Management of Latent Tuberculosis Infection in Children and Adolescents

A Guide for the Primary Care Provider

New Jersey Medical School
Global Tuberculosis Institute
A Founding Component of the International Center for Public Health

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ACKNOWLEDGMENTS

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ORIGINAL DOCUMENT – 2004

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PREFACE

This document is a guide for the pediatric primary care provider. It is not intended to provide in-depth information on the management of latent tuberculosis infection (LTBI), but rather, an overview of the most current recommendations and suggestions for achieving the best patient outcome. Because recommendations for testing and treating children with tuberculosis disease and/or latent infection change as new knowledge and treatment become available, healthcare providers should refer to the attached reference list, as well as other current literature.

The New Jersey Medical School Global Tuberculosis Institute (GTBI) is a Regional Training and Medical Consultation Center (RTMCC) that serves as a resource for healthcare professionals and as a patient referral center. It is one of four centers in the United States and is funded by the Centers for Disease and Prevention (CDC). Physicians at GTBI have expertise in the management of children with TB disease, latent TB infection, and multi-drug resistant TB (MDR TB). The toll-free information number is 1-800-4TB-DOCS (1-800-482-3627). Those with Internet access can find our web site at www.umdnj.edu/globaltb.

INTRODUCTION

Latent tuberculosis infection (LTBI) is defined as infection with the tubercle bacilli without signs and symptoms or radiographic evidence of tuberculosis (TB) disease. Because we know that LTBI is the precursor to TB disease, the early identification of children infected with the *M. tuberculosis* bacillus is a critical factor in preventing morbidity and mortality in the pediatric population. Equally important is the treatment of these children and a plan to ensure treatment completion.

Currently, the emphasis in the United States is on testing only those children identified as having risk factors for tuberculosis. "Targeted tuberculin testing" places priority on groups at highest risk, identifying those at the greatest risk for infection as well as those at risk for developing TB disease if infected.[1] Healthcare providers should also base testing and treatment decisions on local epidemiology and immigration patterns. This approach suggests that providers screen on a regular basis by taking a TB-focused health history.

Rationale for treating LTBI in children includes the following:

- Young children are at greater risk of progression from latent infection to TB disease once infected
- Infection is likely to be recent
- Medications used to treat LTBI are well tolerated by children and there is a low risk of toxicity
- Children have more years to potentially develop TB disease

Attempting to treat healthy children over an extended time period can present challenges to providers, patients, and families. This guide and the additional resources listed will provide pediatric healthcare providers with information about the management of LTBI in children from birth to adolescence.

TESTING FOR TB INFECTION

Two methods of testing for *M. tuberculosis* infection are available. These include the Mantoux tuberculin skin test (TST) and the blood-based interferon-gamma release assays (IGRA), QuantiFERON®-TB Gold, QuantiFERON®-TB Gold In-Tube or T-SPOT®.TB.

IGRAs have been approved for use in adults in all circumstances where a TST would be used. However, there is a lack of published data related to IGRA use in children and the American Academy of Pediatrics only recommends its use in place of TST in immunocompetent children 5 years of age or older. The 2009 Red Book offers the following guidelines for interpretation of IGRA results:[2]

- Children with positive results should be considered infected with *M. tuberculosis*
- Negative results cannot universally be interpreted as lack of infection
- Indeterminate results do not exclude tuberculosis infection
- May be useful in determining whether a reactive TST in a BCG-vaccinated child is due to TB infection or a false positive result caused by BCG

TARGETED TESTING RECOMMENDATIONS

NO RISK NO TEST

Targeted tuberculin skin testing identifies children who are at risk for LTBI and therefore at risk for progressing to TB disease. *Children without risk factors should not be tested.* Because children and adolescents with LTBI represent the future reservoir for cases of TB, it is important that they are identified and treated. The following is a summary of the American Academy of Pediatrics (AAP) testing recommendations that can be found in the *Red Book: 2009 Report of the Committee on Infectious Diseases*. It should be noted that there are some instances where routine testing is required for attendance in school, day care, or camp. This is to be discouraged because the yield of positive results is low, leading to an ineffective use of resources.[2]

Children for whom immediate TST or IGRA is indicated:

- Contacts of persons with confirmed or suspected contagious tuberculosis
- Children with radiographic or clinical findings suggesting tuberculosis disease
- Children immigrating from countries with high prevalence of TB (e.g., Asia, Middle East, Africa, Latin America, and countries of the former Soviet Union), including foreign adoptees
- Children with travel histories to endemic countries or substantial contact with people who live in these countries

  **Countries in Eastern Europe also have a high prevalence of TB*

Children who should have annual TST or IGRA:

- Children infected with HIV (TST only)
- Incarcerated adolescents

Children at increased risk for progression of infection to disease:

Those with other medical conditions, such as diabetes mellitus, chronic renal failure, malnutrition, and chronic or acquired immunodeficiencies deserve special consideration. Underlying immune deficiencies associated with these conditions can increase the possibility for progression to severe TB disease. Information regarding potential exposure to tuberculosis should be elicited from these patients. If histories or local epidemiological factors suggest a possibility of exposure, immediate and periodic TB testing should be considered. In addition, a TST or IGRA should be performed before initiation of immunosuppressive therapy including prolonged steroid administration or use of tumor necrosis factor-alpha antagonists.

Appendix A reviews the technique for administering and measuring the TST.

SCREENING FOR RISK OF TB INFECTION

The AAP suggests that a risk assessment for TB be performed at the provider's first encounter with the child, every six months until age two, and then annually if possible. Testing should be performed only if one or more risk factors are present.[2] The following four questions were validated by several studies and incorporated into a risk assessment questionnaire by the Pediatric Tuberculosis Collaborative Group.[3]

- Was child born in a high-risk country (countries other than U.S., Canada, Australia, New Zealand or Western European countries)?
- Has child traveled and had contact with the resident population in a high-risk country (Africa, Asia, Latin America, countries of the former Soviet Union, or Eastern Europe) for more than a week?
- Has child been exposed to anyone with TB disease?
- Has a family member or close contact had a positive TST?

Some studies have found that other risks and exposures are predictive of a positive TST and should be incorporated into screening systems based on local epidemiology.

Providers should become familiar with the incidence of TB in the countries from which their patients and families are emigrating.The most current data available (2007) suggests that 58% of TB cases in the United States occurred among non-US born individuals. Sixty-two percent of those cases reported in 2007 occurred in people from seven countries. They were Mexico, Philippines. Vietnam, India, China, Haiti, and the Republic of Korea.[4]

SPECIAL CONSIDERATIONS IN TB SKIN TESTING AND INTERPRETATION

Immunizations

Vaccination with live virus vaccines such as MMR, can temporarily suppress tuberculin reactivity. Therefore, the TST should be administered simultaneously with these vaccines or at least 4-6 weeks afterward. While other viral infections may also suppress the immune response, they are not a contraindication for TST administration.

BCG vaccine

A history of Bacille Calmette-Guerin (BCG) vaccine is **not** a contraindication for testing for tuberculosis, provided such testing is part of a targeted testing program. This vaccine is not part of the vaccine schedule in the United States, but is used extensively throughout the world. Since tuberculosis is endemic in many countries, BCG is given for the specific purpose of protecting infants from the serious complications of TB disease. It does not provide lifelong immunity, and, in fact, its effectiveness wanes over time. More than 50% of infants who received BCG at birth will have a non-reactive TST at 9-12 months of age, and the great majority will be negative by 5 years of age.[5]

Therefore, if a child is at risk for tuberculosis, a skin test should be performed regardless of BCG vaccine history. A child with a positive skin test reaction should be evaluated for TB disease and treated accordingly, because it is impossible to distinguish a reaction caused by infection with the TB bacillus and one that is a result of BCG vaccine. The evaluation should include a history, physical examination, and a chest radiograph. This may require a great deal of parental education. The provider can acknowledge that it is possible, though unlikely, that the BCG vaccine has caused the reaction, and that it is safer to treat such a child for TB infection rather than risk progression to disease.

Contacts of person with potentially contagious tuberculosis

Persons who are contacts of patients with contagious tuberculosis are at risk of infection with *M. tuberculosis* and the subsequent development of disease. Infants are at an especially high risk; up to 40% develop disease without treatment. In addition, children less than 4 years of age are at high risk for developing severe forms of disease once infected.[6] Therefore, identifying those children at risk is of great importance in the prevention of tuberculosis disease. When an adult has been diagnosed with TB disease, children who have been in contact with that individual should be identified and evaluated as soon as possible to rule out (exclude) TB disease. The evaluation should include a TST, a chest radiograph (regardless of TST reaction), a history, and physical examination.

