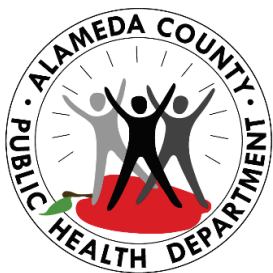


Tuberculosis: A Provider's Guide to Diagnosis and Treatment of Active Tuberculosis (TB) Disease and Screening and Treatment of Latent Tuberculosis Infection (LTBI)






**Alameda County Health Care Services Agency
Public Health Department**

Division of Communicable Disease Control and Prevention - TB Control Section

Phone: (510) 667-3096 Fax: (510) 273-3916 Web: www.acphd.org/tb

Last Updated: March 20, 2017

MANDATORY CALIFORNIA TUBERCULOSIS REPORTING GUIDELINES

WHO MUST REPORT	WHEN TO REPORT	HOW TO REPORT	WHY REPORT
<ul style="list-style-type: none"> <input type="checkbox"/> ALL HEALTH CARE PROVIDERS <input type="checkbox"/> LABORATORY DIRECTORS <p><i>Title 17 California Code of Regulations, Chapter 4, Section 2500, requires medical providers, laboratories, hospitals and other facilities to report all suspected and confirmed tuberculosis (TB) cases to the Alameda County Public Health Department within <u>one</u> working day of diagnosis</i></p> <ul style="list-style-type: none"> <input type="checkbox"/> Suspected TB case means there is high enough suspicion, based on clinical judgment, to start treatment for active TB disease <input type="checkbox"/> Confirmed TB case means there is clinical, radiographic or laboratory evidence confirming active TB 	<ul style="list-style-type: none"> <input type="checkbox"/> WITHIN <u>ONE</u> WORKING DAY <input type="checkbox"/> TB suspects or confirmed cases identified in Alameda County must be reported to Alameda County Public Health regardless of where the patient resides <input type="checkbox"/> TB suspects or confirmed cases who are Alameda County residents but are hospitalized in other counties are still followed by Alameda County Public Health 	<div style="display: flex; flex-direction: column; gap: 10px;"> <div>  Call Alameda County TB Control at: (510) 667-3096 </div> <div>  The TB Confidential Reporting Form is available on our website: www.acphd.org/tb </div> <div>  Fax TB Reporting form to: (510) 273-3916 </div> </div>	<ul style="list-style-type: none"> <input type="checkbox"/> Timely reporting allows the Public Health Department to: <ul style="list-style-type: none"> • Take appropriate measures to prevent further TB transmission throughout the community • Investigate potential sources of infection in young children

DISCHARGE OR TRANSFER OF TB SUSPECTS AND CONFIRMED CASES FROM HEALTH FACILITIES, LOCAL DETENTION FACILITIES, OR STATE CORRECTIONAL INSTITUTIONS

California Health and Safety Code 121361 ("Gotch") requires all health facilities to obtain approval of a written treatment plan from the Public Health Department before releasing or transferring any person known to have confirmed or suspected active tuberculosis disease

WHO SHOULD REQUEST DISCHARGE APPROVAL	WHEN TO REQUEST A DISCHARGE APPROVAL	HOW TO REQUEST DISCHARGE APPROVAL	WHY IS DISCHARGE APPROVAL NEEDED
<ul style="list-style-type: none"> <input type="checkbox"/> Physicians <input type="checkbox"/> Infection Control Practitioners, Nurse Case Managers and Discharge Planners, Medical Social Workers <p>Request discharge approval even if patient was hospitalized for reasons other than TB and/or the patient has a known diagnosis of pulmonary or extra-pulmonary TB upon hospital admission</p>	<ul style="list-style-type: none"> <input type="checkbox"/> Request discharge at least 24 hours prior to the anticipated date of discharge; Public Health has 24 hours to respond <input type="checkbox"/> Approval is not required for transfer to an acute care hospital due to immediate need for a higher level of care 	<ul style="list-style-type: none"> <input type="checkbox"/> Fax ACPHD TB Discharge/Transfer Treatment Plan to Public Health: (510) 273-3916 <input type="checkbox"/> Fax chest imaging reports <input type="checkbox"/> Fax acid fast bacilli results; indicate volume of sputum specimens <input type="checkbox"/> Fax discharge summaries and relevant consult notes. <input type="checkbox"/> Other records may also be requested 	<ul style="list-style-type: none"> <input type="checkbox"/> Continuity of care: Public Health is mandated to track TB cases and suspects through completion of treatment <input type="checkbox"/> Prevent further transmission; conduct household evaluation, identify high risk contacts before approving discharge

Please call TB Control and request medical consultation for any questions regarding when to start TB treatment in absence of microbiologic evidence of TB disease

WHEN TO SUSPECT TB?

