Diagnosis and Treatment of Latent TB Infection (LTBI)

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Aurelia Schmalstieg, MD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

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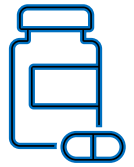
Goals for this hour:

Define LTBI

Discuss testing options for LTBI

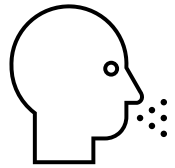


Review treatment options for LTBI

Identifying and treating latent TB infection is an essential part of successful TB elimination in the United States

An estimated 13 million people in the US are living with LTBI

It is estimated that 80% of people in the US who developed active TB had LTBI



Once a person has LTBI, this presents a lifelong risk to their own health as well as the health in their communities, unless they are treated

Am J Respir Crit Care Med 2021

Classic Conceptualization of TB

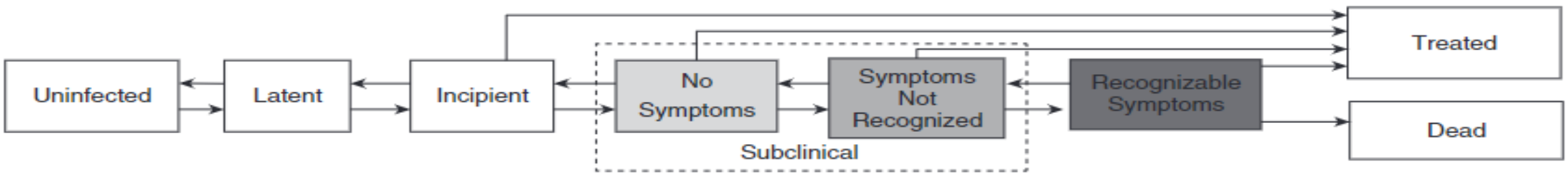
Updated Conceptualization of TB:

Incorporates Three Elements:

1) Subclinical stages from which transmission may occur without recognizable symptoms (extra boxes with grey shading)

2) Regression/resolution to milder disease possible (bidirectional arrows)

3) The potential for diagnosis and treatment before recognizable symptoms develop (upper arrows to "Treated")



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Age	Risk of Progression from TBI to Disease if Untreated, %
<12 mo	40–50
1–2 y	25
School-aged	5–10
Adolescents	10–15
Adults	5–10

Table: Pediatrics 2021

Note: this table refers to the risk in individuals who are not immunocompromised

What are some of the challenges to better testing and treatment of LTBI in our communities?

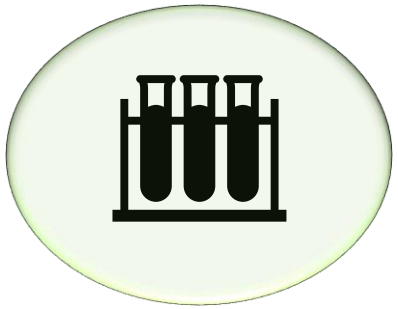
Historical use of long courses of drugs with greater potential for adverse effects

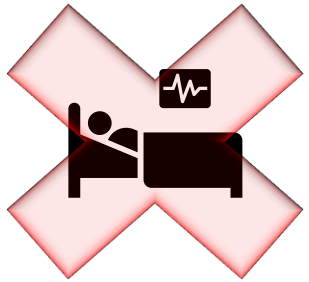
The concept of taking a prolonged course of medication for an infection that is asymptomatic

