

Southern Nevada Health District
Maternal Tuberculosis Investigation Report
December 16, 2015

Introduction

The Health District Tuberculosis (TB) Program and Office of Epidemiology have conducted a TB contact investigation related to the postmortem TB diagnosis in a Clark County resident (Patient A) who delivered premature twins (Patients B & C) two-months before her death in July, 2013. The twins remained in the Neonatal Intensive Care Unit (NICU) until their deaths (in June and August). In accordance with the CDC's prioritized strategies to prevent and control TB in the United States, [1] the objectives of this TB contact investigation were the following:

1. To promptly detect and report persons who have contracted TB; and
2. To protect close contacts of patients with contagious TB from contracting TB infection and disease, by identifying and treating people with active TB disease and identifying and offering treatment to people with evidence of noninfectious Latent TB Infection (LTBI).

Methods

Contact Investigation(s)

The Health District identified, prioritized, and evaluated personal contacts of Patient A for TB (family, friends, coworkers, church-goers, etc.) and supported evaluation of contacts in healthcare facilities (inpatient and outpatient settings). As a proxy for determining the risk of exposure of other NICU infants who had resided in the unit with the twins, we tested healthcare workers (HCWs) in the NICU. If no evidence of transmission to HCWs was found it is reasonable to indicate that no transmission to NICU infants had occurred, as the HCWs would have had closer contact with Patients A—C than other NICU infants. Because it can take 8-10 weeks for tests to reveal TB infection after someone has been exposed to a person with infectious TB disease, contacts were retested >8 weeks of last contact with the TB patients if their first test was performed <8 weeks of last contact.

After test results indicated that transmission to NICU staff members had occurred, the investigation plan was expanded to include an evaluation of infants who resided in the Level 3 NICU (see Appendix for hospital NICU floor plan) at times when infectious persons could have been present. The Health District also evaluated individuals who visited those infants in the NICU. Evaluation of TB infection or disease is different for infants than for adults: Since TB tests can be inaccurate in infants, the Health District consulted experts in pediatric TB, who recommended that evaluations occur immediately (Round 1), at 6 months of age (adjusted for prematurity when applicable; Round 2), and at 1 year of age (adjusted for prematurity; Round 3). Tests are more

accurate after 6 months of age. Depending on the age of the infant during the initial evaluation, up to three rounds of evaluations might be needed. Evaluation of an infant for TB should include a TST, chest radiograph (chest x-ray), and physical examination.

A second TB contact investigation was initiated upon identifying that one of the NICU staff members had developed active (infectious) TB disease. The Health District identified contacts of the newly identified TB case-patient from among hospitalized adult patients, hospitalized infant patients, and HCWs. The Health District prioritized their testing based on their exposure to the case-patient. For the purposes of this report, results of testing for both investigations are combined.

Identifying Active TB Disease Case-Patients / Genotyping

Contacts with clinical, radiographic, or microbiologic evidence of TB disease were considered to have active TB disease and appropriate treatment was initiated. Contacts with indications of infectious TB disease resulted in initiation of new contact investigations to identify their contacts during their infectious periods. When available, *Mycobacterium* isolates were further characterized through genotyping, a technique used to analyze the genetic material (e.g., DNA) (For more information, see: <http://www.cdc.gov/TB/publications/l'actsheets/statistics/genotyping.htm>).

A genotypic match between TB specimens identified in this cluster was considered indicative of cluster-associated transmission.

The Health District defined active TB cases as:

- **Confirmed** — TB disease with G03483 genotype reported in a Clark County, Nevada, resident during January 1, 2013—December 10, 2013.
- **Probable** — TB disease with unknown genotype reported in a Clark County, Nevada, resident during January 1, 2013—December 10, 2013, where an epidemiologic linkage to one of the active cases identified through this investigation exists.
- **Suspect** — suspected TB disease (clinical indications of TB disease, final diagnosis pending) reported in a Clark County, Nevada, resident during January 1, 2013—December 10, 2013, where an epidemiologic linkage to one of the active cases identified through this investigation exists.