If the initial TST is positive (≥ 5 mm) and there is no evidence of disease, treatment for LTBI should be initiated (See Treatment Guidelines, page 12). If the initial TST is negative, a repeat skin test should be administered 8-10 weeks after contact with the source case has been broken or after the source case has been deemed to be non-infectious.

If the child is less than four years of age or has impaired immunity, treatment should be initiated as soon as disease is ruled out, even if the evaluation and TST are negative. This is because of the high risk of progression to disease if infected and because TST reactivity can be delayed for up to 8-10 weeks after infection. If the repeat test is negative, treatment can be discontinued in immunocompetent children. In the immunocompromised and young infants, it may not be possible to exclude LTBI due to cutaneous anergy, and as a result, treatment with INH should be continued for the full course (See Treatment Under Special Circumstances, page 14). If the repeat TST is positive, the child should be reevaluated and, in the absence of disease, complete 9 months of treatment.[2] A repeat chest radiograph is not necessary if the child is asymptomatic and the initial radiograph was normal.

DEFINITION OF POSITIVE TST RESULTS[2]

The interpretation of the TST is based on a person's risk of TB infection and of progression to TB disease if infected.

≥5 mm induration

- Child who is a close contact of a person with known or suspected TB
- Child with radiologic or clinical evidence of TB disease
- Child receiving immunosuppressive therapy or with immunosuppressive conditions, including HIV Infection

≥10 mm induration:

- Child younger than 4 years of age
- Child with medical conditions such as: lymphoma, Hodgkin's disease, diabetes mellitus, chronic renal failure, or malnutrition
- Child born in region of the world with high prevalence of TB
- Child who has frequent exposure to high-risk adults (HIV-infected, homeless, residents of nursing homes, institutionalized, incarcerated, users of illicit drugs, or migrant farm workers)
- Child with a travel history to high prevalence regions of the world

≥15 mm induration

- Child ≥ 4 years with no risk factors

EVALUATION OF CHILDREN AND ADOLESCENTS WITH A POSITIVE TST OR IGRA

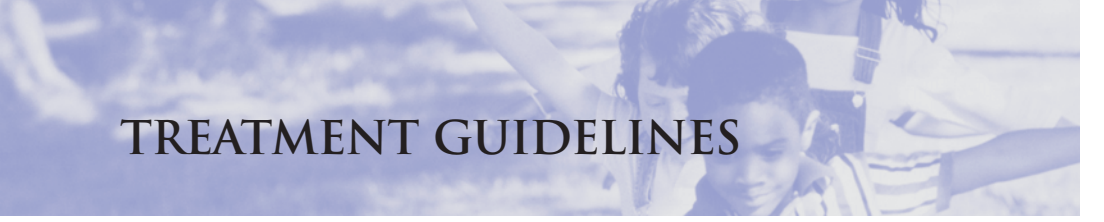
The evaluation of individuals with positive TST or IGRA results includes a detailed health history, a physical assessment, and a chest radiograph. By focusing on the presence of symptoms, the risk of progression to TB disease, and coexisting medical conditions, the practitioner is able to identify or exclude TB disease. **Any child suspected of having TB disease should be referred to a specialist.**

The diagnostic criteria for LTBI includes a positive test for TB infection, the absence of symptoms or physical findings suggestive of TB disease, and a chest radiograph with no evidence of TB disease.[3]*

Chest radiographs are used as a diagnostic tool to evaluate the child with a positive TST or IGRA.[1,3]

- Frontal and lateral views are recommended for children less than 5 years of age
- In children 5 years or older, clinicians may opt to obtain both views to aid in decision making
- Films should be obtained and results reviewed by an experienced radiologist *before* initiation of LTBI treatment
- If the initial chest radiograph is normal and the child remains asymptomatic and completes treatment, no further radiographs are required

**Chest radiographs that reveal isolated calcified granulomata or calcified intrathoracic lymph nodes without other abnormalities are consistent with LTBI not TB disease.*



TREATMENT GUIDELINES

For the following reasons, treatment is recommended for ALL children and adolescents who have been diagnosed with LTBI:

- Young children are at a greater risk for progressing to TB disease
- Infection is likely to have been recent
- Drugs used to treat LTBI are generally safe in the pediatric population
- Pediatric population has more time to potentially develop TB disease

MEDICATION FOR TREATMENT OF LTBI

Isoniazid (INH)[2]

INH is the drug of choice for the treatment of LTBI in children and adolescents. The length of treatment is 9 months.