- Making the diagnosis of TB often requires suspecting or considering TB in the differential diagnosis (***Think TB!***)
- A ***critical first step*** in making a diagnosis of TB is conducting a thorough history

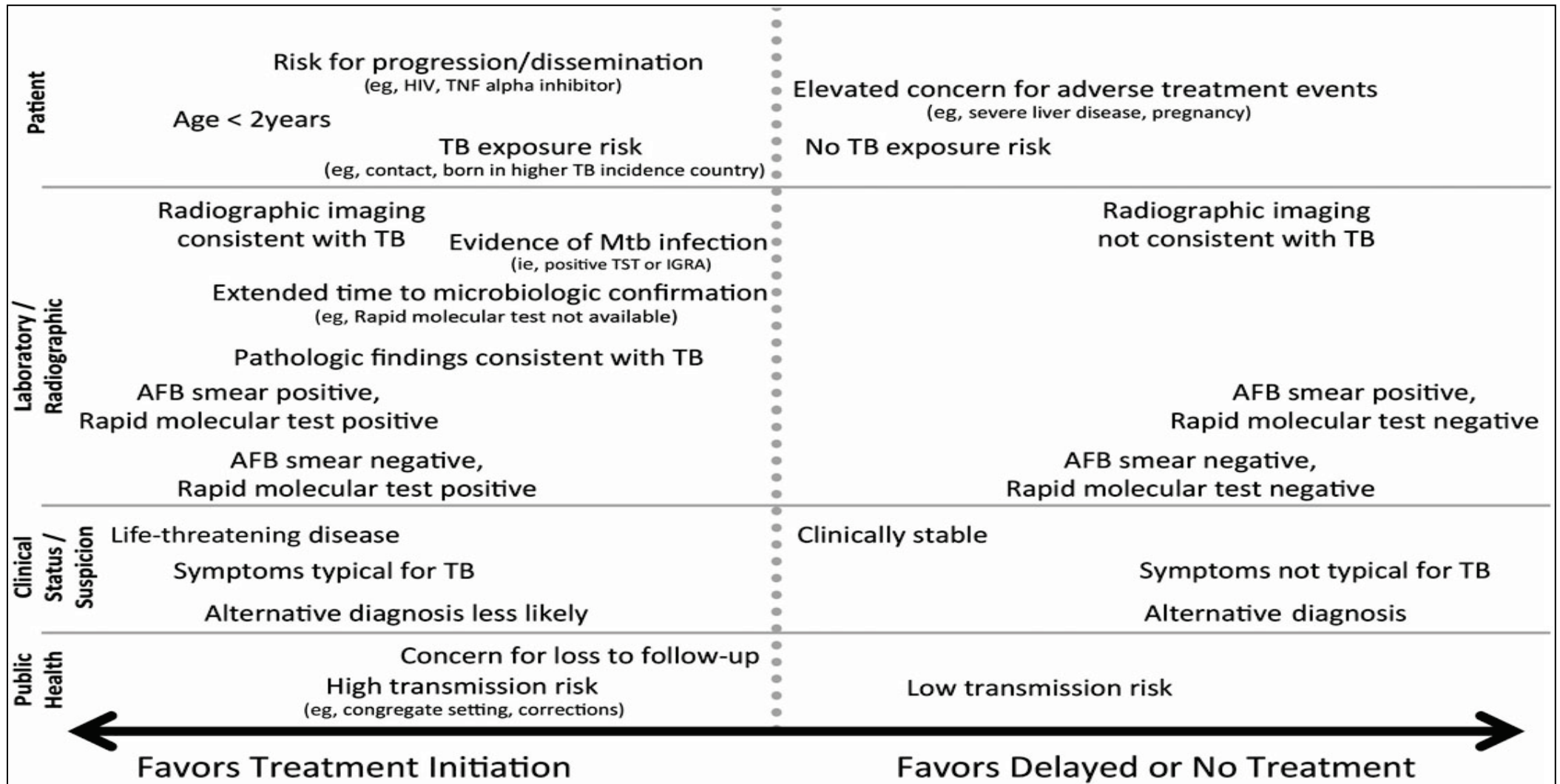
Medical History of a Patient with Suspected TB			
Symptoms of TB	<ul style="list-style-type: none"> • <u>Respiratory Symptoms</u>: Cough > 2 weeks, Chest pain, Shortness of breath, Hemoptysis • <u>Other Symptoms</u>: Weight loss, Fatigue, Fever, Night sweats, Loss of appetite • <u>Extrapulmonary symptoms</u>: Lymph Node (Lymph node swelling or drainage); Meningitis (Headache, Fever, Neck stiffness); etc. 		
Risk of TB exposure	<ul style="list-style-type: none"> • Foreign-born from a country with an elevated TB rate • <u>Factors to consider</u>: Homelessness, Incarcerated or history of incarceration, Healthcare worker with high-risk for TB exposure or previously untreated LTBI 		
History of TB treatment	<ul style="list-style-type: none"> • Prior treatment for TB disease: Determine when and how disease was treated • LTBI that has not been treated or was inadequately treated 		
High risk for progression to active TB dx	<table style="width: 100%; border: none;"> <tr> <td style="vertical-align: top;"> <ul style="list-style-type: none"> • HIV • TNF-alpha antagonist use • Organ transplant recipient with use of immune suppressants • Silicosis • End-stage renal disease requiring hemodialysis </td> <td style="vertical-align: top;"> <ul style="list-style-type: none"> • Leukemia, lymphoma, carcinoma of head and neck • Chemotherapy or other immunosuppressive medication • LTBI diagnosed in the past 2 years, and has not been treated • CXR with apical fibronodular fibrosis </td> </tr> </table>	<ul style="list-style-type: none"> • HIV • TNF-alpha antagonist use • Organ transplant recipient with use of immune suppressants • Silicosis • End-stage renal disease requiring hemodialysis 	<ul style="list-style-type: none"> • Leukemia, lymphoma, carcinoma of head and neck • Chemotherapy or other immunosuppressive medication • LTBI diagnosed in the past 2 years, and has not been treated • CXR with apical fibronodular fibrosis
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- An ***important second step*** is to obtain imaging and clinical specimens to help confirm the diagnosis of TB disease