Identifying Persons with Indications of LTBI

A contact with LTBI is defined as a person who had a positive test (tuberculin skin test (TST), Quantiferon-TB tests (QFT), or T-SPOT test, but is asymptomatic and had a negative chest radiograph. The Health District recommended treatment to persons diagnosed with LTBI.

Definitions

- **Latent TB infection (LTBI)**, also referred to as "TB infection," is a condition in which an individual is infected with the bacterium *Mycobacterium tuberculosis*, or other, closely related species of

Mycobacterium, but does not currently have active disease. Even if infected, people without active disease are not infectious (i.e., they cannot spread the disease). However, they are at risk of their infections progressing to tuberculosis disease, thus LTBI treatment is recommended. Persons are diagnosed with LTBI when they have positive tests for infection with *M. tuberculosis* (which can include a tuberculin skin test (TST), Quantiferon-TB tests (QFT), or a T-SPOT test), but they are asymptomatic and have negative chest radiographs.

- **TB disease**, also referred to as "active TB" or "active TB disease," indicates that the disease caused by *M. tuberculosis* is clinically active. Patients with TB disease generally have symptoms of disease which can include, but are not limited to, unexplained weight loss, fever, cough, night sweats, and shortness of breath. Chest radiograph or a positive culture result for *M. tuberculosis* or a closely related species is an indication of TB disease.
- **Infectious TB disease** refers to TB disease of the lungs or larynx; persons with infectious TB have the potential to transmit *M. tuberculosis* to other persons.

Results

Contact Investigation

Results of the overall TB evaluations performed as part of this contact investigation are shown below (Table).

Adults and children >5 yrs of age: Of 964 persons identified, 893 (92.6%) were found needing evaluation, 1 (0.1%) was diagnosed with active disease, 154 (17.3%) had LTBI, 678 (75.9%) had negative tests, 7 (0.8%) were deceased prior to evaluation, 12 (1.3%) case records were sent out of jurisdiction, 41 (4.6%) had incomplete evaluations. Evaluations may be incomplete as a result of persons refusing testing, persons not completing all testing needed to complete evaluation, or were unable to locate for evaluation.

Children 5 years and under: We identified a total of 239 children and infants. Of these infants and children, 197 (82.7%) were found needing evaluation for possible TB exposure. Further, 6 (3%) contacts were found to be residents of another county and/or state. The Health District appropriately notified their respective health departments of the TB exposure and evaluation recommendations. A total of 191 cases residing in Clark County were identified as needing evaluation. Evaluation for TB was recommended, but not required. To be considered complete, the patient must have a TST, chest x-ray, and physical exam documented, for up to 3 rounds of testing, as indicated. Of the contacts tested, 3 (1.6%) were diagnosed with active disease, 3 (1.6%) had LTBI, 73 (38%) had negative tests, 2 (1.1%) were deceased prior to

evaluation, 110 (57.6%) had incomplete evaluations. Reasons for incomplete evaluations include parental refusal of some or all parts of the evaluation, incomplete documentation (physical examination completed, but documentation not sent to SNHD), loss to follow-up (did not return to provider for TST reading; did not return for follow-up chest x-ray); or inability to contact parents (no accurate contact information). A total of 58 (79.5%) contacts had completed their three Round TST TB evaluations TST, chest x-ray, and physical exam. The remaining 15 cases reported as negative did not have documented physical exam. All three LTBI cases were offered and accepted the recommended LTBI treatment.