Gaps in our testing/diagnostic tools

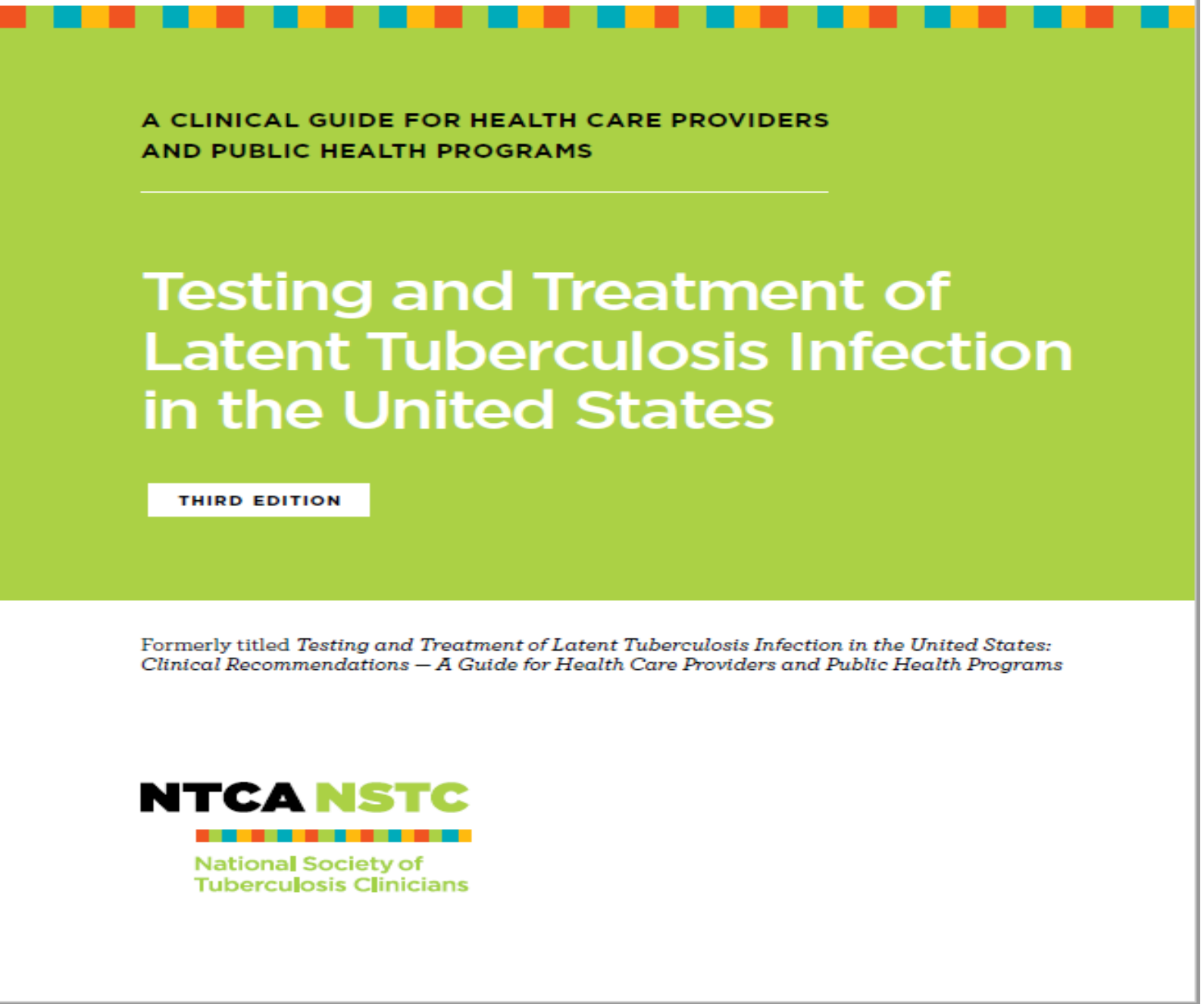
Latent TB Infection =

A symptom free clinical state diagnosed by a positive test result for *Mycobacterium tuberculosis* complex infection and an absence of clinical and radiographic findings of active tuberculosis disease