Imaging and Clinical Specimens			
Imaging	<ul style="list-style-type: none"> • CXR, CT chest, CT or MRI scans of other sections of body as indicated 		
Microbiology	<ul style="list-style-type: none"> • AFB sputum smear and culture • Nucleic acid amplification test (NAAT) (<i>note</i>: Two sputum specimens should be sent for TB PCR) • Gastric aspirates as indicated • Pleural, cerebrospinal, or other bodily fluids 		
Biopsy of tissue	<table style="width: 100%; border: none;"> <tr> <td style="vertical-align: top;"> <ul style="list-style-type: none"> • Pleura • Bone </td> <td style="vertical-align: top;"> <ul style="list-style-type: none"> • Other sites as indicated (e.g., bone, liver, kidney, etc) </td> </tr> </table>	<ul style="list-style-type: none"> • Pleura • Bone 	<ul style="list-style-type: none"> • Other sites as indicated (e.g., bone, liver, kidney, etc)
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FACTORS TO CONSIDER WHEN STARTING TB TREATMENT

- Report all patients who are started on TB medications for treatment of active TB disease
- If you have questions regarding when to start TB treatment in the absence of microbiologic evidence of TB disease, then please call Alameda County TB Control at (510) 667-3096
- Several factors including patient, laboratory and radiographic evidence, clinical status and suspicion, and public health factors need to be considered when starting TB treatment. Some factors outlined in the 2016 TB Treatment guidelines are displayed in the figure below:



DIAGNOSIS AND MANAGEMENT OF ACTIVE TB CASES (SUSPECTS* AND CASES)

Days 1-2

- Isolate patient while work-up underway
- **Collect 3 sputum specimens** a minimum of every 8 hours apart with at least one AM specimen, and send all specimens for AFB smear and culture
 - **Sputa required even for extrapulmonary TB**
 - Two of the 3 sputum specimens should also be sent for TB PCR or NAAT
- Start TB therapy with 4 drugs
- **Report to Public Health**
- **Determine need for Directly Observed Therapy (DOT).**¹ Call Public Health for questions about DOT

Weeks 1-2

- **If AFB sputum smear positive at baseline, then:**
 - Collect one sputum per week until smear negative
 - Once negative, collect 2 additional sputa until 3 consecutive AFB smear negative specimens obtained
- **Patient may not return to work or school until TB Control has approved release from isolation**
 - **Decisions regarding release from isolation are made based on State Health Department Guidance**²

Months 1-2

- **Continue collecting 3 additional sputa monthly until culture conversion documented.** If culture conversion is not documented by 2 months, then 3 sputa need to be collected monthly until evidence of culture conversion

Month 2

- Obtain radiographic imaging to determine response to therapy
- **Pulmonary TB duration of therapy will depend on:** Presence of cavity on initial CXR, culture conversion, and response to TB therapy
- **Extrapulmonary TB duration depends on:** Response to TB therapy and site of TB disease

End of Treatment

- Collect 3 additional sputa if culture-positive TB
- Repeat imaging to obtain end of therapy baseline

***TB Suspect** = TB in differential dx and being worked up. Empiric TB treatment may be started based on clinical suspicion and patient's clinical status.

1. DOT guidance: www.cdph.ca.gov/programs/tb/Documents/TBCB-PMD-DOT.pdf
2. Infectiousness guidelines: www.ctca.org/fileLibrary/file_52.pdf

BASELINE AND FOLLOW UP EVALUATIONS FOR A 6 or 9 MONTH PULMONARY TB REGIMEN

Activity	Baseline	Month of Treatment Completed							End of Treatment (Every 6 Months x2)	
		1	2	3	4	5	6	9	12 or 15	18 or 21
Microbiology										
Sputum smears and culture ¹	X	X	X	X ¹	X ¹		X	X	X	X
NAAT or TB PCR	XX (2 specimens)									
Drug susceptibility testing (DST) ²	X			X ²						
Imaging										
Chest X-ray or other imaging ³	X		X ³				X	X	X	X
Clinical Assessment										
Weight	X	X	X	X	X	X	X	X	X	
Symptoms, side effects, adherence	X	X	X	X	X	X	X	X	X	
Vision assessment ⁴	X	X	X	X ⁴	X ⁴	X ⁴	X ⁴	X ⁴	X ⁴	
Laboratory										
LFTs ⁵ (AST, ALT, Alk Phos, Bilirubin)	X	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	
CBC ⁵	X	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	
Creatinine ⁵	X	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	X ⁵	
HIV	X									
Hepatitis B and C screen ⁶	X									
Diabetes screen ⁷	X									

Note: Since TB patients are at increased risk for relapse 12 months after completion of TB treatment, follow-up imaging and sputum smears and cultures are recommended.

1. If culture conversion has not been documented by 2 months, then additional sputum smears and cultures are recommended
2. Repeat DST should be performed if culture-positive at 3 months; molecular testing should be performed in patients at risk for drug resistance
3. Imaging required at 2 months to document clinical improvement
4. Vision assessment not indicated if ethambutol is discontinued
5. Further laboratory monitoring if baseline abnormalities or clinically indicated
6. Patients with HBV or HCV risk factors (e.g., injection drug use, HIV+, or birth in Asia or Africa) should be screened
7. Patients with diabetes risk factors (e.g., aged > 45 years old; BMI >25 mg/kg²; first degree relative with diabetes; or race/ethnicity of African American, Asian, Hispanic, American Indian/Alaskan Native, Hawaiian Native/Pacific Islander) should be screened