Table. TB Evaluations outcomes for Persons Identified during the investigation

Type of contact	TB Evaluation							Not testing needed	All
	COMPLETE				INCOMPLETE				
	ACTIVE TB	LTBI	NEGATIVE	NTN*	DECEASED	OOJ**	OTHER		
Healthcare Worker	1	91	295	2	.	8	22	.	419
Hospitalized/Outpatient Noninfant	.	4	31	.	8	2	5	.	50
Person Contacts to Patient A	3	20	139	1	1	5	92	35	296
Visitors of Hospitalized Patients	.	42	286	66	.	3	32	9	438
All	4	157	751	69	9	18	151	44	1203

* NTN- No testing needed

** OOJ- Out of jurisdiction

Identifying Active TB Disease Case-Patients / Genotyping

To date, a total of five cases of active TB disease have been identified through contact investigation activities, including the index patient's two infants. An epidemic curve of the cluster is presented (Figure 1), showing three probable cases (Patient C — the twin who died before Patient A was diagnosed; Patient A — maternal patient; Patient E — a personal contact of Patient A), and two confirmed cases (Patient B — twin who survived until August; and Patient D — a healthcare worker in the NICU who could have been exposed to Patients A, B, or C).

Two patients (Patient B and Patient D) identified through contact investigation activities were found to have microbiologic evidence of active TB disease. Sputum culture specimens of these two patients were further characterized through genotyping (G03483) with matching spoligotype patterns consistent with *Mycobacterium bovis*. *M. bovis* belongs to the *M. tuberculosis* complex (MTBC) that comprises the closely related human pathogens *M. tuberculosis* and *M. africanum*, all of which can cause similar TB disease in humans.

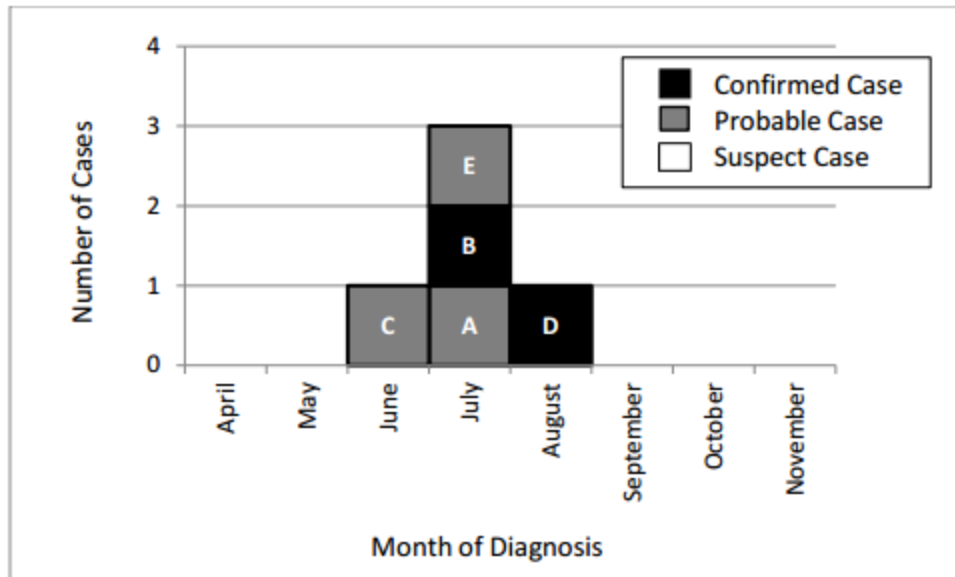


Figure 1. Epidemic Curve of Tuberculosis Disease Cluster Cases — Clark County, Nevada, 2013

Treatment of Persons with TB Disease and LTBI

Of those evaluated for TB in the investigation, the Health District identified and initiated treatment on 55 individuals: 2 with active TB disease completed their treatment, 53 LTBI accepted treatment, 95 high priority cases under 5 years old were offered presumptive treatment and 7 accepted treatment (but who have no evidence of infection). The identification and treatment of persons with active TB disease and those with indications of LTBI infection were top priorities in TB contact investigations as a part of the TB control strategy in the U.S.