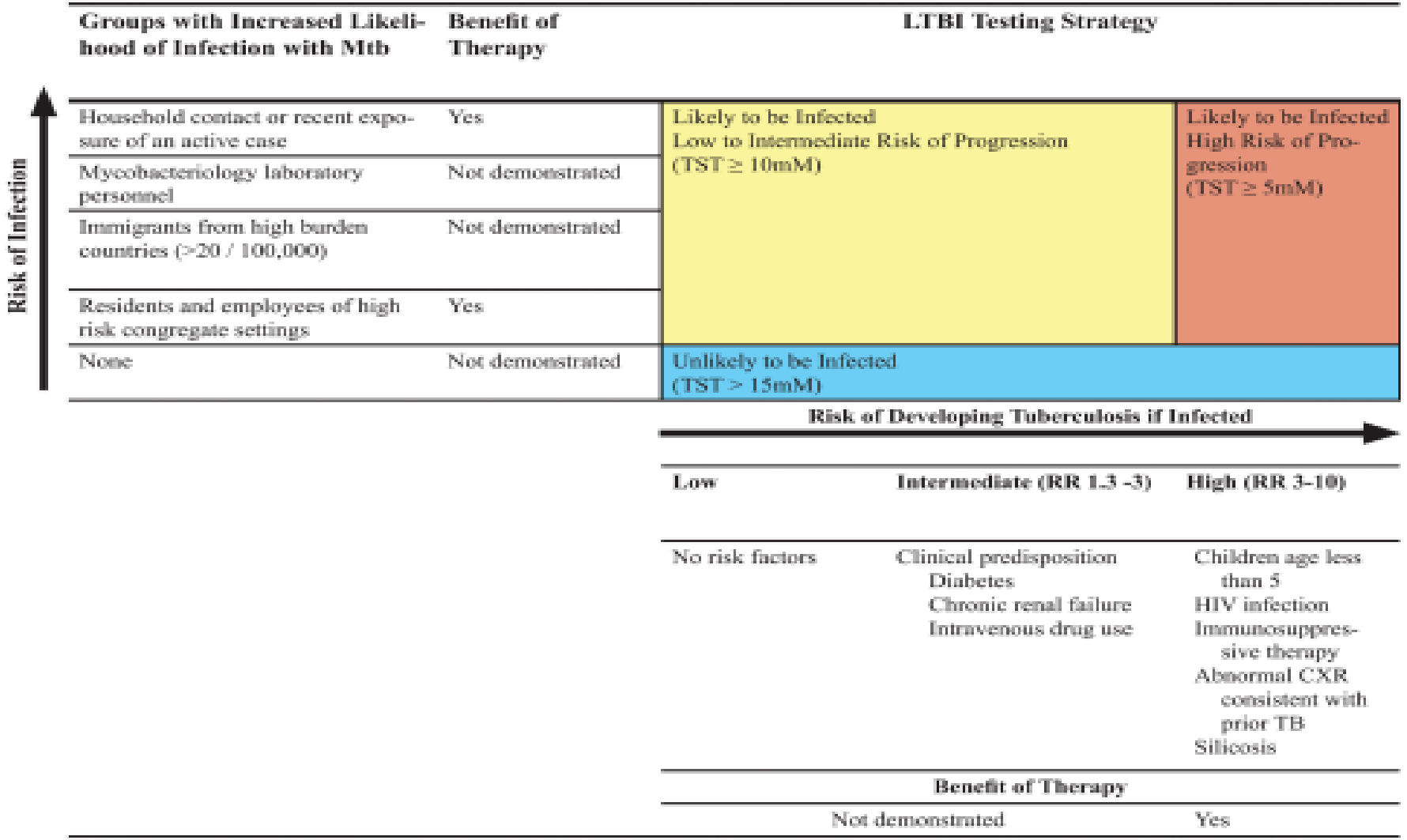




NSTC/NTCA 2023



https://www.tbcontrollers.org/resources/tb-infection/clinical-recommendations/


Groups with Increased Likelihood of Infection with Mtb
Benefit of Therapy
LTBI Testing Strategy
Risk of Infection
Household contact or recent exposure of an active case
Yes
Mycobacteriology laboratory personnel
Not demonstrated
Immigrants from high burden countries (>20 / 100,000)
Not demonstrated
Residents and employees of high risk congregate settings
Yes
None
Not demonstrated
Likely to be Infected
Low to Intermediate Risk of Progression
(TST ≥ 10mM)
Likely to be Infected
High Risk of Progression
(TST ≥ 5mM)
Unlikely to be Infected
(TST > 15mM)
Risk of Developing Tuberculosis if Infected
Low
Intermediate (RR 1-3 -3)
High (RR 3-10)
No risk factors
Clinical predisposition
Diabetes
Chronic renal failure
Intravenous drug use
Children age less than 5
HIV infection
Immunosuppressive therapy
Abnormal CXR consistent with prior TB
Silicosis
Benefit of Therapy
Not demonstrated
Yes

CID 2017

Testing options for LTBI:

1. Interferon-Gamma Release Assay (IGRA):
   - QuantiFERON®-TB Gold Plus
   - T-SPOT®

2. Tuberculin Skin Test (TST)

These tests really just tell us that the host immune response has been sensitized to specific antigens, and that the immune system is working well enough to remember this prior sensitization

T-SPOT (In vitro enzyme-linked immunosorbent spot assay):

- White blood cells are separated from whole blood, washed and transferred to test wells for incubating with the negative control, two antigen mixtures and a positive control.
- Whole blood must be processed within 8-32 hours
- Each cell that releases interferon-gamma is bound by a dye, and the spots are counted
- The spot counts for each antigen (A and B) are adjusted by subtracting the count from the negative control well, and a test kit algorithm
- Possible results: Positive, Negative, Invalid, or Borderline (equivocal)

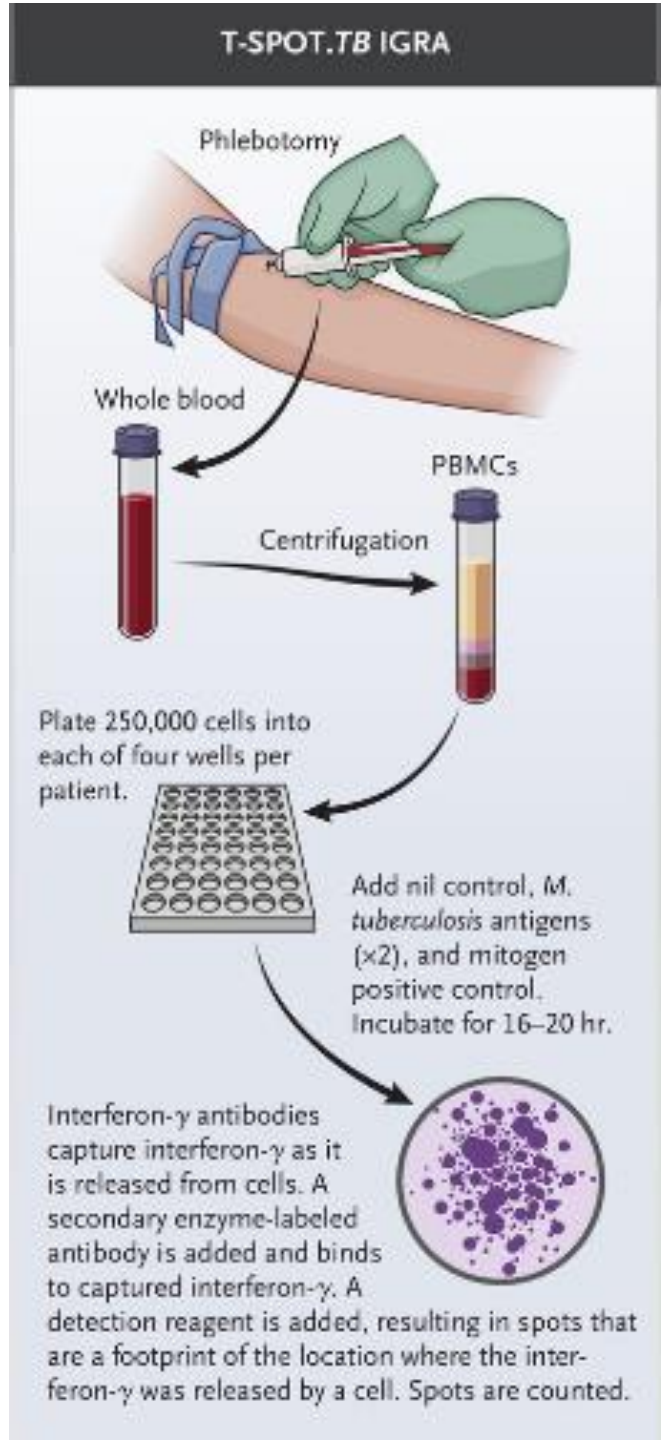


Image: NEJM 2021

QuantiFERON®-TB Gold Plus:

