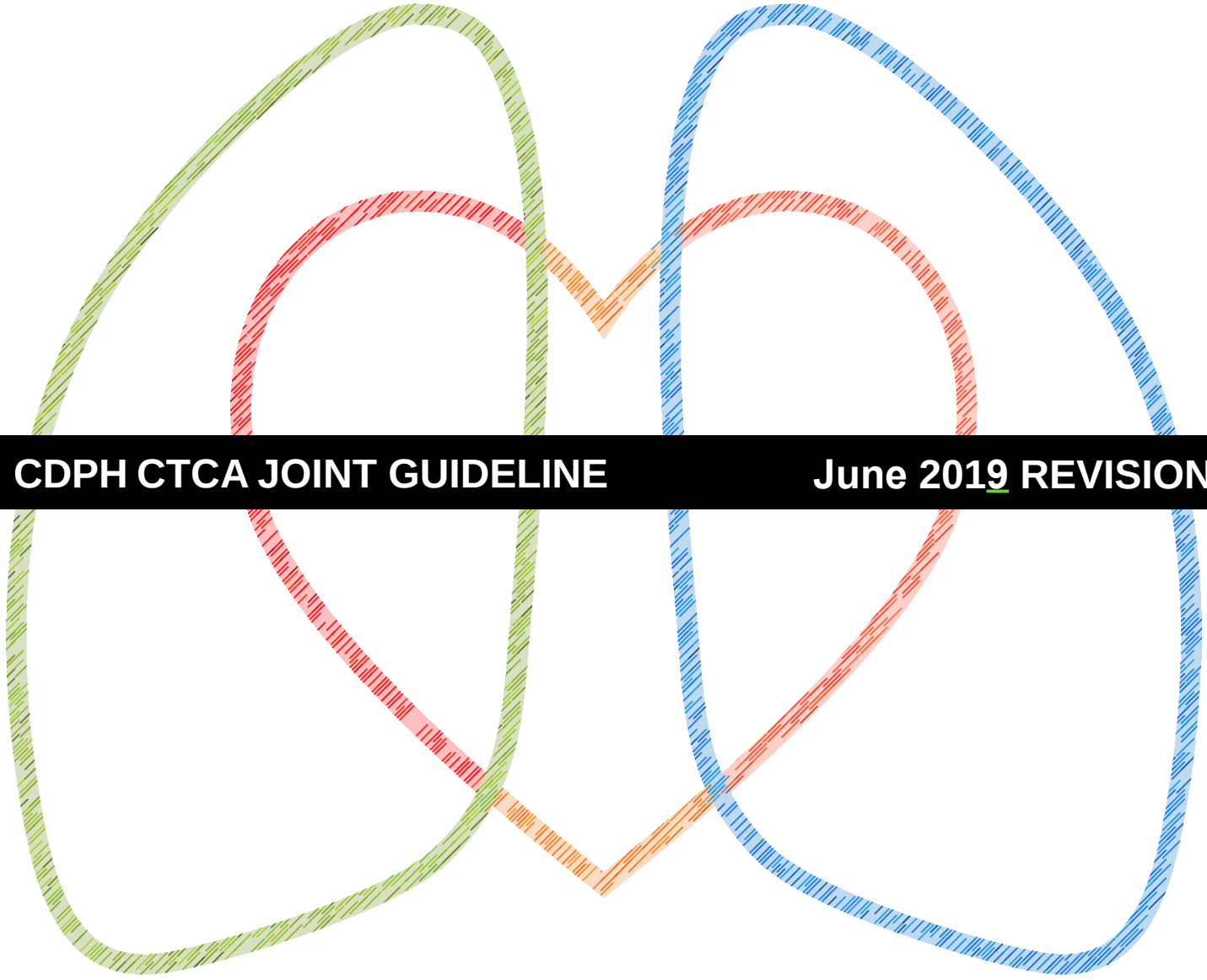
Latent Tuberculosis Infection Guidance for Preventing Tuberculosis in California



CDPH CTCA JOINT GUIDELINE **June 2019 REVISION**

CDPH California Department of PublicHealth

CTCA CALIFORNIA TUBERCULOSIS CONTROLLERS ASSOCIATION

Update: Added ***Definition of a positive tuberculin skin test***
to Selecting a Test for Latent TB Infection (LTBI), pg 10
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Introduction to this *LTBI Guidance*

The purpose of this document is to provide clear, simple guidance for providers in California on preventing tuberculosis. The document consists primarily of a compilation of previously published fact sheets that provide guidance on screening for and treatment of latent tuberculosis infection (LTBI). The content reflects consensus recommendations of experts in the clinical and public health management of LTBI in California based on existing guidelines, medical literature, and clinical practice. The workgroup consisted of members of the California Tuberculosis Controllers Association (CTCA) and staff from the California Department of Public Health (CDPH), Tuberculosis Control Branch.

The intended users of this updated guidance are healthcare providers, public health programs, and healthcare administrators who may be treating, managing, or developing screening and treatment policies for LTBI.

The format of this document is intended to allow busy clinicians to find recommendations easily and quickly. Individual sections of the document can be printed, saved, and altered for incorporation into clinical protocols, educational materials, and electronic health records.

This guidance is not intended to be exhaustive and no guidance can anticipate every situation. Seek consultation from your local TB control program or other sources of expert consultation listed in the Resources section of this document.

Although updated national guidelines for treatment of LTBI are being developed to be released in the future (date unknown), several recent studies as well as the experience of public health programs with using short course regimens for LTBI treatment provide evidence to support the release of updated guidance.

Background

LTBI is the presence of *Mycobacterium tuberculosis* in the body without evidence of TB disease (i.e., signs and symptoms, radiographic, or bacteriologic evidence of TB). People with LTBI are asymptomatic and non-infectious. Because LTBI can persist for decades, people with LTBI are at risk for developing TB disease if LTBI is not treated.

Although rates of TB disease in California have steadily declined, this trend has slowed significantly since 2000. More than 2,000 cases of active TB disease occur in California each year and approximately 200 Californians die each year with active TB disease.

Approximately 80% of TB cases result from longstanding LTBI and therefore represent a missed opportunity for prevention.

In California there are estimated to be more than 2 million people with LTBI, which represents a substantial reservoir of people who may develop TB disease in the future. Most people with LTBI are unaware of their infection and are untreated.

Screening for and treatment of LTBI is an essential component of preventive care as recommended by the United States Preventive Services Task Force.

Preventing TB disease through finding and treating people with LTBI is crucial for ensuring that TB disease continues to decline in California.

