Southern Nevada Health District
Maternal TB Investigation – Interim Report #2
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Background Update

(This is an update. Please refer to Brief Interim Report #1 for background information.)

The Southern Nevada Health District TB Program and Office of Epidemiology have been conducting 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 NICU until their deaths (in June and August). Our goals in conducting this TB contact investigation follow the CDC's prioritized strategies to prevent and control TB in the United States[1]:

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).

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 for 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.

Methods

Contact Investigation(s)

We 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 neonatal intensive care unit (NICU). If no evidence of transmission to HCWs was found, we believed that would reasonably 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 the first test was performed <8 weeks of last contact.

After test results indicated that transmission to NICU staff members had occurred, we expanded our plan to include the evaluation of infants who resided in the Level 3 NICU at times when infectious persons could have been present. We also evaluated people who visited those infants in the NICU. Evaluation of TB infection or disease is different for infants than for adults.[3] Because TB tests can be inaccurate in infants, we 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. We identified contacts of the newly identified TB case-patient from among hospitalized adult patients, hospitalized infant patients, and co-workers (HCW). We 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/factsheets/statistics/genotyping.htm). A genotypic match

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

We 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. We recommended treatment to persons diagnosed with LTBI.

Results

Contact Investigation (as of December 10, 2013)
Results of noninfant TB evaluations performed as part of this contact investigation are shown below (Table 1). Of 977 persons identified as needing evaluation, 735 (75%) had negative tests, 2 (0%) were diagnosed with active disease, 59 (6%) had indications of LTBI, and 181 (19%) had incomplete evaluations. Evaluations may be incomplete as a result of persons refusing testing, persons not completing all testing needing to complete evaluation, or inaccurate contact information.

Of the HCWs found to have active TB disease (1) or LTBI (21), 10 (45%) were staff members primarily working in the NICU. Because these results indicated that transmission occurred to NICU staff members, we determined the risk of TB transmission to infants residing in the NICU and their visitors was still low, but greater than was originally presumed. This information resulted in our new recommendation for TB evaluation for NICU infants and their visitors, and preventive treatment for infants.

We identified 142 infants as needing evaluation for possible TB exposure including 6 (4%) residents of another county and/or state, for which SNHD appropriately notified their respective health departments of their TB exposure and evaluation recommendations. A total of 136 infants residing in Clark County were identified as needing evaluation. Evaluation for TB was recommended, but not required. To date, evaluations for many infants remain incomplete. To be considered complete, the infant must have a TST, chest x-ray, and physical exam documented, for up to 3 rounds of testing, as indicated. Of the infants tested to date, 119 (88%) had TST, 89 (65%) had chest x-ray, and 105 (78%) had physical exams. All TSTs (117) and physical exams (105) completed to date are negative for TB. Several infants require repeat chest x-rays due to inconclusive readings; results are pending. 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 (infant did not return to provider for TST reading; infant did not return for follow-up chest x-ray); or inability to contact parents (no accurate contact information).

A total of 34 (25%) infants have completed their Round 1 TB evaluations including the recommended TST, chest x-ray, and physical exam. All had no indications of TB and were offered preventive treatment per recommendations by pediatric TB experts. To date, 7 infants are on preventive treatment.

Table 1. Noninfant TB Evaluations for Persons Identified as Needing Testing (data as of December 10, 2013)

		TB Evaluation							
		Complete						Incomplete	
		Negative		Active TB Disease		LTBI			
Type of Contact	Total^	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Personal Contacts to Patient A	114	94	(82)	1	(1)	15	(13)	4	(4)
Healthcare Workers	407	340	(84)	1	(0)	21	(5)	45	(11)
Hospitalized / Outpatient Noninfant Patients	41	19	(46)	0	(0)	0	(0)	22	(54)
Visitors of Hospitalized Patients	415	282	(68)	0	(0)	23	(6)	110	(27)
TOTAL	977	735	(75)	2	(0)	59	(6)	181	(19)

^Excluding 24 identified as residents of other states; we notified their state health departments of TB exposure and recommendations for evaluation

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), 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; 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.