- Whole blood is incubated in GFT-Plus tubes- a negative control, two antigen tubes, and a positive control
- Whole blood must be processed within 16 hours
- After centrifugation, the plasma from each tube is removed and the concentration of interferon-gamma in each of the four tubes is measured by ELISA
- Interferon-gamma concentration of each antigen tube and the positive control is adjusted by subtracting the concentration of the negative control tube, along with the test kit algorithm
- Possible results: Positive, Negative, Indeterminate

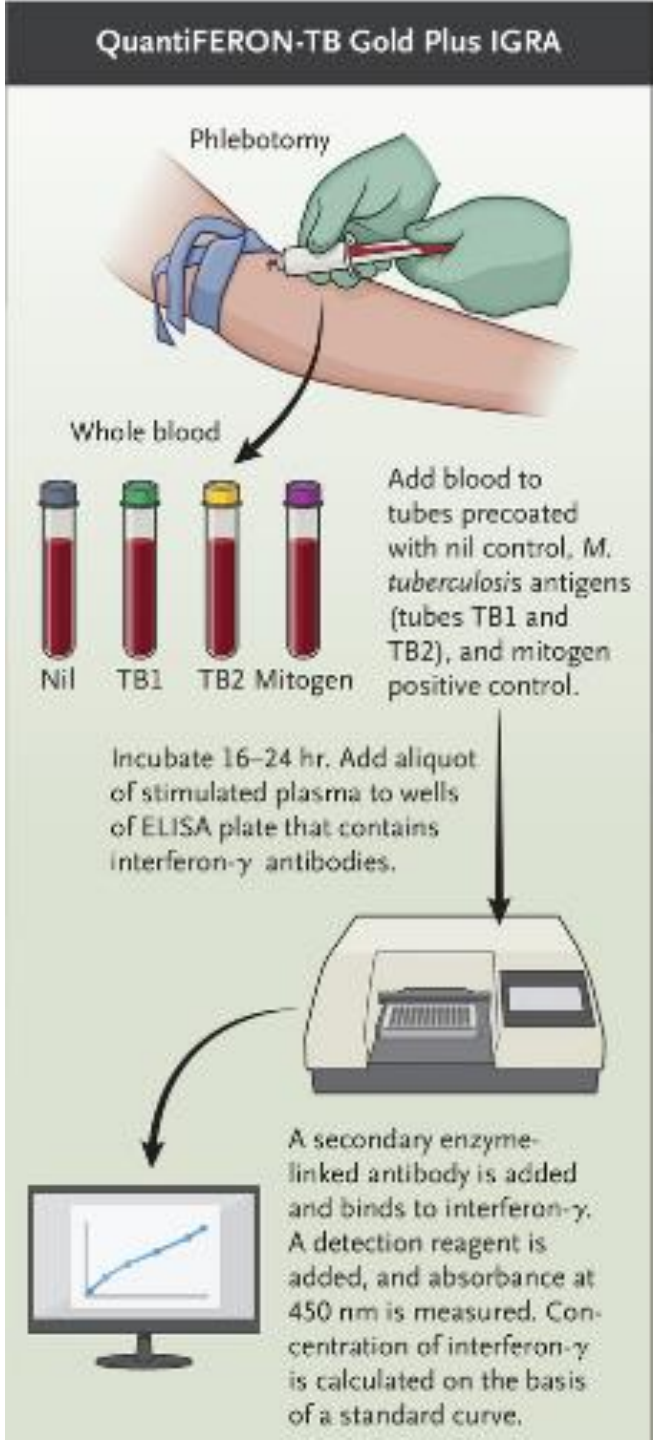


Image: NEJM 2021

Tuberculin Skin Test (TST):

- An "In-vivo" assay

- Not recommended for people who:
  - won't be able to return in 48-72 hours
  - have a history of TB
  - had a prior positive TB test
  - had prior BCG immunization

- TST interpretation is subjective and positivity thresholds are stratified according to "risk"