Who to Test: Using the Risk Assessment

Because approximately 80% of tuberculosis is due to the reactivation of LTBI, routine assessment of TB risk followed by testing and treatment are crucial to preventing TB and its associated morbidity and mortality. However, routine testing of low risk populations is not recommended and may result in unnecessary evaluations and treatment because of falsely positive test results.

CDPH and CTCA created the TB Risk Assessment tools to assist clinical providers in determining whether or not to test for LTBI. There are separate Adult and Pediatric tools in this document that use the same basic testing strategy and risk factors but with minor differences.

The risk assessment tools are meant for use in busy clinical settings. They are designed to be simple and streamlined while being consistent with literature, other guidelines, and with the epidemiology of tuberculosis in California. However, not all situations are addressed in these tools and not all risk factors included in other guidelines are included here. The User Guides that follow each risk assessment provide additional information on specific populations and common situations. Additional guidance and answers to questions may be provided by local or state TB control programs.

California Tuberculosis Risk Assessment Adults

- Use this tool to identify asymptomatic **adults** for latent TB infection (LTBI) testing.
- **Do not repeat testing** unless there are **new risk factors** since the last test.
- Do not treat for LTBI until active TB disease has been excluded:
  For patients with TB symptoms or an abnormal chest x-ray consistent with active TB disease, evaluate for active TB disease with a chest x-ray, symptom screen, and if indicated, sputum AFB smears, cultures and nucleic acid amplification testing. A negative tuberculin skin test or interferon gamma release assay does not rule out active TB disease.

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

☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month
- Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe
- If resources require prioritization within this group, prioritize patients with at least one medical risk for progression (see the California Adult Tuberculosis Risk Assessment User Guide for this list).
- Interferon Gamma Release Assay is preferred over Tuberculin Skin Test for non-U.S.-born persons ≥2 years old

☐ **Immunosuppression,** current or planned
HIV infection, organ transplant recipient, treated with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥15 mg/day for ≥1 month) or other immunosuppressive medication

☐ **Close contact** to someone with infectious TB disease during lifetime

Treat for LTBI if LTBI test result is positive and active TB disease is ruled out.

☐ **None**; no TB testing is indicated at this time.

Provider Name: _____

Assessment Date: _____

Patient Name: _____

Date of Birth: _____

See the California Adult Tuberculosis Risk Assessment User Guide for more information about using this tool. To ensure you have the most current version, go to the RISK ASSESSMENT page at: https://cdph.ca.gov/tbcb

California Adult TB Risk Assessment User Guide

Avoid testing persons at low risk

Routine testing of persons without risk factors is not recommended and may result in unnecessary evaluations and treatment because of falsely positive test results.

Prioritize persons with risks for progression

If health system resources do not allow for testing of all non-U.S. born persons from a country with an elevated TB rate, prioritize patients with at least one of the following medical risks for progression:

- diabetes mellitus
- smoker within past 1 year
- end stage renal disease
- leukemia or lymphoma
- silicosis
- cancer of head or neck
- intestinal bypass/gastrectomy
- chronic malabsorption
- body mass index ≤20
- History of chest x-ray findings suggestive of previous or inactive TB (no prior treatment). Includes fibrosis or non-calcified nodules, but does not include solitary calcified nodule or isolated pleural thickening. In addition to LTBI testing, evaluate for active TB disease.

United States Preventive Services Task Force

The USPSTF has recommended testing persons born in or former residents of, a country with an elevated tuberculosis rate and persons who live in or have lived in high-risk congregate settings such as homeless shelters and correctional facilities. Because the increased risk of exposure to TB in congregate settings varies substantially by facility and local health jurisdiction, clinicians are encouraged to follow local recommendations when considering testing among persons from these congregate settings. The USPSTF did not review data supporting testing among close contacts to persons with infectious TB or among persons who are immunosuppressed because these persons are recommended to be screened by public health programs or by clinical standard of care.

Children

This risk assessment tool is intended for adults. A risk assessment tool created for use in California for children is available at the following URL: http://www.cdph.ca.gov/programs/tb/Documents/TBCB-CA-Pediatric-TB-Risk-Assessment.pdf

Local recommendations

Local recommendations and mandates should also be considered in testing decisions. Local TB control programs can customize this risk assessment according to local recommendations. **Providers should check with local TB control programs for local recommendations.** A directory of TB Control Programs is available at the following URL: https://www.ctca.org/locations.html

Mandated testing and other risk factors

Several risk factors for TB that have been used to select patients for TB screening historically or in mandated programs are not included among the components of this risk assessment. This is purposeful in order to focus testing on patients at highest risk. However, certain populations may be mandated for testing by statute, regulation, or policy. This risk assessment does not supersede any mandated testing. Examples of these populations include: healthcare workers, residents or employees of correctional institutions, substance abuse treatment facilities, homeless shelters, and others.

Age as a factor

Age (among adults) is not considered in this risk assessment. However, younger adults have more years of expected life during which progression from latent infection to active TB disease could develop. Some programs or clinicians may additionally prioritize testing of younger non-U.S.-born persons when all non-U.S.-born are not tested. An upper age limit for testing has not been established but could be appropriate depending on individual patient TB risks, comorbidities, and life expectancy.

Foreign travel

Travel to countries with an elevated TB rate may be a risk for TB exposure in certain circumstances (e.g., extended duration, likely contact with persons with infectious TB, high prevalence of TB in travel location, non-tourist travel). The duration of at least 1 consecutive month to trigger testing is intended to identify travel most likely to involve TB exposure. TB screening tests can be falsely negative within the 8 weeks after exposure, so are best obtained 8 weeks after return from travel.

When to repeat a test
Re-testing should only be done in persons who previously tested negative, and have new risk factors since the last assessment. In general, this would include new close contact with an infectious TB case or new immunosuppression, but could also include foreign travel in certain circumstances.

When to repeat a risk assessment
The risk assessment should be administered at least once. Persons can be screened for new risk factors at subsequent preventive health visits.

IGRA preference in BCG vaccinated
Because IGRA has increased specificity for TB infection in persons vaccinated with BCG, IGRA is preferred over the TST in these persons. Most persons born outside the United States have been vaccinated with BCG.

Previous or inactive tuberculosis
Chest radiograph findings consistent with previous or inactive TB include fibrosis or non-calcified nodules, but do not include a solitary calcified nodule or isolated pleural thickening. Persons with a previous chest radiograph showing findings consistent with previous or inactive TB should be tested for LTBI. In addition to LTBI testing, evaluate for active TB disease.