- Daily dosing: 10-15 mg/kg (maximum 300 mg)
- Twice weekly dosing: 20-30 mg/kg (maximum 900 mg)
  - Consider when adherence with daily therapy cannot be ensured
  - Must be administered via directly observed therapy (DOT)

Formulation - 100-mg and 300-mg tablets

- A liquid preparation is available but may contain sorbitol which can cause diarrhea

Techniques for administration

- For children unable to swallow tablets, the tablets should be crushed and mixed with a spoonful of food the child likes to mask the bitter taste (e.g., undiluted frozen orange juice concentrate, applesauce, mashed bananas, yogurt).[5] Afterwards, a spoonful of food without medicine should be given, followed by liquid to wash down the INH. For accurate dosing, do not add crushed medication to a full glass of water, as the drug will sink to the bottom
- For infants, the tablet may be dissolved in 1 tablespoon of warm water and then mixed with a small amount of breast milk or formula and placed in a nipple for administration

Adverse effects and drug interactions

- Hepatotoxic effects in children are rare; however, parents should be educated about recognition of early signs of hepatotoxicity (flu-like symptoms may precede clinical jaundice)
- Peripheral neuritis or seizures caused by the inhibition of pyridoxine metabolism are rare
- INH may increase serum levels of phenytoin when administered concomitantly; therefore, phenytoin levels should be closely monitored[1]
- INH may also inhibit the metabolism of other drugs such as: carbamazepine, primidone, valproic acid, benzodiazepines, haloperidol, ketoconazole, theophylline, and warfarin through P-450 enzyme inhibition[7]
- Baseline liver function tests are not recommended unless there are conditions that might increase the risk of hepatotoxicity
- INH should be stopped immediately if patient develops significant nausea, vomiting, anorexia, abdominal pain, or jaundice[3]

Pyridoxine (vitamin B6) supplementation is recommended for the following patients receiving INH. The recommended daily dose: Up to 1 mg/kg/ (maximum 25 mg):[2]

- Children on meat and milk-deficient diets
- Exclusively breast-fed infants
- Children with nutritional deficiencies
- Children with symptomatic HIV infection
- Pregnant adolescents

Rifampin[2]

Rifampin should be used in cases of isoniazid intolerance or resistance. The length of treatment is six months

- Daily dosing: 10-20 mg/kg (maximum 600 mg)

Formulation:

- Capsules: 150 mg, 300 mg

Techniques for administration

- For children unable to swallow capsules, the medication can be compounded into suspension by the pharmacy or the total contents of the capsule can be mixed with food to mask the bitter taste

Adverse effects and drug interactions:

- Hepatotoxic effects are rare - most common side effect is gastrointestinal upset
- Temporary orange discoloration of urine, sweat, tears, and other body fluids is a normal and expected side effect. Warn patients that it may cause permanent orange discoloration of soft contact lenses
- Accelerates the clearance of drugs metabolized by the liver (methadone, warfarin, glucocorticoids, hormonal contraceptives, oral hypoglycemic agents, digitalis, anticonvulsants, dapsone, ketoconazole, and cyclosporin)[1]
- Adolescents using oral contraceptives should be advised to use other forms of birth control
- Intermittent dosing (separated by weeks or months) of rifampin (>10 mg/kg) can lead to blood dyscrasia (hemolytic anemia, thrombocytopenia), influenza-like symptoms, and acute renal failure[1]

TREATMENT UNDER SPECIAL CIRCUMSTANCES

Children recently exposed to TB disease

When the source case has drug-sensitive TB:

- Children with impaired immunity and those younger than 4 years of age, treatment with INH should be started even if the initial TST is negative – "window prophylaxis"
- TST should be repeated 8-10 weeks after contact with the source case has been broken or when the source case is no longer infectious
- INH treatment can be stopped in immunocompetent children if the repeat TST is negative
- All children who are contacts should be reevaluated for the presence of TB disease if the repeat TST is positive. If no disease is found, the child should complete the recommended regimen of INH for a total of 9 months

When source case has isoniazid-resistant/rifampin-susceptible TB:

- Consultation with a specialist should be sought
- Treatment of choice is daily rifampin as monotherapy for at least 6 months[2]

When source case has multidrug-resistant TB (MDR TB; resistant to at least INH and rifampin):[1]

- Consult a specialist who has experience in treating MDR TB in children
- Treatment for LTBI in patients exposed to MDR TB should be guided by the in vitro susceptibility test results from the isolate to which they were exposed
- Immunosuppressed contacts should be treated for a minimum of 12 months
- Irrespective of treatment, all patients with suspected MDR TB infection should be followed for at least 2 years

Lapses in treatment of LTBI

Providers should attempt to determine the reason for lapses in treatment.