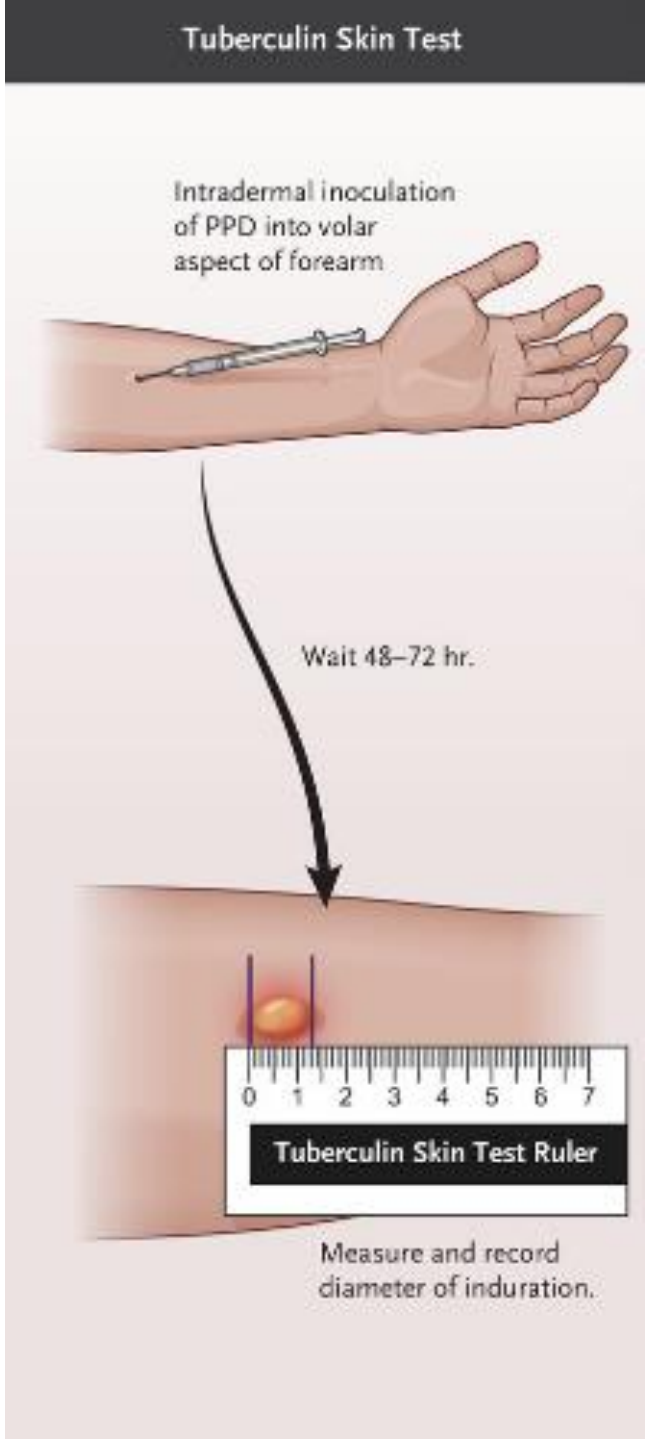


Image: NEJM 2021

5 or more millimeters	10 or more millimeters	15 or more millimeters
An induration of 5 or more millimeters is considered positive for • People living with HIV • Recent contacts of people with infectious TB • People with chest x-ray findings suggestive of previous TB disease • People with organ transplants • Other immunosuppressed patients (for example, patients on prolonged therapy with corticosteroids equivalent to/ greater than 15 mg per day of prednisone or those taking TNF-alpha antagonists)	**An induration of 10 or more millimeters is considered positive for** • People born in countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, and Guatemala, or other countries with high rates of TB • People who abuse drugs • Mycobacteriology laboratory workers • People who live or work in high-risk congregate settings (for example, nursing homes, homeless shelters, or correctional facilities) • People with certain medical conditions that place them at high risk for TB (for example, silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions) • Children younger than 5 years of age • Infants, children, and adolescents exposed to adults in high-risk categories	**An induration of 15 or more millimeters is considered positive for** • People with no known risk factors for TB

CDC Training: Module 3

A false positive TST may result from:

- Infection with non- tuberculous mycobacteria
- Prior BCG vaccination
- Incorrect administration technique
- Incorrect measurement or interpretation of the reaction

A false negative TST may result from:

- Underlying immunosuppression
- Very recent TB infection (within the last 8-10 weeks)
- Incorrect administration
- Live virus vaccination within the last 4 weeks

Pediatrics 2021

IGRA Result	Interpretation
Positive	*M. tuberculosis* infection likely
Negative	*M. tuberculosis* infection unlikely, but cannot be excluded especially if 1. Patient has signs and symptoms of TB 2. Patient has a high risk for developing TB disease once infected with *M. tuberculosis*
Indeterminate (QFT-Plus only)	The test did not provide useful information about the likelihood of *M. tuberculosis* infection. Repeating an IGRA or performing a TST may be useful.
Invalid or Borderline (T-Spot only)	The test did not provide useful information about the likelihood of *M. tuberculosis* infection. Repeating an IGRA or performing a TST might be useful.

Negative IGRA results for contacts to persons with infectious TB should be confirmed with a repeat test 8 to 10 weeks after their last exposure to TB

A positive IGRA result can be caused by certain non-tuberculous mycobacteria (*M. kansasii*, *M. szulgai*, *M. marinum*)