Negative test for LTBI does not rule out active TB disease
It is important to remember that a negative TST or IGRA result does not rule out active TB disease. In fact, a negative TST or IGRA in a patient with active TB disease can be a sign of extensive disease and poor outcome.

Symptoms that should trigger evaluation for active TB disease
Patients with any of the following symptoms that are otherwise unexplained should be evaluated for active TB disease: cough for more than 2-3 weeks, fevers, night sweats, weight loss, and hemoptysis.

How to evaluate for active TB disease
Evaluate for active TB disease with a chest x-ray, symptom screen, and if indicated, sputum AFB smears, cultures and nucleic acid amplification testing. A negative tuberculin skin test or interferon gamma release assay does not rule out active TB disease

Most patients with LTBI should be treated
Persons with risk factors who test positive for LTBI should generally be treated once active TB disease has been ruled out. However, clinicians should not feel compelled to treat persons who have no risk factors but have a positive test for LTBI.

Emphasis on short course 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. Drug-drug interactions and contact to drug resistant TB are typical reasons these regimens cannot be used.

Shorter duration LTBI treatment regimens

Medication	Frequency	Duration
Rifampin	Daily	4 months
Isoniazid + rifapentine	Weekly	12 weeks*

* 11-12 doses in 16 weeks required for completion.

Patient refusal of recommended LTBI treatment
Refusal should be documented. Recommendations for treatment should be made at future encounters with medical services. If treatment is later accepted, TB disease should be excluded and CXR repeated if it has been more than 6 months from the initial evaluation; or more than 3 months if there is immunosuppression, or the prior CXR was abnormal and consistent with potentially active TB disease.

Resources
Fact Sheets for LTBI Regimens, Isoniazid+Rifapentine, Rifampin, and Isoniazid are available at the following URL: www.cdph.ca.gov/LTBITreatment/

U.S. Preventive Services Task Force Latent TB Infection Screening Recommendations are available at the following URL: https://www.uspreventiveservicestaskforce.org/Page/Document/ UpdateSummaryFinal/latent-tuberculosis-infection-screening

Abbreviations
AFB= acid-fast bacilli BCG= Bacillus Calmette-Guérin
CXR= chest x-ray DOT= directly observed therapy
IGRA=interferon gamma release assay LTBI= latent TB infection
MDR =multiple drug resistant NAAT= nucleic acid amplification testing
SAT= self-administered therapy TST= tuberculin skin test

California Tuberculosis Risk Assessment Pediatrics

- Use this tool to identify asymptomatic **children** for latent TB infection (LTBI) testing.
- **Do not repeat testing** unless there are **new risk factors** since the last test.
  If initial negative screening test occurred prior to 6 months of age, repeat testing should occur at age 6 months or older
- Do not treat for LTBI until active TB disease has been excluded:
  For children with TB symptoms or abnormal chest x-ray consistent with active TB disease, evaluate for active TB disease with a chest x-ray, symptom screen, and if indicated, sputum AFB smears, cultures and nucleic acid amplification testing. A negative tuberculin skin test or interferon gamma release assay does not rule out active TB disease.

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

☐ **Birth, travel, or residence** in a country with an elevated TB rate for at least 1 month

- Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe
- If resources require prioritization within this group, prioritize patients with at least one medical risk for progression (see the California Adult Tuberculosis Risk Assessment User Guide for this list).
- Interferon Gamma Release Assay is preferred over Tuberculin Skin Test for non-U.S.-born persons ≥2 years old

☐ **Immunosuppression,** current or planned

HIV infection, organ transplant recipient, treated 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 during lifetime

Treat for LTBI if LTBI test result is positive and active TB disease is ruled out.

☐ **None**; no TB testing is indicated at this time.

Provider Name: _____

Assessment Date: _____

Patient Name: _____

Date of Birth: _____

See the California Pediatric TB Risk Assessment User Guide for more information about using this tool.To ensure you have the most current version, go to the RISK ASSESSMENT page at: https://cdph.ca.gov/tbcb

California Pediatric TB Risk Assessment User Guide

Avoid testing persons at low risk

Routine testing of persons without risk factors is not recommended and may result in unnecessary evaluations and treatment because of falsely positive test results.

Local recommendations, mandated testing and other risk factors

Several risk factors for TB that have been used to select children for TB screening historically or in mandated programs are not included among the 3 components of this risk assessment. This is purposeful in order to focus testing on children at highest risk. However, certain populations may be mandated for testing by statute, regulation, or policy. This risk assessment does not supersede any mandated testing. Testing can also be considered in children with frequent exposure to adults at high risk of TB infection, such as those with extensive foreign travel in areas with high TB rates. Local recommendations should also be considered in testing decisions. Local TB control programs and clinics can customize this risk assessment according to local recommendations. **Providers should check with local TB control programs for local recommendations.** A directory of TB Control Programs is available at the following URL: https://www.ctca.org/locations.html.

Most patients with LTBI should be treated

Persons with risk factors who test positive for LTBI should generally be treated once active TB disease has been ruled out with a physical exam, chest radiograph and, if indicated, sputum smears, cultures, and nucleic acid amplification testing (NAAT). However, clinicians should not feel compelled to treat persons who have no risk factors but have a positive test for LTBI.

When to repeat a risk assessment and testing

Risk assessments should be completed for new patients, patients thought to have new potential exposures to TB since last assessment, and during routine pediatric well-child visits. Repeat risk assessments should be based on the activities and risk factors specific to the child. Children 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 <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.

Immunosuppression

The exact level of immunosuppression that predisposes to increased risk for TB progression is unknown. The threshold of steroid dose and duration used in the Pediatric TB Risk Assessment are based on data in adults and in accordance with ACIP recommendations for live vaccines in children receiving immunosuppression.

Foreign travel or residence

Travel or residence in countries with an elevated TB rate may be a risk for TB exposure in certain circumstances (e.g., extended duration, likely contact with persons with infectious TB, high prevalence of TB in travel location, non-tourist travel). The duration of at least 1 consecutive month to trigger testing is intended to identify travel most likely to involve TB exposure. TB screening tests can be falsely negative within the 8 weeks after exposure, so are best obtained 8 weeks after a child's return.

IGRA preference in non-U.S.-born children ≥2 years old

Because IGRA has increased specificity for TB infection in children vaccinated with BCG, IGRA is preferred over the tuberculin skin test for non-U.S.-born children ≥2 years of age. 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 test results. In BCG vaccinated 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.