STANDARD TB MEDICATIONS

Please consult Alameda County TB Control Staff for usage of alternative TB medications

Drug	Supplied	Interval	Standard Dosage	Side Effects	Monitoring	Comments
Isoniazid (INH)	Tablets: 300 mg, 100 mg Suspension: 50 mg/5 ml	Daily	Adults: 5 mg/kg/day up to 300 mg Children: 10–15 mg/kg/day up to 300 mg	Hepatitis; peripheral neuropathy; mild CNS effects; skin rash; increased phenytoin levels.	Recommended LFTs at baseline. Routine monitoring of LFTs if h/o liver dz, pregnant, HIV+, or other concurrent hepatotoxic drugs used.	Give pyridoxine 25–50 mg/day to prevent neuropathy in patients who are elderly, pregnant, or have diabetes, nutritional deficiencies, HIV, seizure d/o, existing or new-onset peripheral neuropathy, or alcohol abuse.
Rifampin (RIF)	Capsules: 300 mg, 150 mg	Daily	Adults: 10 mg/kg/day, typically 600 mg Children: 10–20 mg/kg/day up to 600 mg	Orange discoloration of secretions; cholestatic hepatitis; febrile (flu-like) reaction; thrombocytopenia; drug interactions; skin rash.	As above for INH. Baseline CBC.	Counsel patient about orange discoloration of urine/other body secretions as well as discoloration of contact lenses. Induces hepatic microsomal enzymes. Significant interactions with some HIV antiretroviral agents.
Ethambutol (EMB)	Tablets: 400 mg, 100 mg	Daily	Adults: 15–25 mg/kg/day (1600 mg/day max dose) Children: 15–25 mg/kg/day (2000 mg/day max)	Optic neuropathy rare at 15mg/kg if renal function is normal; usually reversible if drug stopped. Skin rash.	Red-green color discrimination and visual acuity done at baseline and monthly. Baseline creatinine.	Dose adjustment needed for renal disease; dose AFTER dialysis sessions. Use with caution if visual testing is not feasible (e.g. children under the age of 5).
Pyrazinamide (PZA)	Tablets: 500 mg	Daily	Adults: 20–25 mg/kg/day (2000 mg/day max) Children: 30–40 mg/kg/day (2000 mg/day max)	Hepatitis; GI upset; hyperuricemia; arthralgias; photosensitive dermatitis.	As above for INH Baseline creatinine.	Dose adjustment needed for renal disease; dose AFTER dialysis sessions. Safety not established in pregnancy.

FIRSTLINE ADULT TB DRUG SCHEDULE ACCORDING TO WEIGHT

Drug	Weight in kilograms (kg)	Dose in milligrams (mg)
Isoniazid (INH)	30 → 35 kg	150 mg
	36 → 40 kg	200 mg
	> 40 kg	300 mg
Rifampin (RIF)	< 45 kg	450 mg
	≥ 45 kg	600 mg
Ethambutol (EMB)* <i>*EMB daily dose calculated based on a target of 15 mg/kg.</i>	22 → 26 kg	400 mg
	27 → 40 kg	600 mg
	41 → 53 kg	800 mg
	54 → 66 kg	1000 mg
	67 → 80 kg	1200 mg
	81 → 93 kg	1400 mg
	≥ 94 kg	1600 mg
Pyrazinamide (PZA)** <i>**PZA daily dose calculated based on a target range of between 20 mg/kg to 25 mg/kg</i>	40 → 50 kg	1000 mg
	51 → 60 kg	1250 mg
	61 → 68 kg	1500 mg
	69 → 75 kg	1750 mg
	≥ 76 kg	2000 mg

Note: The recommended EMB and PZA dose for patients with a creatinine clearance < 30 ml/min is:

- EMB 20 mg/kg to 25 mg/kg three times per week
- PZA 25 mg/kg to 35 mg/kg three times per week

LATENT TB INFECTION (LTBI)

What is LTBI?

LTBI is the presence of *Mycobacterium tuberculosis* in the body without signs and symptoms or radiographic or bacteriologic evidence of active TB disease

Who should be screened for LTBI?