IGRA

TST

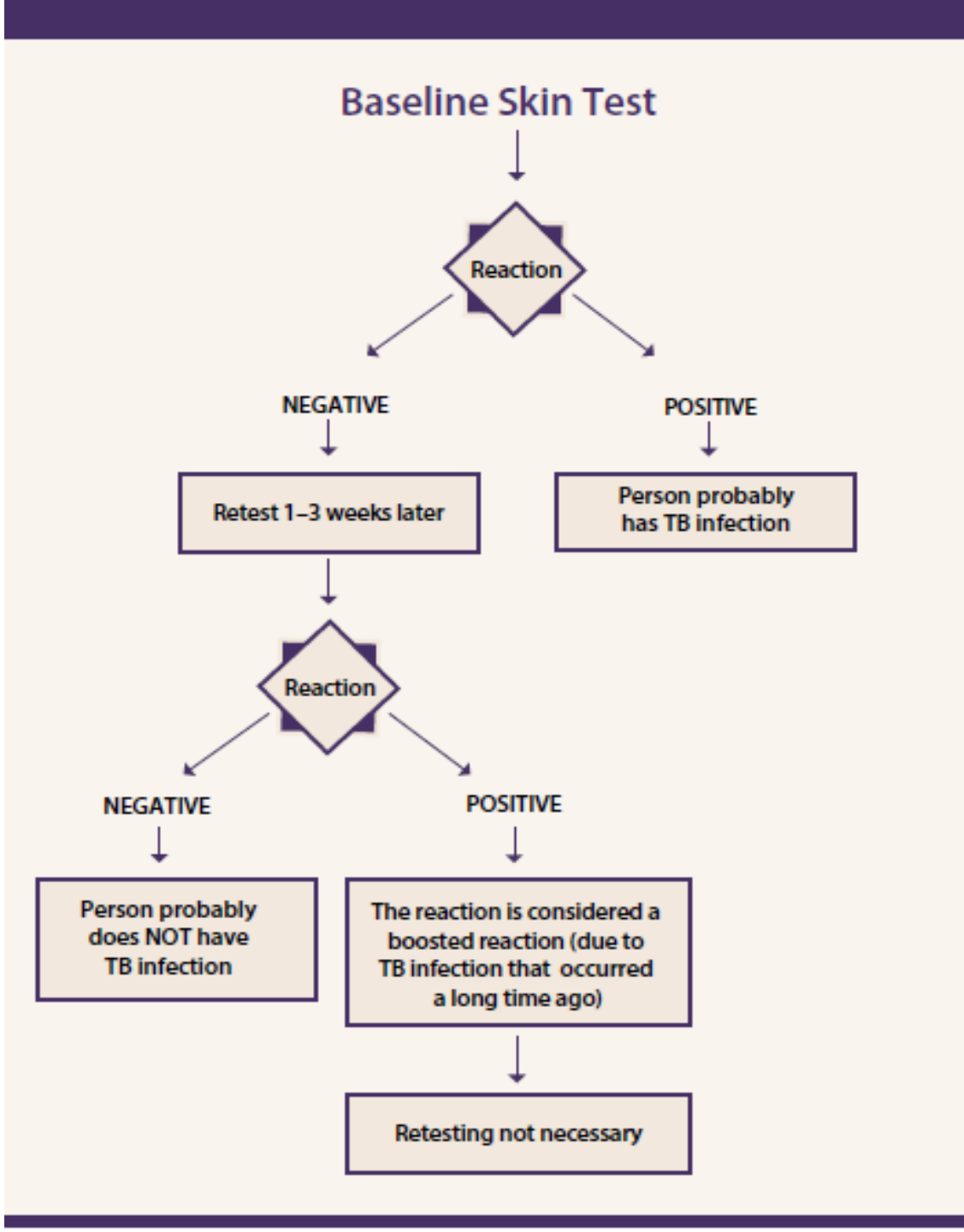
- Antigens are chosen to optimize specificity
- Laboratory instruments are required
- One patient encounter is sufficient
- Little subjectivity
- Does not cross-react with BCG or most NTM
- Previous IGRA does not boost future IGRA
- Results can be available within 24hrs
- Generally more expensive
- Blood must be processed within 8 – 32 hours after collection

- Less specific antigens
- No lab instruments are required
- Requires two visits to complete test
- Interpretation is subjective and risk-stratified
- Cross-reacts with BCG and some NTM
- Can boost subsequent TST or IGRA
- Results available in 48-72 hrs
- Generally lower cost
- No blood draw or specimen collection required, only intradermal injection

Two-step testing:

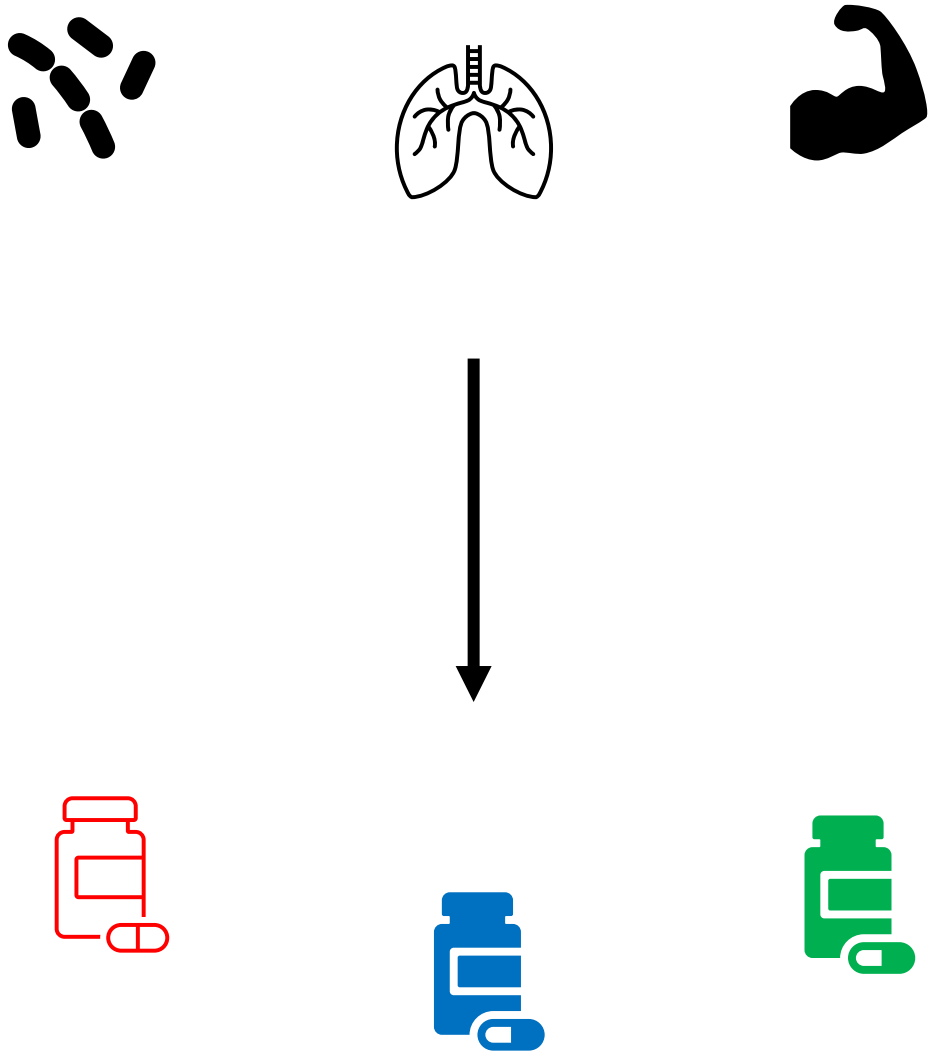
- Two-step testing should be used for the initial TB skin testing of persons who will be retested periodically (serially) due to ongoing risk for TB exposure, if TST is being used.