Negative test for LTBI does not rule out active TB

It is important to remember that a negative TST or IGRA result does not rule out active TB disease. A negative TST or IGRA in a patient with active TB disease can be a sign of extensive disease. Any suspicion for active TB disease or extensive exposure to TB should prompt an evaluation for active TB disease, including physical exam, symptom review, and 2-view chest x-ray.

Emphasis on short course 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 <2 years of age or children on antiretroviral medications. It is under study in pregnancy. Drug- drug interactions and contact to drug resistant TB are other contra-indications for shorter regimens.

Shorter duration LTBI treatment regimens

Medication	Frequency	Duration
Rifampin	Daily	4 months
Isoniazid + rifapentine	Weekly	12 weeks*

* 11-12 doses in 16 weeks required for completion.

Refusal of recommended LTBI treatment

Refusal should be documented. Recommendations for treatment should be made at future encounters with medical services. If treatment is later accepted, TB disease should be excluded and chest x-ray repeated if it has been more than 6 months from the initial evaluation for children 5 years or older and 3 months for children less than 5 years of age.

Symptoms that should trigger evaluation for active TB

Patients with any of the following symptoms that are otherwise unexplained should be evaluated for active TB disease: cough for more than 2-3 weeks, fevers, night sweats, weight loss, lymphadenopathy, hemoptysis or excessive fatigue.

Resources

Fact Sheets for LTBI Regimens, Isoniazid+Rifapentine, Rifampin, and Isoniazid are available at the following URL: www.cdph.ca.gov/LTBITreatment/

American Academy of Pediatrics, Red Book Online, Tuberculosis are available at the following URL: https://redbook.solutions.aap.org/chapter.aspx?sectionid=189640207&bookid=2205

Abbreviations

AFB= acid-fast bacilli BCG= Bacillus Calmette-Guérin
CXR= chest x-ray DOT= directly observed therapy
IGRA=interferon gamma release assay LTBI= latent TB infection
MDR =multiple drug resistant NAAT= nucleic acid amplification testing
SAT= self-administered therapy TST= tuberculin skin test

Selecting a Test for Latent TB Infection (LTBI)

IGRA is preferred; TST is acceptable

Interferon gamma release assays (IGRAs), such as Quantiferon or T-Spot TB, are preferred over the tuberculin skin test (TST) because of increased specificity and lack of need for a second visit for reading the test. A TST is acceptable when an IGRA is not available, too costly or too logistically difficult to obtain.

IGRA in non-U.S.-born

IGRA is especially helpful in persons who have previously been BCG (Bacillus Calmette-Guerin)-vaccinated (most persons born outside the U.S.) For non-U.S. born, immunocompetent, BCG-vaccinated persons with a positive TST, IGRA can be used to confirm or rule out LTBI (i.e., consider TST positive and IGRA negative to not be LTBI). Exceptions might include situations where infection is highly likely such as among recent known contacts to active TB cases where transmission has been confirmed in other contacts with similar level of exposure.

IGRA in children

Because IGRA has increased specificity for TB infection in children vaccinated with BCG, IGRA is preferred over the tuberculin skin test for non-U.S. born children ≥2 years of age. 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 test results. In BCG vaccinated immunocompetent children with a positive TST, it may be appropriate to perform an IGRA to confirm the LTBI diagnosis (i.e., consider TST positive and IGRA negative to not be LTBI). If IGRA is not done, the TST result should be considered the definitive result.

Testing persons with very high risk for progression

In patients with a very high risk for progression if infected (e.g., TNF-α inhibitor use, HIV infection, organ transplant) some experts perform a second test if the first test is negative, using a positive on either test to determine LTBI status. Patients with a CD4 count of <200 cells/μL should be retested when their CD4 count is ≥200 cells/μL.

Testing persons without TB risk factors

Although testing persons without risk factors is discouraged, when it cannot be avoided for administrative or policy reasons (e.g., previously negative healthcare workers who have no known new TB exposure), using two tests might be appropriate: if the first test is positive, a second test (TST or IGRA) can be performed using a negative on either test to determine LTBI status.

Serial testing

Choice of LTBI test for serial testing programs such as for occupational health should consider additional factors such as test performance and TB risk. This choice should be informed by discussion with local TB control programs.

Definition of a positive tuberculin skin test

The definition of a positive tuberculin skin test depends on a person's prior probability of having LTBI and the person's risk of developing active TB.

≥5 mm of induration

- Persons known or suspected to have HIV infection.
- Recent contacts to an active case of pulmonary or laryngeal TB.
- Persons with fibrotic changes seen on chest radiograph consistent with TB.
- Immunosuppressed individuals

≥10 mm of induration

- All persons except those in above

NOTE: The CDC recommends using a 15 mm cutoff for low risk reactors. However, in California, using a 10mm cutoff is the standard due to the higher incidence of TB in the state compared to other parts of the US.

For more in-depth information on LTBI testing, see:

- California TB Controllers Association, Interferon Gamma Release Assay (IGRA) Clinical Guidelines in California: http://ctca.org/menus/cdph-ctca-joint-guidelines.html
- ATS/IDSA/CDC Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children, available at the following URL: www.cdc.gov/tb/publications/guidelines/testing.html

Evaluating Patients with a Positive TB Test

Baseline evaluation for patients with LTBI

All patients with a positive test for latent tuberculosis infection (LTBI) should undergo an evaluation that includes:

Symptom review

Chest radiograph (CXR)

- If the patient is immunosuppressed, less than 5 years of age, a known close contact to a person with infectious TB or has a history of previously abnormal CXR consistent with potentially active TB disease, then the CXR should be no older than 3 months. Otherwise, a previous CXR can be used if it was taken within 6 months and is normal.
- Obtain a new CXR for patients with new symptoms.
- Pregnancy is not considered a contraindication to a CXR, though the abdomen should be shielded.

Medical history

- The medical history should include medical risk factors for TB progression including HIV status, prior TB exposures, history of TB or LTBI treatment, history of liver disease, alcohol use, pregnancy, , and a complete list of medicines in order to review them for potential hepatotoxicity and drug-drug interactions with rifamycins or isoniazid.

Symptoms that should trigger evaluation for active TB disease

Patients with any of the following symptoms that are otherwise unexplained should be evaluated for active TB disease: cough for more than 2-3 weeks, fevers, night sweats, weight loss, and hemoptysis.

