

Diagnosis and Management Guide

Children Under 5 Exposed to Infectious Tuberculosis (TB)



Purpose

This reference guide is intended to provide clinicians, tuberculosis (TB) control programs, and public health professionals with a concise, evidence-based reference on the diagnosis and management of children under five years of age who have had a confirmed exposure to an infectious case of TB.

Introduction

A young child exposed to infectious TB is a complex and potentially high-risk situation. Clinicians must have a high index of suspicion and be able to identify and interpret the often-subtle signs, symptoms and radiologic findings of active TB. Compared to adults, TB presents and progresses differently in young children. Key characteristics of TB in this population include:

- A higher and more rapid risk of progression to active disease (primary rather than reactivation disease). In some cases, particularly in infants, there may be no latent period at all with direct progression from infection to disease within a very short period
- More severe and complex forms of TB, including disseminated and central nervous system involvement, particularly in infants and the very young
- A tendency to develop paucibacillary (low number of bacteria) TB that is typically non-cavitary and often more difficult to confirm microbiologically
- **High frequency of intrathoracic lymph node disease, which may be the only initial manifestation of active TB**

Challenges

Diagnosing and treating TB in young children presents unique challenges. These may include:

- Atypical and often subtle pulmonary and extrapulmonary presentations
- Limitations of chest radiography, including challenges obtaining a quality x-ray as well as identifying subtle abnormalities including intrathoracic adenopathy
- Low bacillary burden, making microbiological confirmation more difficult
- Difficulty obtaining quality specimens for testing (e.g., sputum samples are often not possible, and gastric aspirates require a procedure)
- Special considerations for drug dosing and formulations, particularly in infants

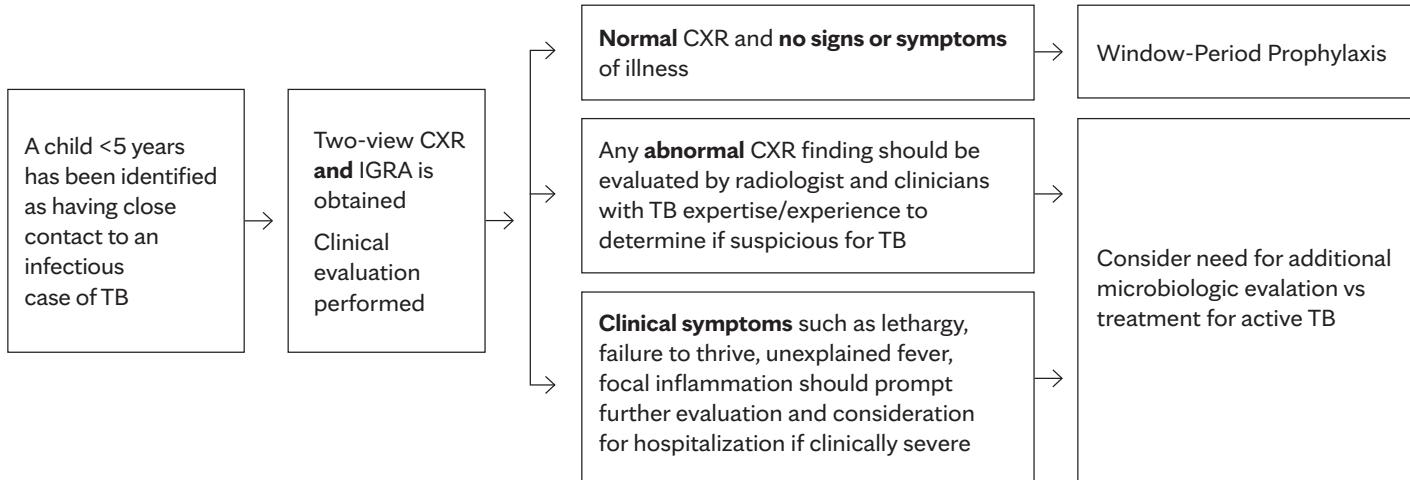
Providers should “**think TB**” when evaluating a young child exposed to an active TB case. They should have adequate awareness to identify and act on findings which might not be worrisome in a child without that exposure.

The good news is children with TB tend to tolerate treatment much better than adults, and most children can be cured in 4 months.

Because TB in young children can progress quickly and present with subtle, hard-to-confirm findings, clinicians must maintain a high index of suspicion and act promptly to ensure timely diagnosis and effective treatment.

Diagnosis

TYPICAL EVALUATION PATHWAY FOR EXPOSED CHILDREN



TESTS FOR LATENT TB OR TB INFECTION

All young children suspected of having TB should have a test for TB infection, which in almost all cases should be an interferon gamma release assay (IGRA).