- Allowing for short gaps, the total number of doses over a specified period is what determines completion of treatment[1]
  - For the 9-month regimen of daily INH, 270 doses should be taken within a period of 12 months. Missed doses can be added on at the end of 9 months to complete 270 doses. Nine bottles of 30 tablets will achieve this goal
  - For the 9-month regimen of twice weekly dosing of INH, 76 doses should be taken within 12 months
  - When there is an interruption of therapy for more than 2 months, a physical examination and repeat chest radiograph are indicated to rule out TB disease before treatment is continued
- If there is lapse of treatment for more than 3 months, the treatment regimen should be restarted after a physical examination and chest radiograph has ruled out TB disease
  - Early symptoms of TB disease in children are subtle and may include poor appetite, failure to gain weight, and general malaise, as well as classic signs such as cough, fever, and weight loss

Immunocompromised children with LTBI

Children whose immune systems are compromised have an increased risk for progression to TB disease. Consultation with an infectious disease specialist is suggested in the following situations:

- Child with HIV infection
- Child receiving immunosuppressive therapy (chemotherapy or long-term/high-dose corticosteroids, e.g. prednisone or equivalent at 2 mg/kg/day for 2-4 weeks)[1]
- Child with diagnosis of leukemia, Hodgkin's disease, or lymphoma
- Child with other chronic diseases that may affect the immune system and increase the risk of progression to disease such as diabetes mellitus, chronic renal failure, or malnutrition

Treatment with INH:

- Though there is no substantial increase in hepatic side effects from INH, baseline testing of AST, ALT, and bilirubin is recommended in HIV-infected patients[1]
- Treatment should continue for at least 9 months[2]
- Pyridoxine supplementation is recommended for children with symptomatic HIV infection[3]

Treatment with rifampin:[8,9]

- When there is INH resistance or intolerance, rifampin for 6 months is recommended
- Rifamycins (rifampin, rifabutin) induce hepatic enzymes (CYP450) causing significant drug interactions with antiretrovirals (ARV)
- Rifabutin is a less potent inducer of CYP450 than rifampin, and therefore effects drug levels of ARV to a lesser extent
- Rifampin can be used with certain ARV combinations (efavirenz, ritonavir-saquinavir, and probably lopinavir-ritonavir)
- Dose adjustments are necessary with both rifamycins. Expert consultation is recommended

Referring to a specialist

Consider consultation with an expert in management of pediatric tuberculosis if the child:

- Is HIV-infected or immunocompromised
- Has a history of liver disease
- Does not tolerate INH
- Is a contact to a person with INH-resistant or multi-drug resistant TB

- Exhibits any signs or symptoms of TB disease such as abnormal chest radiograph, cough, weight loss, anorexia, or change in activity level

State TB Programs or Regional Training and Medical Consultation Centers can arrange consultations with a pediatric TB expert. See Resources on page 26 for links to RTMCC websites.

DIRECTLY OBSERVED THERAPY

Directly observed therapy (DOT) is the term used to describe the observation of TB medication ingestion by a member of the healthcare team. Primary care providers treating children for LTBI should be aware of community resources for directly observed therapy and recommend it whenever possible. While DOT is the standard of care for patients with TB disease, it can also improve adherence in children with LTBI. DOT is a priority for very young children, adolescents, immunocompromised children, and those with evidence of non-adherence.

In the pediatric population, the school can be asked to collaborate in the treatment by providing directly observed therapy. The school nurse can dispense the medication using twice weekly dosing for both LTBI and TB disease, or daily dosing as needed.