CXR abnormalities should trigger evaluation for active TB disease

Unless explained by another known diagnosis, an abnormal CXR finding should trigger evaluation for active TB disease even in the absence of symptoms. This includes even stable lesions consistent with healed previous or inactive TB. A solitary calcified nodule or isolated pleural thickening alone are not concerning for active TB disease. If the abnormality on the CXR is of questionable significance, consultation with an expert is recommended.

Previous or inactive tuberculosis

CXR findings consistent with previous or inactive TB include fibrosis or non-calcified nodules. Persons with a CXR showing findings consistent with previous or inactive TB should be evaluated for active TB disease. A solitary calcified nodule or isolated pleural thickening alone are not concerning for active TB disease.

Under no circumstances should treatment for LTBI be initiated without ruling out active TB disease

If there is clinical suspicion for active TB disease while cultures are pending, empiric treatment for active TB disease can be started.

Evaluation for active TB disease

Symptoms or CXR abnormalities should trigger evaluation for active TB disease with bacteriologic studies:

- At least 3 sputum specimens should be collected at least 8 hours apart.
- At least 1 sputum specimen should be either induced or obtained in the early morning immediately after waking.
- All specimens should be sent for AFB smear microscopy and culture.
- At least 2 specimens should also be tested by nucleic acid amplification testing (e.g., Xpert MTB/RIF).
- Treatment for LTBI should be delayed until all results are finalized as negative, including cultures. This may take up to 8 weeks. For some patients, empiric treatment for active TB may be beneficial.
- Patients who complete 2 months of empiric treatment for active TB disease with a regimen that includes rifampin and pyrazinamide (usually rifampin, isoniazid, ethambutol, and pyrazinamide) and whose evaluation for active TB disease was negative (e.g. sputum AFB cultures are negative and CXR at 2 months is stable) do not need further LTBI treatment.

Evaluating Patients with a Positive TB Test *— continued*

Baseline patient education and counseling

- Provide verbal and written education in the patient's native language
- Provide education about TB and LTBI treatment including the importance of treatment completion. Assess and address barriers to treatment completion

At the start of treatment and at each monthly visit, patients should be instructed to stop taking treatment and to seek medical attention immediately if symptoms of hepatitis such as anorexia, nausea, vomiting, abdominal pain, jaundice, or dark urine develop. They should not wait until the next clinic visit to stop treatment.

Laboratory testing at baseline and during LTBI treatment

- Baseline tests (e.g., CBC, creatinine, AST, ALT, bilirubin, etc) are generally **not** recommended for healthy patients treated with isoniazid and/or a rifamycin.
- Baseline and follow-up serum ALT and bilirubin are recommended for patients with a known or possible liver disorder:
  - history of chronic liver disease (e.g., chronic hepatitis B and C, alcoholic hepatitis, or cirrhosis)
  - regular use of alcohol
  - HIV infection
  - pregnant women, and up to 3 months postpartum
- Baseline testing can be considered on an individual basis especially for patients taking other medications for chronic medical conditions. Some experts recommend patients aged >35 years have baseline and ongoing monitoring of ALT during LTBI treatment.
- For patients with chronic hepatitis or who have hepatotoxicity due to isoniazid, rifampin should be considered in lieu of isoniazid.
- Follow-up abnormal ALT with viral hepatitis screening tests for hepatitis B and C and diagnostic workup as appropriate. Consider further workup and treatment of viral hepatitis in conjunction with a hepatologist or viral hepatitis provider especially in patients with an ALT at least two times the upper limit of normal.
- Follow up clinical and ALT monitoring is recommended for patients with abnormal baseline liver function tests.
- Some programs perform additional tests such as baseline CBC in patients treated with a rifamycin.

Clinical monitoring during LTBI treatment

- Patients should be instructed, at the start of treatment and at each monthly visit, to stop taking treatment and to seek medical attention immediately if symptoms of hepatitis develop, rather than waiting until the next clinic visit.
- Monthly symptom review during LTBI treatment should include assessment for:
  - fatigue, weakness, malaise
  - anorexia, nausea, vomiting, abdominal pain
  - jaundice, pale stools, dark urine
  - chills
  - paresthesias
  - syncope, lightheadedness
  - rash
- ALT and bilirubin should be checked in patients who have symptoms suggestive of hepatitis (e.g., fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, dark urine, and chills) or who have jaundice.
- It is generally recommended that medication be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms or 5 times the upper limit of normal if the patient is asymptomatic.

What should be done when treatment is completed?

- Patients should receive written documentation of TST or IGRA testing results, CXR results, names and dosages of medications, and duration of treatment that can be presented as proof of prior treatment anytime TB testing is requested.
- Providers should re-educate patients about the signs and symptoms of TB reactivation and advise

Evaluating Patients with a Positive TB Test *— continued*

them to seek medical care if these symptoms develop.

- Repeat CXRs are not indicated unless the patient develops symptoms of TB disease.

Resources

California TB Controllers Association website at:
http://www.ctca.org/

Centers for Disease Control and Prevention, Latent Tuberculosis Infection: Guide for Primary Health Care Providers, available at the following URL:
http://www.cdc.gov/tb/publications/LTBI/treatment.htm

California Department of Public Health, Tuberculosis Control Branch (TBCB) website at:
http://www.cdph.ca.gov/tbcb

Curry International Tuberculosis Center Warmline Consultation Service, available at the following URL:
http://www.currytbcenter.ucsf.edu/

Choice of Treatment for Latent TB Infection (LTBI)

Most patients with LTBI should be treated

Persons with risk factors that test positive for LTBI should generally be treated once active TB disease has been ruled out with a CXR, symptom screen, physical exam, and, if indicated, sputum AFB smears, cultures, and nucleic acid amplification testing. However, some patients at low risk for LTBI are tested. Clinicians should not be compelled to treat low risk persons with a positive test for LTBI.

Emphasis on short course 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. Drug-drug interactions and contact to drug resistant TB are typical reasons these regimens cannot be used.

Shorter duration LTBI treatment regimens

Medication	Frequency	Duration
Rifampin	Daily	4 months
Isoniazid + rifapentine	Weekly	12 weeks*

*11-12 doses in 16 weeks required for completion.

12-dose weekly regimen of INH+rifapentine

- First-line regimen with efficacy equivalent to 9 months of INH.
- Completion rates (85-90%) are much higher than 9 months of INH.
- There is a lower risk of hepatotoxicity than with 9 months of INH.
- Initially studied and recommended using directly observed therapy (DOT), but self-administered therapy found to have equivalent rates of completion in U.S. patients.
- Hypersensitivity syndrome (fevers, flu-like symptoms, presyncope/syncope, hypotension) is observed in some patients. Reactions are typically mild and most patients can continue the regimen.