Key Points

- As is the case in adults, IGAs and TB skin test (TST) can be negative, even in severe or invasive disease, so a negative does **not** rule out disease.
- Indeterminate (QuantiFERON) or invalid results (T-SPOT) occur rarely; options include repeating the same assay or testing using the other assay.
- Quantitative results on IGAs in children with active TB can range from negative to very high, but higher positive results (e.g. QuantiFERON antigen result >4) increase the likelihood of active TB.

RADIOLOGY

Lung imaging is a critical component of TB evaluation in young children.

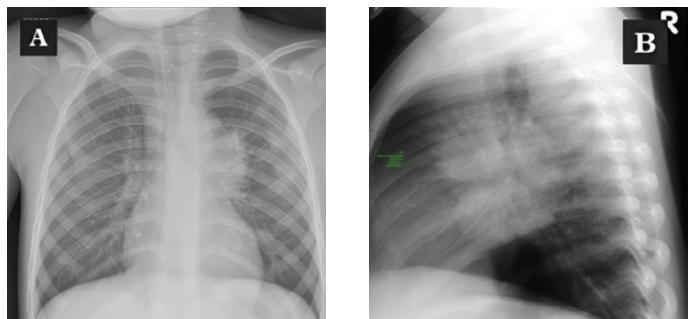
Key Considerations

- All children should receive a two-view CXR; If the x-ray is rotated, under- or over-penetrated, or has poor expansion, the x-ray should be repeated.
- High-quality imaging is especially important in pediatric evaluations—consider utilizing facilities with extensive pediatric experience.

- Interpretation should be performed by both a pediatric radiologist and an experienced pediatric TB clinician; the CDC **TB Centers of Excellence** are useful resources for helping interpret chest x-rays in young children.

Key findings to look for on a chest x-ray

Hilar or mediastinal adenopathy: these findings are **highly specific for TB in this setting and should be considered evidence of active TB.** Hilar adenopathy is easily missed or confused for peri-hilar viral changes which are seen more commonly in U.S. children. Examples below are from the **Diagnostic CXR Atlas for Tuberculosis in Children**, available from the Union Against Tuberculosis and Lung Disease. Education on TB radiology in children can also be found in the document.



Parenchymal lung findings: Any abnormality should be considered potential TB. However, if the appearance is typical of a viral process and there is no adenopathy, consider repeating the x-ray after 2-4 weeks to assess if there is resolution; **failure to improve should be considered more worrisome for TB.**

- Chest CT may be useful when the diagnosis remains unclear and the CXR is not definitive.
- Follow-up CXR is generally recommended after two months of effective combination TB drug therapy for children with pulmonary disease, and again at the end of therapy (note: the CXR may not yet be normal at these time points).
- Follow-up chest CT is generally not needed unless there are additional clinical concerns (e.g., lack of response to treatment, consideration of alternative or additional diagnoses) that cannot be characterized by x-ray.

MICROBIOLOGIC DIAGNOSIS

Microbiologic confirmation of TB disease (e.g., culture or PCR) is challenging and requires significant resources. Even when aggressive diagnostic strategies are employed, microbiologic testing is frequently negative in children with active TB disease. Obtaining any available microbiologic data is essential, including drug-susceptibility results from the source case (person suspected of passing TB to the child). When drug-susceptibility results are obtained from the source case, the information can be utilized for determining the drug regimen for the child.

In some circumstances, obtaining specimens for microbiologic testing may not be necessary when there are:

- Specific findings for TB on CXR, **and**
- Known contact with a confirmed case of active pulmonary TB (with *Mtb* culture and drug susceptibility results available or pending—e.g., parent or close family member).

Follow-up cultures to assess treatment response are rarely needed in children <5, unless there is a concern for treatment failure.



Sample Collection

Collecting samples for AFB stain, PCR, and mycobacterial culture in hospitalized children is routine. Children who are less ill generally do not require hospitalization solely for diagnostic purposes.

Sample collection is important when:

- Diagnosis remains uncertain
- There is no known contact from whom microbiologic data can be obtained
- Severe disease is present
- Additional infectious or non-infectious diagnoses are being considered

Sample Collection Approaches

- **Induced sputum** (via aerosolized hypertonic saline) can be performed, even in infants but requires a facility with expertise (nebulizing saline, performing a nasopharyngeal aspirate, treating bronchospasm if it occurs).
- **Gastric aspirates** are the traditional technique for obtaining samples for respiratory specimens. Hospitalization is required, often for multiple nights to capture very early AM aspirate; 2–3 specimens are recommended.
 - Each specimen should be sent to a lab for AFB stain, *Mtb* PCR, and culture
 - Negative results do **not** exclude active TB as the sensitivity is only 30–40%
- **Stool testing** may be useful and easy to perform, though sensitivity is low.
 - Consider stool collection for PCR in children not eligible for gastric aspirates or as an initial test prior to more invasive procedures; a positive test provides useful information but not full susceptibility data, whereas a negative test does **not** rule out TB due to low overall sensitivity.