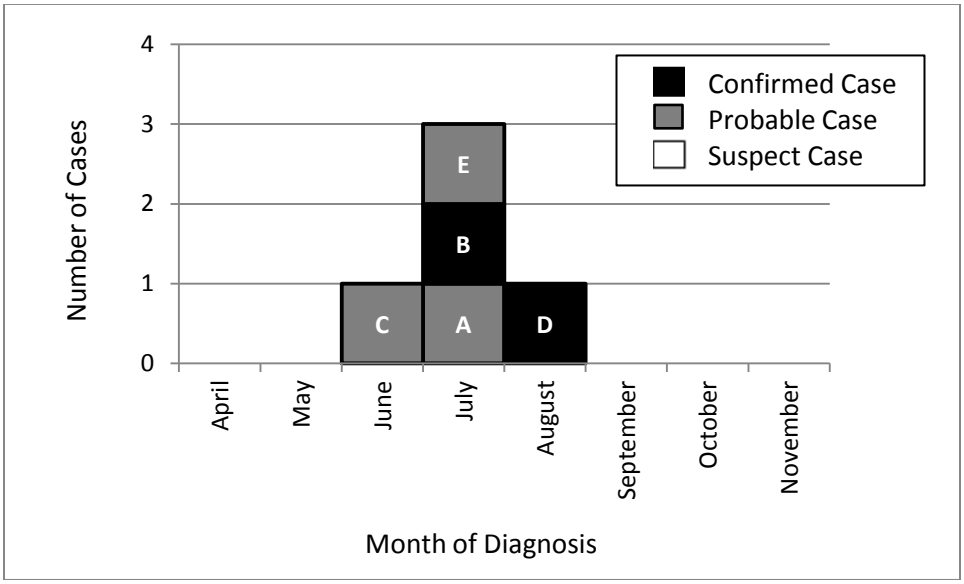

Figure. Epidemic Curve of Tuberculosis Disease Cluster Cases — Clark County, Nevada, 2013
(data as of December 10, 2013)

Treatment of Persons with TB Disease and LTBI
Of those evaluated for TB in our investigation, SNHD has identified and initiated treatment on 48 individuals (Table 2): 2 with active TB disease, 39 with indications of LTBI disease, and 7 infants on preventive TB 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 are top priorities in TB contact investigations as a part of the TB control strategy in the U.S.

Table 2. Contacts Currently Undergoing Treatment for TB (data as of December 10, 2013)

Type of Contact	Active TB Disease*	LTBI†	Preventive^	
Personal Contacts to Patient A	1/1 (100%)	14/15 (93%)	N/A	
Healthcare Workers	1/1 (100%)	14/21 (67%)	N/A	
Hospitalized Noninfant Patients	0	0	N/A	
Visitors of Hospitalized Patients	0	12/23 (52%)	N/A	
Hospitalized Infant Patients (NICU)	0	0	7	
TOTAL	2	39	7	**48**

N/A - Not applicable

*Treatment for Active TB Disease is required.

†Treatment for LTBI was recommended, but not required.

^Preventive treatment was recommended for infants regardless of negative evaluation results, but not required.

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 treat contacts to active TB patients.
- Our initial recommendation **not** to perform TB testing on infants who resided in the NICU concurrently with the twins was based on two main reasons: 1) our understanding that transmission of TB from one infant to another infant is extremely rare, and 2) our belief that contact between the mother and infants in the NICU other than her own was minimal. However, when our findings indicated that disease transmission to some hospital staff members did occur within the NICU, we sought further consultation with experts in pediatric TB. Because the risk of TB transmission to infants was low, but greater than was 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).[3] As demonstrated in this investigation, *M. bovis* can also be transmitted person-to-person. We will never be able to identify the specific source, route, or date Patient A became infected. We 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

- SNHD 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.
- SNHD will continue to ensure that any person for whom treatment is indicated is offered treatment according to CDC's TB treatment guidelines.
- Finally, SNHD will continue this contact investigation to attempt to identify additional persons who could have been exposed to TB.

Recommendations:

- After consulting with experts in pediatric TB, SNHD recommends prompt TB evaluations on infants with possible TB exposure as part of this contact investigation. We encourage parents of infants to ensure that all evaluations are completed (TB skin tests, chest x-rays, physical examinations, and follow-up testing as needed) and encourage the infants' providers to report all results to SNHD (TB Program secure fax 702-633-0975).
- We also encourage parents and providers to ensure the completion of Round 2 and Round 3 TB evaluations. Thorough evaluation is important because infants can have nonspecific presentations of TB, the TB tests can be falsely negative in infants, and, if infected, infants can have rapid and severe disease progression.
- SNHD distributed a technical bulletin to providers regarding Pediatric TB on October 7, 2013. It included information on the differences between pediatric TB and adult TB clinical presentation, screening recommendations for infants with possible TB exposure, and preventive treatment recommendations for pediatric patients associated with this TB investigation. The document can be found at: http://southernnevadahealthdistrict.org/download/epi/tb-pediatric-tuberculosis-100713.pdf
- Any cluster or outbreak of TB emphasizes the importance of prompt physician TB diagnosis and initiation of appropriate infection control procedures for preventing 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. We encourage providers to review this information and remain proactive in efforts to support TB elimination through TB 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. MMWR 2005;54(RR12):1-81. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm
2. Southern Nevada Health District. Pediatric TB (Technical Bulletin). Released on October, 7, 2013. Accessible from:

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3. 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