Rifampin for 4 months

- Preferred treatment in many United States TB clinics.
- Equally effective as isoniazid with higher completion rates.
- Lower risk of hepatotoxicity than with isoniazid
- Potential drug-drug interactions are the major contraindication for use. Check for drug interactions before prescribing.

Isoniazid for 6 or 9 months

- Isoniazid for 6 or 9 months has low completion rates, often less than 50%.
- Risk of hepatotoxicity is higher with INH than with rifampin or the 12-dose regimen of INH+rifapentine.
- There is a large body of evidence supporting its effectiveness if taken to completion.
- Isoniazid should be used in patients with significant drug-drug interactions with rifamycins.
- Isoniazid should be used with caution in patients with baseline liver disease or who are being administered other hepatotoxic drugs.
- INH can increase the blood level of phenytoin, carbamazepine and some benzodiazepines.
- Refer to product insert or other drug interaction resource for full list of interactions.

Children

Ensuring that children complete treatment is important, particularly those under 5 years who have a high risk for progression to active TB disease because of their young age.

- Clinical trial data supports the use of the INH+ rifapentine regimen in children 2 years and older.
- Clinical trial data supports the use of 4 months of rifampin in children under 18.

Liver Disease

- Rifampin for 4 months or the 12-dose INH+rifapentine regimen have lower risk of hepatotoxicity, thus are preferred for patients with baseline liver disease or hepatotoxicity risk who are not taking medications that have potential drug interactions with rifamycins.
- For those with ALT > 2.5 to 3 times the upper limit of normal, chronic alcohol consumption, or severe liver disease manifested by low albumin and

Choice of Treatment for Latent TB Infection (LTBI) *—cont.*

coagulopathy or encephalopathy, the risks of LTBI treatment may outweigh benefits. If LTBI treatment is undertaken, close monitoring is indicated.
- When there is an indication for LTBI treatment in patients with advanced liver disease such as future plans for liver transplantation, contact a TB or liver disease expert for LTBI treatment advice.

HIV
- Persons living with HIV are a priority group for LTBI treatment because of elevated risk for progression to TB disease.
- Drug interactions might complicate a rifamycin-containing regimen. Rifabutin in place of rifampin for 4 months is an option to avoid certain interactions.
- Both rifampin and rifabutin interact with the newer tenofovir formulation, tenofovir alafenamide.
- National HIV guidelines recommend INH as the preferred option; rifampin for 4 months and the 12-dose INH+rifapentine regimen as alternatives.
- Treatment should be pursued with consultation with an HIV TB expert.

Immunosuppression (current or planned)
- Significant non-HIV immunosuppression includes organ transplantation, treatment with TNF-alpha antagonist (e.g., infliximab, etanercept, others), steroids (equivalent of prednisone ≥15 mg/day for ≥1 month in adults and ≥2 mg/kg/day for ≥2 weeks in children) or other immunosuppressive medication.
- Immunosuppressed persons are a priority group for LTBI treatment because of higher progression risk to TB disease.
- Drug-drug interactions, particularly with rifamycins, might complicate LTBI treatment and may require additional monitoring.
- For patients with planned immunosuppression, ideally LTBI treatment would be completed prior to immunosuppression. When not possible, at least one month of LTBI treatment should be the goal.

Pregnancy and Breastfeeding
- Pregnancy is not a risk factor for progression to active TB disease.
- Pregnant women with a positive test for LTBI and a risk for rapid progression (e.g., HIV infection, recent exposure and conversion to positive such as in the context of a contact investigation) should be considered for LTBI treatment.
- For women not at risk for rapid progression, LTBI treatment can be delayed until at least 3 months postpartum.
- Both INH and rifampin are considered safe in pregnancy. The INH+rifapentine regimen is under study in pregnancy.
- INH and rifamycins are found in breast milk in small quantities, but are considered safe. There is insufficient data on use of rifapentine in breastfeeding women to recommend use.
- Most experts recommend that exclusively breastfed infants treated with INH should receive pyridoxine supplementation. Pyridoxine supplementation of a breastfed baby whose mother is taking INH is not necessary, but the mother should receive pyridoxine supplementation.

Contact to MDR TB
Treatment of persons with LTBI who are close contacts to a person with infectious MDR TB should be offered treatment for LTBI with a regimen based on the resistance pattern of the index case. Consultation with a clinician with MDR TB expertise is recommended.

Resources
Centers for Disease Control and Prevention, LTBI: Guide for Primary Health Care Providers: cdc.gov/tb/publications/LTBI/treatment.htm

California Department of Public Health Tuberculosis Control Branch (TBCB): cdph.ca.gov/tbcb

California TB Controllers Association: www.ctca.org/
Curry International Tuberculosis Center Consultation Service:currytbcenter.ucsf.edu/ or (877) 390-6682

12-dose Isoniazid (INH) + Rifapentine Regimen for Latent TB Infection (LTBI) Treatment

NOTE: It is imperative to rule out active TB disease in all persons prior to initiating treatment for LTBI

What is the 12-dose INH+rifapentine regimen?

An LTBI treatment regimen consisting of 12 once-weekly doses of INH and rifapentine. This is a preferred LTBI treatment regimen because it is a short-course treatment with higher completion rates.

Is the regimen effective?

Randomized controlled trials in adults and children showed that the 12-dose regimen administered by DOT is as effective as 9 months of daily INH by SAT for LTBI treatment. The 12-dose regimen was more likely to be completed when compared to 9 months of daily INH.

What are the advantages of this regimen?

- The 12-dose regimen reduces treatment time by two-thirds (from 9 months to 3 months)
- Weekly dosing offers convenience
- Higher rates of treatment completion
- Lower rates of hepatotoxicity

Who should be considered for treatment with the 12-dose regimen for LTBI?

- The 12-dose regimen is recommended as an equal alternative to 9 months of daily INH by SAT for treating LTBI
- Short course regimens are preferred whenever possible to enhance the likelihood of LTBI treatment completion

Who is *NOT* recommended for treatment with the 12-dose regimen?

- Children under 2 years of age
- HIV infected persons taking antiretrovirals that have unacceptable drug interactions with rifapentine
- Persons taking medications that may have drug interactions that are difficult to manage with the 12-dose regimen
- Persons presumed infected with *M. tuberculosis* resistant to INH or rifampin
- Pregnant or breastfeeding women or women planning to become pregnant during treatment
- Persons who have had prior adverse events or hypersensitivity to INH or rifampin

What are the doses?