Discussion

- TB transmission occurred in one Clark County hospital, including to HCWs.
- It is extremely important in any setting for physicians to make a prompt TB diagnosis, initiate appropriate infection control procedures for preventing the spread of TB disease, and rapidly identify and, as necessary, treat contacts to active TB patients.
- The Health District initial recommendation **not** to perform TB testing on infants who resided in the NICU concurrently with the twins was twofold: 1) transmission of TB from one infant to another infant is extremely rare [2,3], and 2) our belief that contact between the mother and infants in the NICU other than her own was minimal. The Health District findings indicated that disease transmission to some hospital staff members did occur within the NICU. As a result the Health District sought further consultation with experts in pediatric TB. Because the risk of TB transmission to infants was low, but greater than originally presumed, we initiated TB evaluations on NICU infants and their visitors.
- *M. bovis*, a member of the bacterium that causes TB disease, accounts for

approximately 1% of all genotyped cases of TB in Nevada. *M. bovis* is found in cattle or other animals, and people are most commonly infected by eating or drinking contaminated, unpasteurized dairy products (such as milk and soft cheeses like queso fresco) [4]. As demonstrated in this investigation, *M. bovis* can also be transmitted person-to-person. The specific source, route, or date Patient A became infected is unknown. The Health District did not identify a human case-patient who could have been the source of Patient A's TB disease. Because Patient C's strain appears indicative of presumptive *M. bovis* and Patient A's family members reported that she had consumed unpasteurized dairy products from Mexico, it is possible that Patient A became infected through ingestion and not as a result of contact to another human with TB disease. Consumption of unpasteurized dairy products carries multiple health risks. We encourage providers to educate their patients on the risks of consuming unpasteurized dairy products. More information can be found at:

<http://www.Fda.gov/ForConsumers/ConsumerUpdates/ucm122062.htm>

- The Health District continues to work with hospitals and healthcare providers to ensure prompt completion of TB screening for healthcare workers having had contact to any active case of TB.
- The Health District will continue to ensure that any person for whom treatment is indicated is offered treatment according to CDC's TB treatment guidelines.

Recommendations:

- The Health District recommends prompt TB evaluations on children with possible TB exposure. We encourage parents of children under 5 years of age to ensure that all evaluations are completed (TB skin tests, chest x-rays, physical examinations, and follow-up testing as needed) and encourage providers to report all positive and negative test results to the Health District (TB Program secure fax 702-633-0975).
- Any cluster or outbreak of TB emphasizes the importance of prompt physician TB diagnosis and initiation of appropriate infection control procedures for preventing the spread of TB disease. Diagnosing TB earlier in a patient's clinical course helps ensure fewer contacts are exposed and fewer people develop latent or active TB. The CDC has resources for providers including a fact sheet that describes "when to suspect TB in a patient" and "how to evaluate persons suspected of having TB" <http://www.cdc.gov/tb/publications/factsheets/testing/diagnosis.htm>. The Health District recommends and encourages providers to review this information and remain proactive in the effort to support TB elimination through testing and diagnosis.

