

Pediatric Tuberculosis

Current Situation

The Southern Nevada Health District (SNHD) is investigating potential tuberculosis (TB) exposures to infants and others at Summerlin Hospital. Families of infants admitted to the Level III NICU between May 11 and August 8, 2013 are being contacted and advised to be evaluated by their health care providers. SNHD is offering testing and treatment to infants exposed in the NICU and testing for their family members.

Pediatric Tuberculosis (TB)

If infected, infants and young children are more likely than adults to develop active TB disease, which can occur in a matter of weeks or months. In addition, the presentation of TB in children is often distinctly different than that in adults. Young children suffer more extrapulmonary and disseminated TB than adults. Very young children are at particular risk of acute hematogenous dissemination (miliary disease) and meningitis. Children frequently have more subtle and modest symptoms when diagnosed with active TB disease.

Diagnosis of TB in Infants and Young Children

As in adults, TB in children is diagnosed on the basis of TB test results, histories, physical examinations, and chest radiographs. However, diagnosis in children is challenging because TB tests can be unreliable in infants, and many children have no symptoms. Approximately 30–60% of children diagnosed with active TB disease in the United States have no symptoms reported by their parents at the time of diagnosis. Sometimes, poor feeding and poor weight gain are the only findings of active TB disease.

Frontal and lateral chest radiographs are recommended by experts for the evaluation of

children suspected of having intrathoracic TB. Adenopathy is reported to be present in 85% of children with active TB disease who are less than 3 years of age. Because radiologic findings for active TB disease in children can be different from those commonly seen in adults, it is important that radiographs be interpreted by someone experienced with pediatric radiographs.

Laboratory confirmation of active TB disease in infants and young children is often challenging because of the difficulty in obtaining a specimen for mycobacterial culture. Unless a child is able to produce sputum, gastric aspiration provides the best clinical specimen.

Signs and Symptoms of Active TB Disease in Infants and Young Children

In infants, common clinical manifestations of active TB disease are nonspecific and can include respiratory symptoms (cough and increased work of breathing), fever, hepatic and/or splenic enlargement, poor feeding, irritability, lethargy, lymphadenopathy, skin lesions (papulopustular, necrotic, or atrophic), and ear discharge. In addition, infants are more likely to have CNS manifestations.

Symptoms in children include cough, fever, and weight loss or failure to thrive. Miliary or acute disseminated TB may cause additional nonspecific symptoms such as fatigue, anorexia, vomiting, and diarrhea.

Health Care Provider's Role in Evaluating Patients as Part of this TB Contact Investigation

SNHD is asking providers to perform physical examinations on pediatric patients who have been potentially exposed to TB to help diagnose or rule out active TB disease. A physical examination form is available from SNHD upon request. If you

believe your patient was exposed at Summerlin NICU, please contact SNHD at 702-759-0707.

Moving forward, please remain alert for signs and symptoms of active TB disease in your patient. Feel free to refer parents to SNHD at 702-759-0707 if they would like more information.

Testing and Treatment Recommendations for Potentially Exposed Infants

Although the Mantoux tuberculin skin test (TST) is a common method of diagnosing TB infection in both children and adults, the test is unreliable in infants less than 6 months of age. Because infants less than 1 year of age have a 42% chance of progressing to active TB disease if infected, failure to treat because of a false negative TST result could have serious consequences. Therefore, SNHD is recommending and offering preventive treatment to all potentially exposed infants, regardless of TST result.

As with any infectious disease investigation, but especially due to the complexity of this situation, SNHD strongly encourages a collaborative relationship with practicing health care providers. TB testing and treatment in infants requires expertise and experience to ensure the best results. Therefore, SNHD is offering to accept referrals based on the following:

- 1) SNHD is consulting with pediatric TB experts to ensure the most appropriate care is provided to infants potentially exposed to TB in the NICU. We are obtaining advice on testing recommendations, clinical guidelines for preventive therapy, clinical guidelines for treatment of active TB disease, and recommendations for how to monitor treatment.
- 2) For best results, daily treatment should be given under direct observation to ensure adherence and close monitoring. Providing this level of care may not be practical for all health care providers and SNHD is ready to assist.

SNHD is required to closely monitor TB contacts to determine the spread of infection resulting from

this cluster. If you are caring for one of these patients, please contact SNHD at 702-759-1370.

In consultation with TB staff from the Centers for Disease Control and Prevention and pediatric TB experts from the Curry International Tuberculosis Center, SNHD recommends the following approach because detection of TB through TST testing is inherently unreliable in infants under six months of age:

- 1) Perform baseline TST, physical examination, and CXR (PA and lateral) now. A positive TST result is one that shows 5 mm or greater of induration. Compare CXR to existing films, if available. Offer preventive treatment to this group and ...
- 2) Empirically start a 6- to 9-month course of preventive therapy per the LTBI protocol for all infants who are less than 6 months of age (adjusted for prematurity at the time of the baseline test and exam). If the TST result is positive, treatment duration should span 9 months, as this infant would now be diagnosed as having LTBI.
- 3) If the infant was less than 6 months old and the TST result was negative at baseline, repeat TST and physical examination at 6 months of age (adjusted for prematurity) and continue the LTBI treatment until complete.
- 4) If TST result at 6 months of age is still negative, repeat TST at 1 year of age.
- 5) *At any point, if the infant shows signs or symptoms of active TB disease or has a positive TST result, contact the SNHD pediatric TB physician at 702-759-1370.*
- 6) As the investigation continues, additional recommendations may follow.

Treatment of Infants and Children with Latent TB Infection (LTBI)

LTBI treatment consists of 270 doses of isoniazid (INH), corresponding to 9 continuous months of daily INH. To promote adherence and maximize

the benefits of therapy, children should be treated under direct observation.

Treatment of Children Diagnosed with Active TB Disease

Because the presumed exposure was to tuberculosis caused by *Mycobacterium bovis*, which is inherently resistant to pyrazinamide, the recommended treatment is 9 months of INH and rifampin with 2 months of ethambutol during the initial phase, dependent on the patient's clinical course. To promote adherence and maximize the benefits of therapy, all children should be treated under direct observation. Historically, patients have been treated at the SNHD TB clinic. We welcome the opportunity to coordinate the care of your patients.

Potential Side Effects of Recommended Treatment

In general, children respond well to TB treatment and experience fewer adverse side effects than adults. Potential side effects of the three drugs include the following:

- **Isoniazid (INH):** While INH rarely causes hepatotoxicity in children, families should be educated thoroughly to watch for associated symptoms. These include anorexia, malaise, abdominal pain, and vomiting. If these symptoms are observed, therapy should be stopped and the child should be evaluated as quickly as possible. Children taking antiepileptic drugs should be monitored closely because INH can affect hepatic metabolism of some of these medications.
- **Rifampin:** A common side effect of rifampin is orange or red coloration of secretions (e.g., tears or urine). This side effect is not harmful.
- **Ethambutol:** In adults, higher doses of ethambutol can cause optic toxicity. However, there are no confirmed reports of this adverse effect caused by ethambutol in children. Still, the use of ethambutol should be limited to a maximal dose of 15 mg/kg/day in children when toxicity cannot be monitored carefully.

References

Loeffler, A.M. Pediatric Tuberculosis. *Seminars in Respiratory Infections*, Vol 18, No. 4(December), 2003: pp272-291.

Centers for Disease Control and Prevention. Guidelines for the Investigation of Contacts of Persons with Infectious TB. *MMWR* Dec 16, 2005/54(RR15);1-37