Some guidelines for administering medication in the school setting:

- Due to the stigma of TB, it is critical to maintain confidentiality
- For LTBI, the treatment period can be extended if doses are missed for illness or vacation
- Ongoing communication and collaboration between the school and healthcare provider are necessary to achieve success in a school DOT program
- Parental consent is needed for administration of medication in school
- Communication with the parent during the treatment course is essential

For information on establishing a school DOT program, refer to the Tuberculosis School Nurse Handbook and Guidelines for Initiating a School-based Directly Observed Therapy Program developed by the New Jersey Medical School Global Tuberculosis Institute.
www.umdnj.edu/globaltb/products/schoolnursehandbook.htm
www.umdnj.edu/globaltb/products/schoolbaseddot.htm

MONITORING DURING LTBI TREATMENT

Whenever possible, children should be monitored by the physician on a monthly basis. This enables the physician to perform an ongoing evaluation of the treatment plan and develop a relationship with the child and caregiver. When a monthly physician visit is not feasible, an evaluation should be performed by a nurse with knowledge of TB. At a minimum, the physician should also see the patient at least twice after the initial visit, and then intermittently if questions or problems arise. Visits should be as convenient and brief as possible.

Periodic monitoring offers the opportunity to:

- Stress the importance of adherence
- Perform a physical examination, checking for any signs and symptoms of TB disease or possible medication side effects
- Address concerns the patient or caregiver may have regarding treatment
- Educate the patient and family about possible medication side effects
- Inquire about status of skin testing for family and other contacts, as well as identification of a source case

Monthly assessment should include a history and physical examination and should document:

- Child's weight – compare to previous weight
- Adherence to medication regimen
- Medication side effects such as: decreased appetite, malaise, abdominal complaints (nausea, vomiting, pain)
- Indications of drug toxicity such as icterus, jaundice, dark urine
- All prescription and non-prescription medications
- Alcohol use
- Oral contraceptive use in adolescents
- Date of last menstrual period

FAMILY EDUCATION

Education of the patient and family is an ongoing process. It is very important to clearly explain the benefits of treatment for LTBI at the first encounter. Sharing anecdotal stories of children with tuberculosis and providing educational materials is an effective way to help parents realize the importance of treatment. *What Parents Need to Know About TB Infection in Children* is a brochure that can be downloaded from the Global Tuberculosis Institute website: www.umdnj.edu/globaltb/products/pedsltbi.htm. Ideally, written material should also include instructions to stop INH immediately and contact provider if parent notes any of the signs of medication intolerance or toxicity mentioned above.

Addressing the following will help improve adherence:

- Length of treatment. Remind patient and family that once treatment is completed they will not have to be concerned with future testing or treatment
- Ways to make medication administration easier for parent and child. Suggest crushing medication and mixing it with food the child likes. In cases of mild nausea, try giving INH at bedtime
- Benefits of establishing a routine for medication administration. For example, taking medication at mealtime or bedtime or after child brushes teeth

In addition, consider the use of incentives and enablers to improve adherence and keep in mind the age and developmental level of the child (See Appendix B).

DOCUMENTING COMPLETION OF TREATMENT

When the treatment for LTBI is completed, written documentation should be provided to the family. See Appendix C for sample form letters. There will be instances when this information will be necessary, such as entrance to college, armed services, or employment in the healthcare industry. When this documentation is given to the family, it is important to review what has transpired over the course of treatment. The following information must be recorded:

- The dates when the tuberculin skin test was administered and interpreted with results expressed in millimeters of induration
- The date and result of the chest radiograph

- The diagnosis and treatment given, including the medication, dosage, and duration of treatment
- A statement that the patient is not contagious
- A statement that no further tuberculin skin testing should be performed and no chest radiograph is required unless symptoms suggestive of TB (unexplained/prolonged cough, weight loss, fever) are noted
- Contact information for provider/facility

Be sure that the family understands both the child's diagnosis of LTBI and the treatment that has been completed. Advise the family to keep the original letter in their possession and provide a copy when requested. When this process has been completed, the patient can be discharged from care with a final reminder that if either the child or a family member develops symptoms of TB such as persistent cough, fever, or weight loss, the possibility of TB should be considered and medical care should be sought.