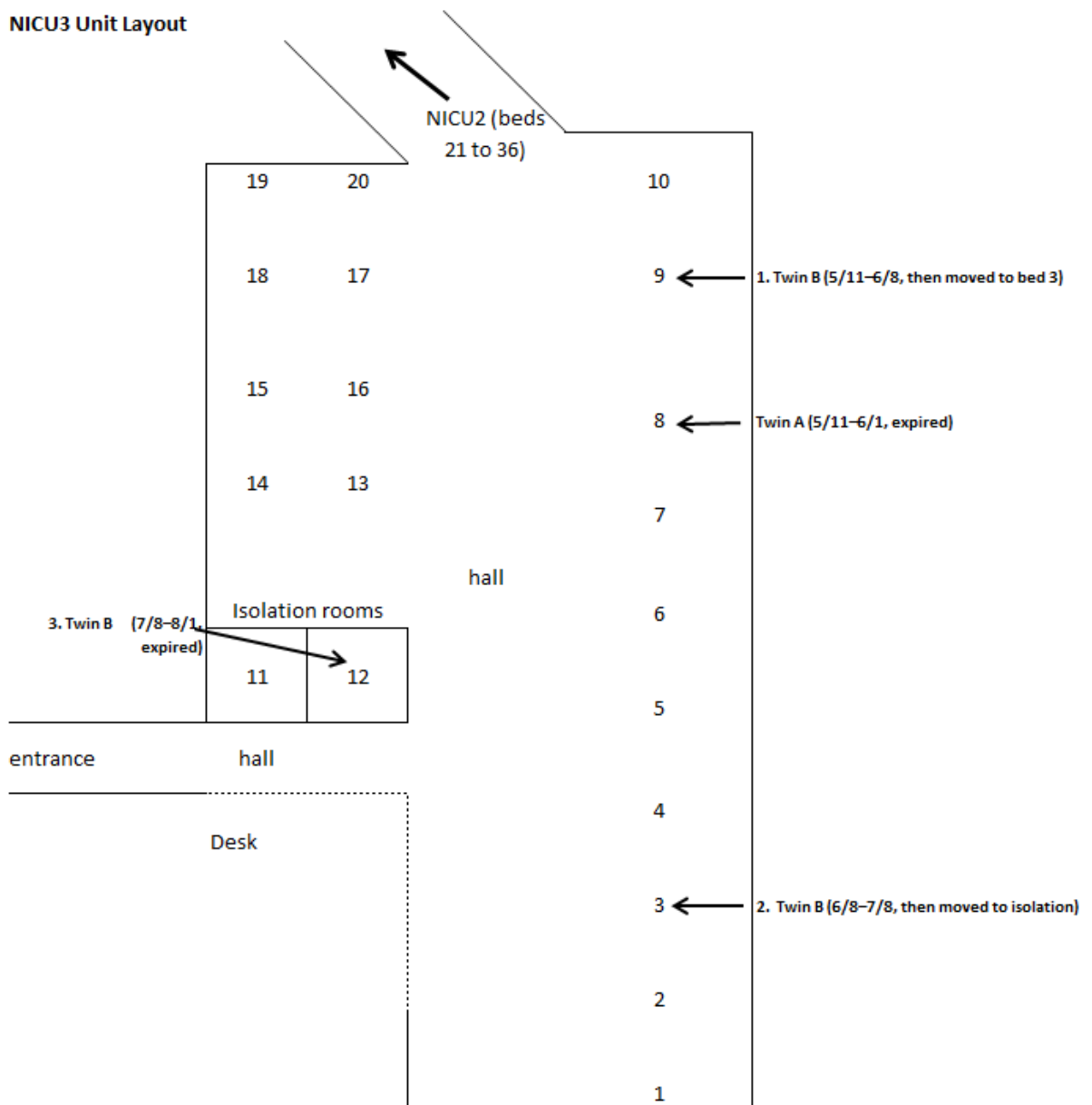
References

- 1) CDC. Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MM WR 2005;54(RR12):1-81
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm>
- 2) Lucia H. Lee, Charles M. LeVea, and Paul S. Graman. Congenital Tuberculosis in a Neonatal Intensive Care Unit: Case Report, Epidemiological Investigation, and Management of Exposures. *Clinical Infectious Diseases*. 1998;27:474–7
- 3) Maryanne Crockett, Susan M. King, Ian Kitai, Frances Jamieson, Susan Richardson, Patricia Malloy, Barbara Yaffe, Donna Reynolds, Jonathan Hellmann, Ernest Cutz, and Anne Matlow. Nosocomial Transmission of Congenital Tuberculosis in a Neonatal Intensive Care Unit. *Clinical Infectious Diseases*. 2004; 39:1719–23
- 4) CDC. *Mycobacterium bovis* (Bovine Tuberculosis) in Humans. Fact Sheet. Accessed on December 10, 2013 from
<http://www.cdc.gov/tb/publications/factsheets/general/mbovis.htm>

Appendix

Map of NICU3 Including Locations of Twin A and Twin B

NICU3 Unit Layout



NOTE: The NICU has no enclosed rooms except 2 isolation rooms. Incubators are in open spaces.