologic links

All eight cases included in the investigation met the outbreak case definition. Table 1 shows the characteristics of these patients. All patients were Hispanic, five were U.S.-born, and two were children aged <15 years. The most frequently reported social TB risk factor among adult patients was illicit substance use (primarily methamphetamine).

TB was transmitted among a social network of people reported to be engaged in the sale and use of methamphetamine (Figure 1). The index patient, whose infectious period lasted approximately two years due to treatment interruptions, served as the direct source of TB for six secondary cases, including his own child. Patient 5, who bought methamphetamine from the index patient, was the source for his son, patient 8. Patient 7, a brother of the index patient, was a resident of Arizona who was identified through the index patient's contact investigation. In addition to patient 7, patients 3 and 8 were identified with active TB disease as part of contact investigations; the remaining patients (i.e., patients 2, 4, 5, and 6) were missed contacts who were diagnosed with TB only after they presented with symptoms.

Index patient

A 26-year-old Mexico-born male was diagnosed with non-cavitary acid-fast bacilli (AFB) smear-positive, drug-susceptible pulmonary TB in April 2006 while detained in ICE custody. The patient was asymptomatic but discovered to have TB disease during routine intake screening. The patient's TB risk factors included substance abuse: he consumed alcohol heavily and also

Table 1. Characteristics of TB outbreak patients in Nevada and Arizona, May 2006–August 2008 (n=8)

Characteristics	N (percent)
Demographic	
Foreign-born (Mexico)	3 (38)
Hispanic	8 (100)
Male	4 (50)
Children aged <15 years	2 (25)
Median age (in years) (range)	25 (4 months–37 years)
Clinical	
Pulmonary disease only	7 (88)
Both extrapulmonary and pulmonary disease ^a	1 (13)
Sputum AFB smear-positive ^b	5 (63)
Sputum culture-positive	6 (75)
Cavity on chest radiograph	3 (38)
TB symptoms present	6 (75)
Median infectious period (in months) (range) ^c	8.5 (0.5–28.0)
Medical and social TB risk factors	
Diabetes	1 (13)
HIV infection ^d	0 (0)
Drug use within one year of TB diagnosis ^e	5 (63)
Excess alcohol use within one year of TB diagnosis	3 (38)
Incarceration at TB diagnosis	2 (25)
Homeless within one year of TB diagnosis	0 (0)

^aExtrapulmonary disease site was meningeal in a pediatric case.

^bOne adult patient had negative results for sputum AFB and two patients (both children <5 years of age) had no sputum specimens.

^cTwo pediatric cases were excluded from infectious period estimation.

^dOf six adult patients and one pediatric patient who were tested for HIV infection.

^eAll five patients used methamphetamine. No injection drug use was noted.

TB = tuberculosis

AFB = acid-fast bacilli

HIV = human immunodeficiency virus

used marijuana, cocaine, and methamphetamine. He had an extensive social network of family and friends across the U.S.-Mexico border, some of whom reported being engaged in the sale or use of methamphetamine with the patient. He had a history of several deportations to Mexico with subsequent reentry into the U.S.

The index patient started TB treatment at a local detention facility while in ICE custody but was deported four weeks later (i.e., before the minimum six months needed for TB treatment completion). Although he was enrolled before deportation in Cure TB, a U.S. and Mexico binational TB program that coordinates care across the U.S.-Mexico border,¹⁷ he provided a false address in Mexico and was thus lost to follow-up.