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Additional Diagnostic Considerations

In the U.S. almost a third of young children will have extrapulmonary disease; commonly this occurs coincident with pulmonary disease but also occurs in isolation. Other sites of suspected disease (e.g. meningeal, disseminated, lymphatic, abdominal/gastrointestinal, musculoskeletal TB) should be considered for imaging, sampling and microbiologic testing.

- Due to **high TB meningitis risk in infants, lumbar puncture (CSF exam) is recommended for all children <12 months with suspected or confirmed active TB**; infants with TB meningitis do **not** always have obvious clinical signs such as is seen in typical bacterial meningitis.
- Brain imaging is not routinely required unless there are clinical concerns. Imaging should be strongly considered if there are abnormal CSF findings; CT is the most common initial neuroimaging study if acute concerns exist.
- Additional evaluation for sites of extrapulmonary TB are based on careful history and physical exam. Advanced imaging (CT, MRI) may be needed to characterize areas of concern.

Specific Testing Modalities

- Given the limitations of microbiologic testing, all available samples should have complete testing performed: AFB staining, PCR and culture, pathology (when applicable).
- In the United States, Xpert MTB/RIF assays are currently limited to respiratory specimens, but additional PCR assays are available from Mayo Clinic Laboratories and others for testing additional specimens, including stool.

WHEN SHOULD A CHILD WITH SUSPECTED TB BE HOSPITALIZED?

Hospitalization should be considered when there are concerns for severe or invasive TB, when the child has symptoms of severe disease that may be due to TB or may be due to other active infections, or when the hospital setting is needed to facilitate or accelerate diagnostic testing.

Signs of severe TB include any sign of meningitis or CNS infection, including sub-acute symptoms:

- Persistent headache
- Neck pain or stiffness
- Lethargy or altered mental status

Additional concerning signs and symptoms of disseminated or severe disease include:

- Poor oral intake or failure to thrive
- Respiratory distress
- Persistent fever
- Focal pain or inflammation that might suggest localized extrapulmonary TB disease



Recognizing when hospitalization is warranted is critical to ensure timely diagnosis and management of severe or complicated TB in children.

Treatment

LAB TESTING PRIOR TO TREATMENT

Routine baseline labs at the start of treatment (e.g. liver function tests) are not necessary unless the child is taking other hepatotoxic medications or has underlying concerns for liver dysfunction; however, many county health departments will require baseline labs (and HIV testing) for all patients.

DOSING AND DURATION

- Pediatric TB drug dosing requires careful attention, as it differs from adult recommendations and is weight-based—refer to [Table 3](#) in the [Official American Thoracic Society/ Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis](#).
- A 4-month course of combination therapy (2 months RIF, INH, PZA +/- EMB followed by 2 months of RIF and INH) is the standard of care in the United States for treating drug-susceptible, non-severe pulmonary TB in children, including in children with HIV.
- Higher doses of rifampin (20–40 mg/kg) are frequently used in infants and toddlers with active TB disease.
- Suspensions of TB medications may be difficult to source. A more practical approach is to:
 - Open capsules (e.g., rifampin),
 - Crush tablets (e.g., INH, PZA, EMB),
 - Administer with flavored syrups or favorite foods (need to assure that the entire dose is ingested).
 - If the capsule or tablet size does not align well with the patient's weight, it is generally better to use a higher dose rather than a lower dose.
- Children with severe forms of TB or extrapulmonary disease require at least 6 months of treatment.
- Treatment of active TB in children should always be done in coordination with local and state public health programs.

INFECTION CONTROL

- Children under 5 with pulmonary TB are rarely infectious, and stigmatizing or frightening infection control or isolation procedures are not needed for children <5.
- Active TB in children often signals recent transmission and is frequently linked to an infectious case, often a family member. Infection prevention measures in health care settings should focus on identifying potential infectious family members who might also be present.
- Parents and other family members should be tested promptly (symptom check, IGRA, x-ray) if the child is hospitalized, to allow visitors, and avoid unnecessary hospital isolation; hospital teams should help facilitate these activities. Coordinate with public health to complete evaluations as efficiently as possible.
- Standard precautions are sufficient for hospitalized children <5 with active TB. Airborne precautions (N-95 masking, negative airflow, etc.) are typically reserved for adolescents or adults with active pulmonary TB.

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