SUMMARY

The role of the pediatric primary care provider is important in the prevention and control of tuberculosis. Early identification and management of LTBI in children and adolescents involves the following:

- Assessing each individual child for risk of LTBI
- Testing if one or more risk factors are present
- Evaluating all positive reactors to rule out TB disease
  - Evaluation includes a history and physical examination and a chest radiograph
- Initiating appropriate treatment and monitoring for side effects
- Educating the patient and family about tuberculosis, LTBI treatment, medication side effects, and importance of adherence
- Providing follow up to ensure completion of therapy
  - Local health departments and school health programs may serve as resources for providers, patients, and families

APPENDIX A

ADMINISTRATION AND READING OF THE TST

The Mantoux test is the recommended TST. It is administered by injecting 0.1 ml of 5 TU of purified protein derivative (PPD) solution intradermally into the volar surface of the forearm using a 27-gauge needle with a tuberculin syringe.[4]

- Purified protein derivative (PPD) solution must be stored at 36-46° F and separate from other biologics, for example DTaP
- To avoid fluctuations in temperature, do not store on the refrigerator door
- Label the vial with date it was opened and discard unused portion within 30 days
- Syringes must be filled immediately prior to administration
- Avoid areas of skin with veins, rashes, or excess hair
- Cleanse the area with alcohol swab and inject PPD solution just below the surface of the skin, forming a 6-10 mm wheal (a pale, raised area with distinct edges)
- Measure the wheal. If no wheal forms or if it is less than 6 mm, the test should be repeated immediately at a site that is approximately 2 inches from the original site or on the opposite arm
- If minor bleeding occurs, dab the area with cotton at the injection site
- Do not cover the area with a bandage
- Record date, time, and site of the intradermal injection
- Record the brand name of the PPD solution, the lot number, manufacturer and expiration date
- Instruct child and parent not to scratch the site or cover it with a bandage
- Inform parent and child of the importance of returning for a reading of the TST within 48-72 hours (2-3 days)
- Give written appointment to return for TST reading
- TST interpretation should be performed by a trained healthcare professional

Measurement of TST reactions

- Locate the skin test site and verify with patient/family
- Inspect and palpate area with fingertips to identify areas of induration rather than erythema

Measure area of induration perpendicular to the long axis of the arm

- Use ballpoint pen to mark edges of induration
- Use a TST ruler or ruler with millimeters to measure the distance between the two edges

Recording/documentation

- Record date TST was administered
- Record the results in millimeters of induration (00 mm if there is no induration) rather than as positive or negative
- Record date and time of reading
- Record name of person reading TST
- Interpret TST results based on established breakpoints (See page 10)

Patient Education

- Explain the significance of a positive TST and the next steps in evaluation
- Provide patient/parent with appropriate educational materials
- Provide documentation of TST

A reaction (induration) that develops more than 48-72 hours after administration should be measured and considered the result. Instruct patients who had no reaction at 48-72 hours to return for evaluation if this occurs

- Inform family of possibility that TB control personnel will test other household members in search of a source case, especially in TST reactors who are less than 5 years old

Counsel family that there is no need for further TB skin testing if the child has a positive TST result

APPENDIX B

ADHERENCE STRATEGIES AT VARIOUS AGES

AGE	ADHERENCE STRATEGY
Infant birth-1 year	Parents and caregivers must comprehend need for treatment. To promote compliance, offer medication when baby is hungry. Pill can be crushed and dissolved in small amount of warm water, then mixed with milk. Mix with approximately 10 cc of breast milk or formula. INH liquid contains sorbitol, which can cause diarrhea. Therefore, it is not recommended. Crushed INH can also be mixed with baby food such as cereal or fruit and given by spoon.
Toddler 1-3 years	Use distraction. Disguise taste by mixing with a food of the child's choice. Expect difficulty but be persistent. Give simple explanations. Use incentives for each daily dose if needed.
Preschooler 3-5 years	Give simple explanations. Allow some negotiation for time of medication administration or vehicle used. Offer rewards and verbal praise, but be consistent and assertive.
School age 5-12 years	Discuss treatment plan with child. Provide simple and accurate information. Child may be able to swallow pills whole. Child should receive DOT if possible. School DOT 2 or 3x/week may be an option. May be indicated to reduce dose-related side effects.
Adolescent 12-18 years	Use a calendar to document adherence Involve adolescent in decision making. Potential for poor adherence. School DOT is an excellent option, if available.