Figure 1. Epidemiologic links of TB outbreak patients in Nevada and Arizona, May 2006–August 2008 (n=8)

Note: The relationship to the index patient and date (month and year) of TB diagnosis is indicated for each patient.
 TB = tuberculosis

Returning to the U.S. several times during the next two years, the patient's worsening TB symptoms prompted him to seek care several times at hospitals in Nevada from December 2007 through May 2008, but each time under different aliases, and each time leaving prematurely against doctor's orders, evading follow-up with public health staff for TB management. The SNHD staff went to extensive efforts to locate the patient by sending alerts to numerous hospitals, health clinics, and law enforcement agencies. Finally, while traveling to Arizona with his brother in May 2008, severe TB symptoms caused him to be rehospitalized, again using an alias. However, this time he was recognized by the hospital staff because of alerts sent out by Arizona Public Health Services based on a notification it received by SNHD, which had learned of the patient's travel to Arizona through one of his contacts. At the hospital, his sputum was still AFB smear-positive, and chest radiograph showed progression of TB disease, with new cavitory lesions. Sputum cultures grew *Mycobacterium tuberculosis*, still susceptible to all first-line TB medications, and the genotype was also unchanged. The patient's TB treatment was reinstituted, and he completed treatment under an Arizona state public health court order that mandated treatment to prevent TB spread to others.

Contact investigation and prevention of additional cases

Prioritization of contacts for TB screening is shown in Figure 2. Contacts with the highest risk of TB infection (e.g., household contact) or with the highest risk of progression to TB disease (e.g., human immunodeficiency virus infection) were classified as high priority. Contacts ascertained through cell phones of three of the five adult patients, who readily granted permission to do so, were categorized as low priority because of their unknown extent of exposure. The outcome of contact investigations of the five AFB smear-positive cases, based on prioritization for screening, is shown in Table 2. Among all contacts, including ones with newly diagnosed LTBI, those categorized as high priority for evaluation had the highest percentage of LTBI (51.2%), followed by low-priority (30.8%) and medium-priority (15.6%) contacts.

Of the 130 contacts with LTBI, 71 (54.6%) started treatment and, of those 71 contacts, 52 (73.2%) completed treatment with isoniazid for nine months. Multiple incentives and enablers were used to achieve LTBI treatment completion and prevent additional cases, including \$10 gift cards for grocery stores or to purchase gasoline or baby items. On multiple occasions, TB staff delivered LTBI medication to contacts at their workplaces to prevent missed refills.

Figure 2. Prioritization of contacts of outbreak patients for TB screening during an outbreak investigation: Nevada, August 2008

<i>High priority</i>	<i>Medium priority</i>	<i>Low priority</i>
<ul style="list-style-type: none"> Household contact Younger than 5 years of age Diabetes HIV infection Immunosuppressed (non-HIV) Health-care workers Congregate setting contact (inmates who shared cell) 	<ul style="list-style-type: none"> Substance abuse^a History of incarceration Congregate setting contact (classmates, coworkers, other inmates, or jail officers) 	<ul style="list-style-type: none"> Contacts identified via patient's cell phone (without additional identifying or locating information) Casual encounter

^aIllicit drugs or excessive alcohol use within one year of diagnosis

TB = tuberculosis

HIV = human immunodeficiency virus

Post-investigation genotype surveillance

From September 2008 through June 2012, 23 additional cases with the outbreak genotype were reported in the U.S., including six cases in Nevada and two cases in Arizona. None of these eight cases (from Nevada and Arizona) had previously been identified by public health authorities as contacts of outbreak cases. Of the six Nevada cases, two cases (diagnosed in July 2009 and January 2012) were found to be linked to the

outbreak through self-reported close contact with the index patient. Although epidemiologic links could not be established for the four remaining cases, all four cases reported a history of methamphetamine use. Of the two cases in Arizona, only one patient, who was diagnosed with TB disease in June 2011 while incarcerated in Arizona, and who abused illicit substances and had a history of multiple incarcerations, was linked to the outbreak. This linkage was based on self-reported

Table 2. Contact investigation results of five sputum smear-positive TB cases in Nevada by contact prioritization, May 2006–August 2008

