

TUBERCULOSIS

RATIONALE

The number of tuberculosis (TB) cases, and the TB rate, remained level from 2014 to 2015 with 2,133 cases and a rate of 5.5 per 100,000 population.¹ In contrast, the number of TB cases reported nationwide increased by nearly three percent, to 9,563 cases (3.0 per 100,000). In 2015, California reported 20 percent of the nation's cases.² Although declines in TB have been small in recent years; TB cases in California have declined by 60 percent since the most recent peak in 1992. Thirty-six cases of TB were reported in children under the age of five in 2015, a decline from the previous year when 56 cases were reported in this most vulnerable group. During 2011-2015, 10% of TB cases in children younger than 5 years of age involved the central nervous system, a serious manifestation of TB disease that leaves many children with permanent disability. TB in children less than 15 years old made up 4% of overall California TB cases during 2011-2015.³ Children with TB represent only a small percentage of California's total cases, but indicate recent disease transmission, most likely from an undiagnosed family member or caretaker and a missed opportunity for preventing the spread of TB disease. TB infection might manifest as TB disease or latent tuberculosis infection (LTBI). LTBI is a condition in which a person is infected with *M tuberculosis*, does not currently have active TB disease, but is at risk of progression to active disease. Individuals with LTBI are asymptomatic and not infectious. In order to prevent substantial morbidity and disability as well as to achieve the goal of elimination of TB in California, TB prevention through screening and treating for LTBI is crucial, particularly in children who have an entire lifetime during which they could progress to active TB disease if TB infection is not identified or treated.

The most important steps to reducing the number of children with TB disease are prompt and thorough contact investigation of persons with known or suspected TB and active monitoring of infected contacts until completion of treatment.

The California Child Health and Disability Prevention (CHDP) Program supports the recommendations of the California Department of Public Health's Tuberculosis Control Branch for tuberculosis screening. The California Department of Public Health, Tuberculosis Control Branch recommends screening:

1. Those who are at increased risk of exposure to TB and thus increased risk of LTBI;
2. Those at increased risk of progression from LTBI to active disease based on immunosuppressing medical conditions.^{4,5}

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Only the Mantoux tuberculin skin test (TST) using purified protein derivative is currently approved for reimbursement by CHDP. However, both the TST and the Interferon- γ Release Assay (IGRA) are covered by Medi-Cal starting at birth, for identification of children infected with *M. tuberculosis*. The TST is preferred for routine targeted testing for latent TB infection for US-born children, while the IGRA is preferred for routine targeted testing for latent TB infection among foreign-born children 2 years of age or older.

SCREENING REQUIREMENTS

- Assess all children for risk of exposure to tuberculosis at least at each preventive pediatric health care visit according to American Academy of Pediatrics' Bright Futures schedule (1 month, 6 months, 12 months, and then annually). Questions for determining risk of LTBI in children in California may be found in Table 1: [California Tuberculosis Risk Assessment: Pediatrics](#).⁶
- Children with TB symptoms or an abnormal chest x-ray consistent with active TB should be evaluated for TB disease. A negative TST or IGRA does not rule out active TB disease.
- For children who are at increased risk of acquiring LTBI (including those with an identified risk factor on the risk assessment), test for LTBI.
- For children who are more likely to progress to active TB if exposed (children with HIV, organ transplant, TNF-alpha inhibitors, or other condition associated with significant immunosuppression), test for LTBI
- When LTBI testing is indicated, the clinician may place a TST or draw an IGRA, depending on the child's birthplace and age.
- The *only* contraindication to the TST is history of a severe reaction (e.g., necrosis, blistering, anaphylactic shock, or ulcerations) to a previous TST.⁷
- Administer the TST as described in Basics of TST Administration section.
- Read the TST 48 to 72 hours after placement and record the results in millimeters (mm) of induration, not erythema. Measure the diameter of the induration transversely to the long axis of the forearm. Trained personnel, not parents, must read the skin test. (Please see Table 2: Guidelines for Definition of a Positive Tuberculin Skin Test)
- If the child fails to return for scheduled reading:
 - Only a positive reaction may still be measured up to one week after testing.