- ❑ A standardized risk assessment should be utilized when deciding to screen for LTBI
- ❑ Routine testing of low-risk populations is not recommended because it may result in unnecessary testing and treatment due to false-positive results
- ❑ **For individuals who are known contacts to patients with infectious TB disease, the Alameda County Public Health Department will send out a separate letter with instructions for testing and recommendations for treatment**
 - If you do not know if a patient is a known contact, then please call Alameda County TB Control at (510) 667-3096

Are there sample risk assessment tools?

- | | |
|--|---|
| <ul style="list-style-type: none">❑ For <u>adults</u>, the California Department of Public Health TB risk assessment tool can be utilized ¹<ul style="list-style-type: none">• LTBI screening is recommended if any of the 3 risk factors below are checked:<ul style="list-style-type: none">❑ Foreign-born from a country with an elevated TB rate<ul style="list-style-type: none">○ Includes any country other than the United States, Canada, Australia, New Zealand or a country in Western or Northern Europe❑ Immunosuppression current or planned<ul style="list-style-type: none">○ 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 at any time | <ul style="list-style-type: none">❑ For <u>pediatric patients</u>, the California Department of Public Health TB risk assessment for pediatrics can be utilized ²<ul style="list-style-type: none">• LTBI screening is recommended if any of the 4 risk factors below are checked:<ul style="list-style-type: none">❑ Foreign-born from a country with an elevated TB rate (similar definition as adult risk assessment)❑ Immunosuppression current or planned (similar definition as adult risk assessment)❑ Close contact to someone with infectious TB disease at any time❑ Foreign travel or residence of ≥ 1 month consecutively in a country with an elevated TB rate |
|--|---|

1. California Department of Public Health TB risk assessment tool: www.cdph.ca.gov/programs/tb/Documents/TBCB-CA-TB-Risk-Assessment-and-Fact-Sheet.pdf
2. California Department of Public Health TB risk assessment for pediatrics: www.cdph.ca.gov/programs/tb/Documents/TBCB-CA-Pediatric-TB-Risk-Assessment.pdf

LTBI TESTING and TREATMENT

How should I test for LTBI?

- ❑ There are two types of tests available:
 - Interferon-gamma release assay (IGRA) [e.g. QuantiFERON®–TB Gold In-Tube or T-SPOT®.TB]
 - Tuberculin skin tests (TSTs), which are known as Mantoux TST or purified protein derivative (PPD)
- ❑ IGRAs are the *preferred test* over TSTs because:
 - Not affected by BCG vaccination and most non-tuberculous mycobacteria
 - No need for a return visit for interpretation of the test
 - Interpretation is objective
 - Test result can be easily located in the electronic medical record
- ❑ If an IGRA is not available or the patient refuses a blood draw, then the TST is an acceptable alternative screening test for LTBI
- ❑ Although current CDC guidelines do not recommend IGRA for screening of healthy children aged < 5 years old, the California Department of Public Health as well as pediatric infectious disease experts have recommended the IGRA over the TST for foreign-born children aged ≥ 2 years old

What do I do if I have a positive test for LTBI?

- ❑ Obtain a ***chest x-ray and conduct a symptom review and physical exam*** to rule out active TB disease
(*note*: for more information see pages titled Frequently Asked Questions Regarding LTBI and When to Suspect TB?)

What should I prescribe for treatment of LTBI?

- ❑ Short course treatment regimens (e.g., isoniazid and rifapentine, or rifampin) are preferred for treating LTBI because of higher completion rates and lower hepatotoxicity compared to 9 months of isoniazid
 - Check for drug-drug interactions before starting rifampin or rifapentine
- ❑ For patients who have LTBI and have been exposed to a patient with:
 - INH-resistant TB disease, then treat LTBI with rifampin
 - Multidrug-resistant TB disease, then call ***Alameda County TB Control at (510) 667–3096***

FREQUENTLY ASKED QUESTIONS REGARDING LTBI

Q: How should I rule out active TB disease before starting LTBI treatment?