Drug	Dosage	Maximum dose
INH	15 mg/kg rounded up to nearest 50/100 mg in patients ≥12 years	900 mg
	25 mg/kg rounded up to the nearest 50/100 mg in patients 2-11 years	
Rifapentine*	10.0 – 14.0 kg = 300 mg	900 mg
	14.1 – 25.0 kg = 450 mg	
	25.1 – 32.0 kg = 600 mg	
	32.1 – 50 kg = 750 mg	
	> 50 kg = 900 mg	

*Rifapentine and INH tablets can be crushed and administered with semi-solid food for patients unable to swallow pills

What is completion of therapy?

Completion of therapy is 12 doses in 16 weeks. In situations where 12 doses cannot be completed, at least 11 weekly doses of treatment within 16 weeks can be considered complete. Doses must be given at least 72 hours apart.

Does this regimen have to be administered via DOT?

- CDC recommends either SAT or DOT in persons aged ≥2years
- DOT vs SAT should be based on local practice, individual patient characteristics and preferences considering the following:
  - The burden and expense of DOT on patients and providers is greater than for SAT.
  - In a randomized trial of INH+rifapentine completion, SAT has been shown to be non-inferior to DOT among adults in the United States.
  - DOT may be beneficial for patients in whom risk for progression to severe forms of active TB disease if adherence is poor. Examples include age less than 5 years and immunosuppression.
- Contact your local TB control program regarding local recommendations.

How frequently were toxicities observed in the 12-dose regimen in the clinical trial participants?

- Possible hypersensitivity (3.8%)
- Rash (0.8%)
- Hepatotoxicity (0.4%)
- Thrombocytopenia (infrequent)
- Other toxicities (3.2%)
- Refer to product insert for full list of side effects

What is a hypersensitivity reaction and how should I respond?

Hypersensitivity reactions may include a flu-like syndrome (e.g., fever, chills, headaches, dizziness, and musculoskeletal pain), thrombocytopenia, shortness of breath or other signs and symptoms including wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema, hypotension or shock.

- If moderate to severe reaction (e.g., thrombocytopenia, hypotension, syncope), hospitalization or life-threatening event →*Discontinue treatment*
- If mild reaction (e.g., rash, dizziness, fever) →*Continue to monitor patient closely with a low threshold for discontinuing treatment*

How do I report an adverse event regarding the 12-dose regimen?

All adverse events should be reported to FDA MedWatch:acessdata.fda.gov/scripts/medwatch/medwatch-online.htm

Report adverse events leading to death or hospitalization to the local health department, who will report to the CDPH TB Control Branch (TBCB). TBCB then reports to the CDC.

Are there drug-drug interactions?

- INH increases blood levels of phenytoin carbamazepine and some benzodiazepines.
- Rifapentine decreases blood levels of many drugs including hormonal contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and some antibiotics including fluoroquinolones
- Rifapentine has interactions similar to rifampin; it induces cytochromes P450 3A4 & P450 2C8/9 (less than rifampin)
- Refer to product insert or other drug interaction resource for full list of interactions.

What type of monitoring do I need to do?

Monthly interview and brief physical examination to identify treatment-associated adverse events is ideal. Telephone or other patient communication can also encourage adherence and identify problems.

- Baseline hepatic chemistry is recommended for patients with specific conditions:
  - HIV infection
  - Liver disorders
  - In the immediate (within 3 months) postpartum period
  - Regular alcohol use
  - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with at least monthly testing and consider viral hepatitis testing.

How do I get rifapentine?

Rifapentine can be ordered from your distributor or wholesaler, or directly from the manufacturer, Sanofi-Aventis, at www.sanofi.us and can be found in the "other products" link.

For questions or assistance in accessing rifapentine, contact the TB Control Branch: 510-620-3000.

Resources

California Department of Public Health Tuberculosis Control Branch (TBCB): cdph.ca.gov/tbcb

California TB Controllers Association: ctca.org

CDC Division of Tuberculosis Elimination: cdc.gov/tb

Curry International Tuberculosis Center Consultation currytbcenter.ucsf.edu/consultation or (877) 390-6682

Abbreviations

AFB= acid-fast bacilli BCG= Bacillus Calmette-Guérin
CXR= chest x-ray DOT= directly observed therapy
IGRA=interferon gamma release assay LTBI= latent TB infection
MDR =multiple drug resistant NAAT= nucleic acid amplification testing
SAT= self-administered therapy TST= tuberculin skin test

Rifampin for Latent TB Infection (LTBI) Treatment

NOTE: It is imperative to rule out active TB disease in all persons prior to initiating treatment for LTBI

How is rifampin used to treat LTBI?

Rifampin is taken once daily for 4 months to treat LTBI.

Is the regimen effective?

Rifampin daily for 4 months has been shown to be as effective as 9 months of INH, and there is substantial clinical experience with its use.

What are the advantages of this regimen?

- Four month regimen reduces treatment time (compared to 9 months of isoniazid)
- Higher rates of treatment completion
- Lower rates of hepatotoxicity

Who should be considered for treatment with 4 months of rifampin for LTBI?

- Persons of any age with LTBI
- Adults or children exposed to isoniazid-resistant TB

Can rifampin be used in patients with HIV?

Rifampin can be considered for people living with HIV being treated with certain combinations of antiretroviral drugs (ARVs) as long as possible interactions can be properly managed. Rifabutin can often be substituted for rifampin in patients taking ARVs and other medications that may interact with rifampin.

Who is *NOT* recommended for treatment with 4 months of rifampin?

- Those with a significant drug interaction (see below)
- People presumed infected with *M. tuberculosis* resistant to rifampin
- People who have had prior adverse events or hypersensitivity to rifamycins

What are the possible side effects?

- Rash and pruritis
- Upset GI tract
- Hepatotoxicity
- Hematologic abnormalities including thrombocytopenia
- Orange staining of body fluids

What are the doses?

Drug	Dosage
Rifampin	Adults 10mg/kg up to 600mg
	Children 15–20 mg/kg up to 600mg
Rifabutin	Adults 5mg/kg up to 300mg
	Children Not recommended

*Rifampin and rifabutin capsules can be opened and the contents mixed with semi-solid food for patients who are unable to swallow pills

What is completion of therapy?

Four months is the recommended length of treatment with rifampin, and should be completed within 6 months.

Are there drug-drug interactions?