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- Repeat the TST if no positive reaction can be measured when the child does return.
- When questions arise about the reading of a TST, consult your local health department TB Control Program.
- Testing for tuberculosis is not a universal requirement for school entry in California. However, California law allows local health departments to require TB testing for school entry based on local epidemiology.⁸ Check with your local health department for local policy.

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Table 1: California Tuberculosis Risk Assessment: Pediatrics⁶

Use this form to identify **asymptomatic children** for latent TB infection (LTBI) testing. Re-testing should only be done in persons who previously tested negative¹, and have new risk factors since the last assessment.

If initial negative screening test occurred prior to 6 months of age, repeat testing should occur at age 6 months or older

Check appropriate risk factor boxes below.

LTBI testing is recommended if any of the 5 boxes below is checked.

If LTBI result is positive and active TB disease is ruled out, LTBI treatment is recommended.

- Foreign-born** person from a country with an elevated TB rate
*Any country other than the United States, Canada, Australia, New Zealand, or a country in Western or Northern Europe.
Interferon Gamma Release Assay (IGRA) is preferred over Tuberculin Skin Test (TST) for foreign-born persons ≥2 years old.*
- Immunosuppression**, current or planned
HIV infection, organ transplantation, treatment with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥2 mg/kg/day, or ≥15 mg/day, for ≥2 weeks) or other immunosuppressive medication
- Close **contact** to someone with infectious TB disease at any time
Recent cases of infectious TB should be reported to your local public health department.
- Foreign travel or residence** of ≥ 1 month consecutively in a country with an elevated TB rate
*Any country other than the United States, Canada, Australia, New Zealand, or a country in Western or Northern Europe.
TB testing should occur at least 8 weeks after the child left the country with elevated TB prevalence*

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Table 2: Guidelines for Definition of a Positive Tuberculin Skin Test⁴

Reaction Size*	Definition of Mantoux Skin Test (5 TU PPD)
5-9 mm induration	<p>Positive</p> <p>Persons known or suspected to have HIV infection</p> <p>Recent contacts to an active case of pulmonary or laryngeal TB</p> <p>Persons with fibrotic changes seen on chest radiograph consistent with TB</p> <p>Immunosuppressed individuals</p>
≥ 10 mm induration	<p>Positive</p> <p>All persons except those in above</p>

*Interpretation of the skin test should be made without regard to previous Bacillus of Calmette-Guérin (BCG) vaccine administration.

NOTE: The Centers for Disease Control and Prevention classification of positive reactions includes a category 15 mm for all other children, e.g., low risk groups. This classification is not recognized by public health departments in California because PPD cross reactivity to other mycobacteria is low and TB prevalence rates are higher due to a greater number of individuals in high risk groups compared to the rest of the United States.

Bright Futures*

Please refer to the [AAP Bright Futures Recommendations for Preventive Pediatric Health Care](#) for TB risk assessment and testing guidelines.

[Bright Futures 3rd Edition Guidelines, Pocket Guide, Tool & Resource Kit](#)

CONSIDERATIONS FOR REFERRAL TREATMENT AND/OR FOLLOW-UP

- Refer any child for diagnosis and treatment who has symptoms consistent with active TB disease regardless of LTBI test results.
- Evaluate all children with positive TST or IGRA results and provide or refer for a medical evaluation, chest x-ray, and any other laboratory studies needed for the diagnosis of TB disease.
- Report to the local health department any confirmed or suspected case of TB disease within one day of identification (California Code of Regulations, Title 17, Section 2500). Contact your local health department for specific instructions about reporting children with latent TB infection, or converters, and for additional information regarding therapy.

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- If TB disease is not found, place children and adolescents with positive TST/IGRA on LTBI therapy, unless medically contraindicated.
- Consult with your local health department Tuberculosis Control Program for guidance on the recommended treatment regimen. See “Emphasis on shorter regimens for treatment of LTBI” below.
- Close contacts of persons with active TB disease are candidates for LTBI therapy if:
 - TST/IGRA is positive and active TB disease has been ruled out with a chest x-ray, symptom screen, and if indicated, sputum acid-fast-bacilli smears, cultures, and nucleic acid amplification testing.
 - TST/IGRA is negative, and child is less than 5 years of age or immunosuppressed. These children should be treated for LTBI (“window prophylaxis”) until the child is at least 6 months old and the screening TB test is repeated at least 8 weeks after their last possible exposure to TB. If the second test is positive, or the child is still severely immunosuppressed, a full course of LTBI treatment should ensue. Otherwise, treatment can be stopped after a negative screening test at 8 weeks.
 - In all individuals with negative TST/IGRA, ensure that the screening test occurred at least 8 weeks after the last contact when the TB case was infectious; if not, repeat the test at this point.
- Refer all household contacts of persons being treated for active TB disease to the local health department for follow-up or contact tracing.