APPENDIX C

SAMPLE LETTERS FOR DOCUMENTING TST AND LTBI TREATMENT

Tuberculin Skin Test Record

To Whom it May Concern:

The following is a record of Mantoux tuberculin skin testing:

Name:_____ Date of birth: _____

Date/time test administered: _____

Administered by:_____

Manufacturer of PPD:_____

Expiration date: _____ Lot Number: _____

Date/time test read: _____ Read by: _____

Results: _____mm of induration

Treatment Completion Letter

To Whom it May Concern:

The following is a record of evaluation and treatment for TB infection:

Name:_____ Date of birth: _____

TB Skin Test: Date: _____ Results: _____mm of induration

Chest x-ray: Date: _____ Results: _____

Date medication started: _____ Date completed:_____

Medication(s): _____

This person is not contagious. He/she will always have a positive TB skin test. The skin test should not be repeated.

Annual or serial chest radiographs are not necessary for follow up, and are only indicated in the presence of serious or chronic respiratory illness. If you need any further information, please contact this office.

_____

Signature of Provider Date

REFERENCES

1. American Thoracic Society and Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Resp Crit Care Med.* 2000; 161 (4): s221-243.
2. American Academy of Pediatrics, Committee on Infectious Diseases. Tuberculosis. In L.K. Pickering (Ed.), 2009 *Red Book: Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2009:680-701.
3. Pediatric Tuberculosis Collaborative Group. Targeted Tuberculin Skin Testing and Treatment of Latent Tuberculosis Infection in Children and Adolescents. *Pediatrics* 2004; 114 (4): 1175-1201.
4. Centers for Disease Control and Prevention. National Center for HIV, STD, and TB Prevention, Division of Tuberculosis Elimination. Surveillance Slides Available: www.cdc.gov/tb/pubs/slidesets/surv2007/default.htm
5. Starke, J.R. & Smith, M. Tuberculosis. In R. Feigen & J.D. Cherry eds., *Textbook of Pediatric Infectious Diseases*. 5th ed. Philadelphia, PA: WB Saunders; 2004:1337-1379.
6. Donald, P.R., Fourie, P.B., & Grange, J.M. eds. The tuberculin skin test. In *Tuberculosis in Childhood* (1st ed., pp. 119-131) Hatfield, Pretoria: J.L. van Schaik Publishers; 1999:119-131.
7. *Physicians' Desk Reference*, 57th ed. Montvale, NJ. Medical Economics Company. 2003:765.
8. Working Group on Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children; June 20, 2008; 1-250. Available at: http://aidsinfo.nih.gov/contentfiles/Pediatric_OI.pdf
9. Centers for Disease Control and Prevention. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2000; 49(9) 185-189.

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RESOURCES

For Healthcare Providers

CDC Fact Sheets: www.cdc.gov/tb/pubs/TBfactsheets.htm

CDC Mantoux TST Wall Chart:
www.cdc.gov/tb/pubs/Posters/Mantoux.htm

Loeffler AM, Lobato MN. Tuberculosis. In: McInerny TK, Adam HM, Campbell D, Kamat DM, Kelleher KJ, eds. *American Academy of Pediatrics Textbook of Pediatric Care*. Elk Grove Village, IL: American Academy of Pediatrics; 2006

Pediatric TB for the Private Provider, Southeastern National Tuberculosis Center: sntc.medicine.ufl.edu/products.aspx

Pediatric Tuberculosis: A Guide to the Gastric Aspirate Procedure:
www.nationaltbcenter.edu/products/product_details.cfm?productID=ONL-06

Pediatric Tuberculosis: An Online Presentation:
www.nationaltbcenter.ucsf.edu/pediatric_tb/resources.cfm

Centers for Disease Control and Prevention. *Guidelines for the prevention and treatment of opportunistic infections among HIV-exposed and HIV-infected children*]. MMWR 2009;58 (RR-4):19-28.

LTBI Card (Testing & Treatment Record):
www.umdnj.edu/globaltb/products/ltbicard.htm

For Parents

What Parents Need to Know About Tuberculosis (TB) Infection in Children:
www.umdnj.edu/globaltb/products/pedsltbi.htm

Websites

Find TB Resources: www.findtbresources.org/scripts/index.cfm

Charles P. Felton National TB Center: www.harlemtbcenter.org/index.htm

Regional Training & Medical Consultation Centers

Francis J. Curry National Tuberculosis Center:
www.nationaltbcenter.ucsf.edu

Southeastern National Tuberculosis Center: sntc.medicine.ufl.edu

NJMS Global Tuberculosis Center: www.umdnj.edu/globaltb

Heartland National TB Center: www.heartlandntbc.org

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Global
Tuberculosis
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