- A TST can boost a subsequent IGRA. IGRAs do not boost subsequent test results because, unlike the TST, the patient is not exposed to the *M. tuberculosis* antigens.



Wait, when was the last :

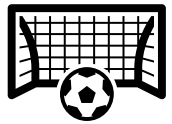
- Clinical assessment?
- Chest x ray?



Choosing the best treatment option:

- Consider the person's risk for exposure to TB, and their underlying biologic risk factors for progression to active TB disease
- Consider drug-drug interactions with current medications the person is taking for other medical conditions
- Consider the risk of hepatotoxicity based on the treatment regimen being considered, and other concurrent medical conditions
- Consider pregnancy status

A shorter treatment is more likely to be completed!



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Morbidity and Mortality Weekly Report (*MMWR*)

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Recommendations and Reports / February 14, 2020 / 69(1);1–11

Timothy R. Sterling, MD[1]; Gibril Njie, MPH[2]; Dominik Zenner, MD[3]; David L. Cohn, MD[4]; Randall Reves, MD[4]; Amina Ahmed, MD[5]; Dick Menzies, MD[6]; C. Robert Horsburgh Jr., MD[7]; Charles M. Crane, MD[8]; Marcos Burgos, MD[8,9]; Philip LoBue, MD[2]; Carla A. Winston, PhD[2]; Robert Belknap, MD[4,8] (VIEW AUTHOR AFFILIATIONS)

View suggested citation

TABLE 4. Dosages for recommended latent tuberculosis infection treatment regimens

Drug	Duration	Dose and age group	Frequency	Total doses
Isoniazid* and rifapentine†	3 mos	**Adults and children aged ≥12 yrs** Isoniazid: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum Rifapentine: 10–14.0 kg, 300 mg 14.1–25.0 kg, 450 mg 25.1–32.0 kg, 600 mg 32.1–49.9 kg, 750 mg ≥50.0 kg, 900 mg maximum **Children aged 2–11 yrs** Isoniazid*: 25 mg/kg; 900 mg maximum Rifapentine†: see above	Once weekly	12
Rifampin¶	4 mos	**Adults:** 10 mg/kg **Children:** 15–20 mg/kg** **Maximum dose:** 600 mg	Daily	120
Isoniazid* and rifampin¶	3 mos	**Adults** Isoniazid*: 5 mg/kg; 300 mg maximum Rifampin¶: 10 mg/kg; 600 mg maximum **Children** Isoniazid*: 10–20 mg/kg††; 300 mg maximum Rifampin¶: 15–20 mg/kg; 600 mg maximum	Daily	90
Isoniazid*	6 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	180
		Adults:15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	52
	9 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	270
		Adults: 15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	76

* Isoniazid is formulated as 100-mg and 300-mg tablets.
† Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.
§ Intermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).
¶ Rifampin (rifampicin) is formulated as 150-mg and 300-mg capsules.
** The American Academy of Pediatrics acknowledges that some experts use rifampin at 20–30 mg/kg for the daily regimen when prescribing for infants and toddlers (**Source:** American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:829–53).
†† The American Academy of Pediatrics recommends an isoniazid dosage of 10–15 mg/kg for the daily regimen and 20–30 mg/kg for the twice-weekly regimen.

MMWR 2020

Latent Tuberculosis Infection Treatment Regimens

Treatment regimens for latent TB infection (LTBI) use isoniazid (INH), rifapentine (RPT), or rifampin (RIF). **CDC and the National Tuberculosis Controllers Association preferentially recommend short-course, rifamycin-based, 3- or 4-month latent TB infection treatment regimens over 6- or 9-month isoniazid monotherapy.**

Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coexisting medical conditions (e.g., HIV*), and potential for drug–drug interactions.

https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w

	DRUG	DURATION	FREQUENCY	TOTAL DOSES	DOSE AND AGE GROUP
Preferred	**ISONIAZID† AND RIFAPENTINE†† (3HP)**	3 months	Once weekly	12	**Adults and children aged ≥12 yrs** INH: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT: 10–14.0 kg; 300 mg 14.1–25.0 kg; 450 mg 25.1–32.0 kg; 600 mg 32.1–49.9 kg; 750 mg ≥50.0 kg; 900 mg maximum
					Children aged 2–11 yrs INH†: 25 mg/kg; 900 mg maximum RPT††: See above
	RIFAMPIN§ (4R)	4 months	Daily	120	**Adults:** 10 mg/kg; 600 mg maximum
					Children: 15–20 mg/kg; 600 mg maximum
	ISONIAZID† AND RIFAMPIN§ (3HR)	3 months	Daily	90	**Adults** INH†: 5 mg/kg; 300 mg maximum RIF§: 10 mg/kg; 600 mg maximum
					Children INH†: 10-20 mg/kg#; 300 mg maximum RIF§: 15-20 mg/kg; 600 mg maximum
Alternative	**ISONIAZID† (6H/9H)**	6 months	Daily	180	**Adults** Daily: 5 mg/kg; 300 mg maximum Twice weekly: 15 mg/kg; 900 mg maximum
			Twice weekly¶	52	
		9 months	Daily	270	**Children** Daily: 10-20 mg/kg#; 300 mg maximum Twice weekly: 20–40 mg/kg#; 900 mg maximum
			Twice weekly¶	76	