- Rifamycins are inducers of cytochromes P450 3A4 & P450 2C8/9 and can decrease blood levels of many drugs including hormonal contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and some antibiotics including fluoroquinolones.
- Rifampin is contraindicated in HIV infected persons being treated with certain combinations of antiretroviral drugs (ARVs). In some cases rifabutin may be substituted for rifampin. Note that both rifampin and rifabutin interact with tenofovir alafenamide.
- More information on interactions with ARVs is available at these URLs:
  - https://aidsinfo.nih.gov/guidelines
  - http://arv.ucsf.edu/insite?page=ar-00-02
- Refer to product insert or other drug interaction resource for full list of interactions.

What type of monitoring do I need to do?

- Monthly interview and brief physical examination to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions:
  - HIV infection
  - Liver disorders
  - In the immediate (within 3 months) postpartum period
  - Regular alcohol use
  - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with at least monthly testing and consider viral hepatitis testing.

Resources

California Department of Public Health Tuberculosis Control Branch (TBCB) website:
http://www.cdph.ca.gov/tbcb

California TB Controllers Association website:
http://www.ctca.org/

Centers for Disease Control and Prevention Division of Tuberculosis Elimination website:
http://www.cdc.gov/tb/

Curry International Tuberculosis Center Warmline Consultation Service, available at:
http://www.currytbcenter.ucsf.edu/
(877) 390-6688

American Academy of Pediatrics, Red Book Online, Tuberculosis:
https://redbook.solutions.aap.org/chapter.aspx?sectionid=189640207&bookid=2205

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Isoniazid (INH) for Latent TB Infection (LTBI) Treatment

NOTE: It is imperative to rule out active TB disease in all persons prior to initiating treatment for LTBI

Is the regimen effective?

Nine months of Isoniazid is a regimen that has been historically used for the treatment of LTBI. Clinical studies of this regimen have indicated it can be ~95% effective in preventing progression to active TB with full compliance in immunocompetent subjects. However, due to poor compliance and low rates of completion, newer short-course regimens of INH/rifapentine and rifampin have much higher rates of completion and may be more appropriate for patients with no contraindications to these newer regimens.

What is the dose and regimen of INH for LTBI?

Duration	Age
9 months daily	Children - 10-15 mg/kg per day up to 300 mg/day (270 doses)
9 months daily	Adults - 5mg/kg daily (Not to exceed 300 mg/day) (270 doses)
6 months daily	Children –Not recommended
6 months daily	Immunocompetent Adults- 5 mg/kg not to exceed 300 mg/day
6 months / 9 months biweekly	Adults – 15 mg/dose not to exceed 900 mg/dose (Given 2 times/ week by DOT) Children – Not recommended

Are there situations when INH should not be used?

- Patients with known allergies to INH
- Contacts to persons with INH-resistant TB
- Other regimens are preferred for patients with liver disease or who are being administered other hepatotoxic drugs.
- There may be an increased risk of INH induced hepatotoxicity in pregnant and postpartum women. Consider postponing treatment with INH until 3 months postpartum unless the patient is at high risk for progression to active TB disease (e.g., recent TB infection, HIV positive).

What are the adverse effects of INH?

- Ten to 20% of patients taking INH experience asymptomatic LFT elevation that resolves with discontinuation of the drug.
  - INH should be discontinued when LFTs are 3 times the upper limits of normal (ULN) if the patient has symptoms of drug induced hepatitis (e.g., anorexia, fatigue, abdominal pain, jaundice) and should be discontinued if LFTs are 5 times ULN without symptoms.
  - Significant hepatoxicity occurs very rarely in those <20 years of age, but occur with increased incidence with advancing age, liver disease, during the post-partum period, in persons with pre-existing liver disease, regular alcohol use, or taking other hepatotoxic medications.
  - Cases of fatal hepatitis have been associated with continued administration of INH after the onset of clinical hepatitis symptoms.
- Dizziness, headaches, fatigue, seizures, and peripheral neuropathy occur rarely
- Vitamin B6 (Pyridoxine) supplementation can decrease odds of peripheral neuropathy in persons who are pregnant or breast feeding, or who have HIV, renal failure, alcoholism, diabetes, or underlying peripheral neuropathy. B6 should be given to exclusively breastfed infants on INH.
- Neutropenia (very rare)

Are there drug-drug interactions with INH?

- INH can increase the blood level of phenytoin, carbamazepine and some benzodiazepines.
- Refer to product insert or other drug interaction resource for full list of interactions.

What type of monitoring is needed for INH treatment?

- Monthly interview and brief physical examination to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions.
  - HIV infection
  - Liver disorders
  - In the immediate (within 3 months) postpartum period
  - Regular alcohol use
  - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with at least monthly testing and consider viral hepatitis testing.
- See "Evaluation of patients with a positive test for latent TB infection" for more information.

What is completion of treatment?

- 270 doses taken within a 12 month period or 180 doses taken within a 9 month period is considered adequate treatment.

Resources

California Department of Public Health Tuberculosis Control Branch (TBCB) website:
http://www.cdph.ca.gov/tbcb

California TB Controllers Association website:
http://www.ctca.org/

Centers for Disease Control and Prevention Division of Tuberculosis Elimination website:
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Resources

ATS/IDSA/CDC Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children at: www.cdc.gov/tb/publications/guidelines/default.htm

BCG Atlas: http://www.bcgatlas.org/
Online source for BCG vaccination global policies. Use to determine likelihood of BCG vaccination in a patient.

California Department of Public Health TB Control Branch: https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/TBCB.aspx *Source for TB surveillance data and information on prevention and control of TB. Also provides clinical and public health consultation to local TB control programs.*

California Tuberculosis Controllers Association
http://www.ctca.org
Source for Californian TB surveillance data and information on prevention and control of TB. Also provides clinical and public health consultation to local TB control programs.

Centers for Disease Control and Prevention, Division of Tuberculosis Elimination: http://www.cdc.gov/tb/
Source for epidemiologic data, clinical guidelines, and patient information.

Curry International Tuberculosis Center: http://www.currytbcenter.ucsf.edu/
Source for educational materials, training, and clinical consultation for providers and TB programs

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TST in 3D: http://www.tstin3d.com/en/calc.html
Online calculator that can assist with interpreting tuberculin skin test and interferon gamma release assay results. Note that as of February 2017 the calculator does not include risk of hepatotoxicity for any LTBI treatment regimen other than INH.

US Preventive Services Task Force Latent TB Infection Screening Recommendations: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/latent-tuberculosis-infection-screening *Statement recommending LTBI screening among adults with risk factors.*

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