BACILLUS of CALMETTE-GUÉRIN (BCG) VACCINATION

Many countries use BCG as part of their TB control programs, especially for infants, to prevent the development of disseminated or meningeal disease. BCG can cause false positive TST reactions in some patients. For this reason, IGRA is preferred over the tuberculin skin test for foreign-born children ≥ 2 years of age. In BCG vaccinated, asymptomatic, immunocompetent children with a positive TST, it may be appropriate to confirm a positive TST with an IGRA. If IGRA is not done, the TST result should be considered the definitive result. IGRAs can be used in children < 2 years of age, however, there is an overall lack of data in this age group, which complicates interpretation of negative or indeterminate results. However, a positive IGRA in a child < 2 years should be considered reliable.

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BASICS OF TST ADMINISTRATION

The Mantoux tuberculin skin test (TST) is the preferred screening method for most US-born children and children younger than 2 years of age. The antigen is aspirated into a disposable plastic syringe with a No. 26 gauge, short-bevel needle no more than one (1) hour before use. Purified protein derivative containing five tuberculin units (5 TU) in 0.1 ml by intradermal injection on the volar aspect of the forearm to produce a six to ten mm wheal. If no wheal is formed then the TST must be placed on an alternative site and documented.

The TST may be placed on the same day that a measles-containing vaccine is given. If not placed on the same day, it is recommended that you wait four to six weeks before placing a Mantoux tuberculin skin test.⁷

When to repeat a risk assessment and testing

Risk assessments should be completed on new patients, patients thought to have new potential exposures to TB since last assessment, and during routine pediatric well-child visits, according to the American Academy of Pediatrics' Bright Futures schedule. Repeat risk assessments should be based on the activities and risk factors specific to the child. High-risk children and adolescents who volunteer or work in health care settings might require annual testing and should be considered separately. Re-testing should only be done in persons who previously tested negative and have new risk factors since the last assessment (unless they were less than 6 months of age at the time of testing). In general, new risk factors would include new close contact with an infectious TB case or new immunosuppression, but could also include foreign travel.

Emphasis on shorter regimens for treatment of LTBI

Shorter regimens for treating latent TB infection have been shown to be as effective as 9 months of isoniazid, and are more likely to be completed. Use of these shorter regimens is preferred in most patients, although the 12-week regimen is not recommended for children under age 2 years, children on antiretroviral medications, or pregnant adolescents. Drug-drug interactions and contact to drug resistant TB are other contra-indications for shorter regimes.

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Shorter duration LTBI treatment regimens

Medication	Frequency	Duration	Notes
Rifampin	Daily	4 months	
Isoniazid + rifapentine	Weekly	12 weeks*	Directly observed treatment currently recommended by CDC

*11-12 doses in 16 weeks required for completion. Doses should be given at least 72 hours apart. See CDPH Fact Sheet for more information on the 12-dose regimen: <http://www.cdph.ca.gov/programs/tb/Documents/TBCB-INH-RIF-LTBI-fact-sheet.pdf>

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Resources

[Curry International Tuberculosis Center](#)

[California Department Public Health Tuberculosis Control Branch:](#)

TB in Teenagers Fact Sheet (<http://www.cdph.ca.gov/programs/tb/Documents/TBCB-TB-In-Teenagers-CA-Fact-Sheet.pdf>)

Fact Sheet: 12-dose Isoniazid/Rifapentine Regimen for Latent TB Infection Treatment (<http://www.cdph.ca.gov/programs/tb/Documents/TBCB-INH-RIF-LTBI-fact-sheet.pdf>)

References

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8. California Health and Safety Code. §121485 – 121520. Retrieved July 26, 2016.

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