- A:**
- ❑ For all patients, ask about signs and symptoms of TB disease, conduct a physical exam, and obtain a PA/Lateral CXR
 - If there are no symptoms of active TB disease and the CXR is normal, start LTBI treatment
 - If the patient ***has any symptoms of active TB disease or the CXR is abnormal*** (does not include calcified granulomas or isolated pleural thickening), then evaluate for TB disease
 - Evaluation for TB disease includes *all of the following*:
 - Obtain induced or expectorated sputum x 3 for AFB smear and culture. Sputum specimens should be 8 hours apart, and at least one specimen should be from the early AM
 - An adequate sputum specimen is 3–5 ml
 - Send two sputum specimen for TB PCR or NAAT
 - Follow-up AFB cultures until finalized at 6–8 weeks
 - If evaluation for TB disease is negative, then start LTBI treatment

Q: How often should the LTBI risk assessment be performed?

- A:**
- ❑ An assessment should be performed upon entry into care
 - For pediatric patients the risk assessment (i.e., asking the screening questions) should be conducted annually
 - ❑ Patients with a negative risk assessment should have a subsequent annual risk assessment if new risk factors are present
 - If it is unclear if a patient has acquired a new risk factor, then the risk assessment questionnaire should be administered

Q: Is there a way to further prioritize LTBI screening among adults?

- A:**
- ❑ If resources do not allow for testing all foreign-born persons, then prioritize those foreign-born who also have one of the following medical conditions that increase the risk for progression of TB disease
 - Diabetes
 - Smoker within past year
 - End-stage renal disease
 - Leukemia or lymphoma
 - Head and neck cancer
 - Silicosis
 - Intestinal bypass/gastrectomy
 - Chronic malabsorption
 - BMI \leq 20
 - CXR findings of previous or inactive TB disease (does not include isolated pleural thickening or calcified granuloma)

TREATMENT OF LTBI

	Drug	Duration	Dose (Maximum)	Comments
Preferred Regimens	Isoniazid (INH) and Rifapentine (RPT)	12 weeks (12 doses)	<p><u>Adults and Children ≥ 2 years old:</u></p> <p>INH:</p> <ul style="list-style-type: none"> ❑ 25 mg/kg weekly rounded to nearest 50/100 mg in patients aged 2–11 years old ❑ 15 mg/kg weekly rounded to nearest 50/100 mg in patients aged ≥ 12 years old (900 mg) <p>RPT:</p> <ul style="list-style-type: none"> • 10.0 – 14.0 kg: 300 mg weekly • 14.1 – 25.0 kg: 450 mg weekly • 25.1 – 32.0 kg: 600 mg weekly • 32.1 – 49.9 kg: 750 mg weekly • ≥ 50.0 kg: 900 mg (max) weekly 	<p>** Administration via directly observed preventive therapy (DOPT) is recommended. However, preliminary data suggest that self-administered therapy (SAT) is non-inferior to DOPT in the United States. Many clinicians are using SAT or modified DOPT.</p> <p>** Review concomitant medications to determine drug-drug interactions</p> <p>** Administer with 25 mg pyridoxine weekly in patients with increased risk of peripheral neuropathy (e.g., diabetes, alcoholism, renal failure, HIV, pregnancy, breast feeding)</p> <p>Regimen NOT recommended for:</p> <ul style="list-style-type: none"> • Children younger than 2 yrs; • HIV/AIDS on antiretroviral meds; • Possible exposure to INH or RIF-resistant TB; • Women who are pregnant or may become pregnant while on treatment
	Rifampin (RIF)	<p><u>Adults:</u> 4 months (120 doses)</p> <p><u>Children:</u> 4 months (120 doses)</p>	<p><u>Adults:</u> 10 mg/kg (600 mg) daily</p> <p><u>Children:</u> 10–20 mg/kg (600 mg) daily</p>	<p>** Interacts with many medications including some antiretrovirals</p> <p>** Review concomitant medications to determine drug-drug interactions</p>
Acceptable Regimen	Isoniazid (INH)	9 months (270 doses)	<p><u>Adults:</u> 5 mg/kg (300 mg) daily</p> <p><u>Children:</u> 10–15 mg/kg (300 mg) daily</p>	<p>** Administer with pyridoxine 25 mg daily in patients with increased risk of peripheral neuropathy (e.g., diabetes, alcoholism, renal failure, HIV, pregnancy, breast feeding)</p>