<i>Characteristic</i>	<i>All contacts N (percent)</i>	<i>High priority N (percent)</i>	<i>Medium priority N (percent)</i>	<i>Low priority N (percent)</i>
Total contacts	667 (100.0)	107 (16.0)	500 (75.0)	60 (9.0)
Contacts evaluated ^a	590 (88.5)	84 (78.5)	454 (90.8)	52 (86.7)
Prior diagnosis of LTBI (baseline positive TST) ^b	19 (3.2)	4 (4.8)	14 (3.1)	1 (1.9)
Positive TST result (≥ 5 mm) with unknown baseline ^c	108 (18.3)	38 (45.2)	55 (12.1)	15 (28.9)
Positive TST result (≥ 5 mm) with negative baseline ^c	3 (0.5)	1 (1.2)	2 (0.4)	0 (0.0)
Total with LTBI ^d	130 (22.0)	43 (51.2)	71 (15.6)	16 (30.8)
Initiated LTBI treatment	71 (54.6)	28 (65.1)	37 (52.1)	6 (37.5)
Completed treatment	52 (73.2)	19 (67.9)	29 (78.4)	4 (66.7)
Negative TST ^e	414 (70.2)	40 (47.6)	341 (75.1)	33 (63.5)
Incomplete TST evaluation ^e	46 (7.8)	1 (1.2)	42 (9.3)	3 (5.8)

^aContact evaluation entailed symptom review, TST (performed twice, if the first TST was placed <8 weeks since end of TB exposure) if no previous history of LTBI, and chest radiograph if indicated.

^bPeople with a history of LTBI based on a positive baseline TST result

^cTST placed ≥ 8 weeks after end of TB exposure

^dSum of all contacts with a positive TST result

^eAll had negative TST results; however, TST after eight weeks of exposure was not performed.

TB = tuberculosis

LTBI = latent tuberculosis infection

TST = tuberculin skin test

mm = millimeter

relationships with people associated with the index patient and suspected involvement with methamphetamine use and distribution.

In addition to the incentives and enablers, such as those used with LTBI patients, TB patients diagnosed with the outbreak genotype after the outbreak investigation were given pay-as-you-go cell phones with 100 prepaid minutes as a reward for treatment completion, which was achieved by all patients.

DISCUSSION

This outbreak highlights the potential for extensive TB transmission from incomplete treatment of TB disease among people diagnosed in ICE custody. Although the health department and Cure TB were appropriately engaged to facilitate continuity of care, the index patient was lost to follow-up for two years. During this time, he reportedly remained engaged in the use and sale of methamphetamine and evaded medical treatment, ultimately requiring a court order to complete TB treatment. During his prolonged infectious period, seven additional TB cases, representing two generations spread, occurred in people who were part of his methamphetamine network or with whom he had social ties.

Each year, thousands of foreign nationals without legal status in the U.S. are detained; in 2010, approximately 363,000 people were detained by ICE.¹⁸ In 2004 and 2005, respectively, 76 and 142 cases of TB were reported among ICE detainees, representing estimated case rates (of 83 and 122/100,000 people)⁶ that were 4–6 times higher than the overall case rate among foreign-born people in the U.S.,¹² highlighting the importance of effective TB control in this population. Most forms of TB require 6–9 months of treatment,¹⁹ but ICE detainees with TB disease receive an average of 2.5 months (83 days)⁶ of treatment and, before release or deportation, are given a two-week supply of medications, along with education about self-administration during the transition period in the receiving country.²⁰ However, if lost to follow-up, these cases represent missed opportunities in TB control, because the patients involved may be at increased risk for TB-related morbidity, including developing drug-resistant TB because of treatment interruptions⁸ and, as this outbreak demonstrated, for spreading the disease.

Coordination of care, not only in the receiving country if the patient is deported but also within the U.S. if the patient is released, is one of the major challenges to treatment completion among ICE detainees.^{6,9} Discharge planning has been identified as one of the weakest areas of collaboration between public health

and correctional facilities, attributed in large part to a lack of advance knowledge of release time.²¹ In 2002, the Advisory Council for the Elimination of TB recommended the development of policies and protocols to allow for better communication and coordination among agencies to ensure treatment completion.^{5,8} In the same year, ICE adopted a policy of short-term medical holds of people with TB disease to make arrangements for continuity of care through programs such as Cure TB, TB Net, and the Binational Card Project, which facilitate TB referrals and follow-up of patients who are mobile between the U.S. and other countries.^{9,22} In addition, measures such as “meet and greet,” where national TB program staff members of the receiving country meet the deportee at the airport or border crossing, have been promoted as best practices to ensure continuity of care.²⁰ However, based on a preliminary assessment of outcomes of TB patients in ICE custody, an estimated 18% of patients enrolled in such programs are lost to follow-up.²³ The index patient reported in this outbreak was one such case, exemplifying that people engaged in the sale or use of illicit substances are a very mobile group at particularly high risk for loss to follow-up and failure to complete TB treatment.^{5,24}

The index patient’s prolonged infectious period, resulting primarily from treatment nonadherence but also a delay in seeking medical care, was the main factor that fueled this outbreak. Delayed diagnosis is a well-known risk factor for TB transmission,^{14,25} and it has previously contributed to at least two known TB outbreaks involving undocumented people.^{26,27} Undocumented foreign-born people are more likely than documented people to delay seeking care for symptoms,²⁸ thereby prolonging the infectious period when TB can be transmitted to others. Socioeconomic factors (e.g., cost, unemployment, and language barrier) and fear of immigration authorities have been associated with such a delay.^{28,29} In this outbreak, the involvement of substance abuse, another well-recognized risk factor for TB transmission,^{14,30–32} likely exacerbated fear of authorities among patients, contributing to delayed diagnosis and treatment nonadherence. Reducing diagnostic delays, through access to medical care without fear of legal repercussions, has been recognized to be of public health importance.³³

Incomplete contact investigations also contributed to this outbreak. Both undocumented status and illicit substances likely limited the completeness of contact investigation, a key U.S. TB control strategy to find and prevent additional TB cases (i.e., through treatment of LTBI).¹ Fear of deportation, arrest, or repercussions from other members of the drug network seemingly

made some individuals reluctant to share contact information of people exposed to TB. As a result, most of the outbreak patients were not found during contact investigations but, rather, as a result of symptoms causing them to seek medical attention. In fact, contact investigations yielded an overall LTBI rate of 22%, a percentage in the low end of the expected range of 20%–30%, suggesting that relatively lower-risk contacts whose names were easier to elicit had been found and evaluated. Because actual names of contacts were difficult to elicit, we resorted to evaluating people identified through the patients' cell phones. Interestingly, we found that a higher percentage of these contacts had LTBI compared with medium-priority contacts, suggesting either closer recent contact with infectious TB or a higher baseline prevalence of LTBI than anticipated. This approach of finding close contacts might be useful in other outbreaks involving hard-to-reach populations, in whom name-based contact investigations are known to be challenging.^{13,34}

Approximately 5%–10% of people with LTBI develop TB disease and represent future cases that could have been prevented.¹³ Prospective surveillance of genotyped cases indeed detected additional cases linked to this outbreak. During the two years after the peak of the outbreak, six cases with the outbreak genotype emerged in Nevada and Arizona, none of which were among the known contacts. Awareness of these cases prompted health department staff to search for linkages to the outbreak through interviews and implement control measures such as appropriate incentives and enablers to achieve treatment completion for both TB and LTBI. Other outbreaks have also demonstrated the utility of TB genotyping data in defining the epidemiology and scope of the outbreak^{30,32,35} and as an important surveillance tool to monitor possible ongoing or recurrent transmission after an outbreak investigation.¹⁶

CONCLUSIONS

This outbreak, along with other documented instances of TB transmission related to incomplete treatment among deportees, demonstrates the need for extra attentiveness and strong multiagency coordination in TB management of people released from custody before treatment completion.^{5,8} When such people are engaged in the sale or use of illicit substances, even more thorough discharge planning and active continuity-of-care measures are recommended to ensure TB treatment completion.

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