*For persons with HIV/AIDS, see Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV available at: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/367/overview.
†Isoniazid is formulated as 100-mg and 300-mg tablets.
††Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.
¶Intermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).
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#The American Academy of Pediatrics recommends an INH dosage of 10–15 mg/kg for the daily regimen and 20–30 mg/kg for the twice weekly regimen.

CDC

CDC and the National TB Controllers Association
LTBI Treatment Guidelines

Potential adverse events of drugs used for latent tuberculosis infection (LTBI) treatment

Drug	Potential adverse effects	Comments
Isoniazid	Elevation of aminotransferases Symptomatic hepatitis Peripheral neuropathy	Close follow-up and caution in patients with baseline liver disease
Rifamycins (includes rifampin,rifapentine, and rifabutin)	Cutaneous rash Hematologic abnormalities Flu-like illness Elevation of aminotransferases Symptomatic hepatitis Orange discoloration of body fluids	Consider multiple potential drug-drug interactions (i.e., warfarin, anticonvulsants, opioids, antiretrovirals) Isoniazid-rifapentine not recommended in pregnant women or women expecting to be pregnant during treatment Isoniazid-rifapentine not recommended for children < 2 years of age

Clin Chest Med 2019

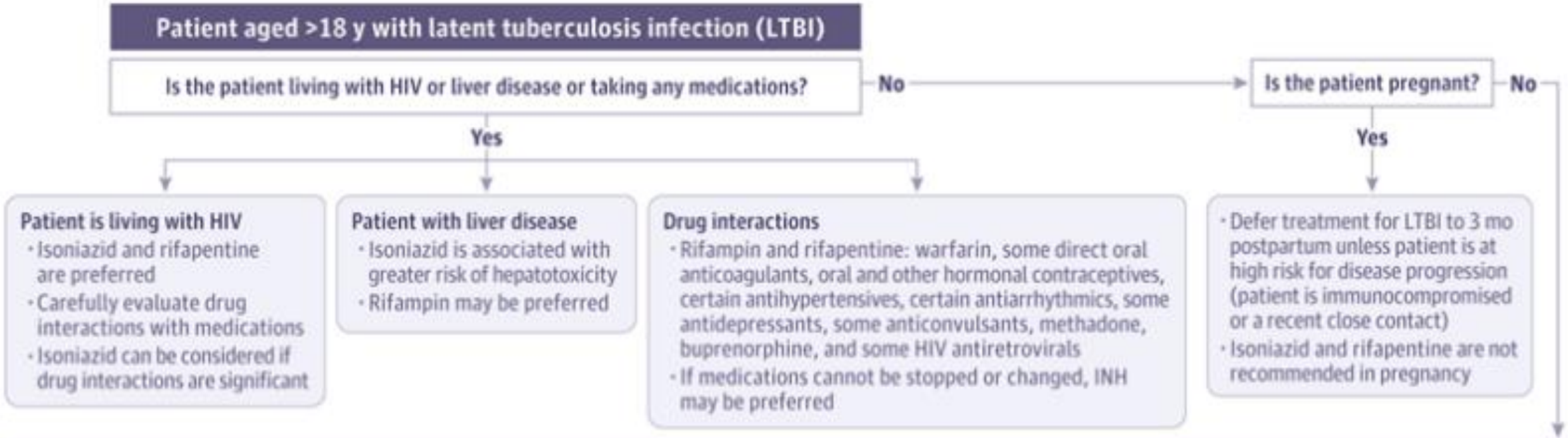
So it looks like the rifamycin-based regimens have many advantages for many people..

- Nitrosamine contamination of rifamycins
(resources at https://www.tbcontrollers.org/resources/nitrosamines/)

- Be mindful of which of the several similar sounding rifamycins are being given

- As well as potential drug-drug interactions

Figure. Proposed LTBI Treatment Algorithm for Clinicians



Medication	Duration, frequency	Dosage	Adverse effects and other considerations
Rifampin	4 mo, daily	10 mg/kg (maximum dose, 600 mg)	Hepatotoxicity, rash or other allergy, thrombocytopenia, gastrointestinal upset
Isoniazid and rifapentine	3 mo, weekly	**Isoniazid:** 15 mg/kg rounded to nearest 50 or 100 mg (maximum dose, 900 mg) **Rifapentine:** 750-mg dose if patient weight is 32.1-49.9 kg; 900-mg dose if patient weight is ≥50 kg (maximum dose, 900 mg)	Rash, hepatotoxicity, hypersensitivity reaction; administer pyridoxine to patients at risk for neuropathy For weekly isoniazid and rifapentine regimen, directly observed therapy is preferred by some state departments; self-administered therapy should include weekly communication with the patient
Isoniazid	6 or 9 mo, daily	5 mg/kg (maximum dose, 300 mg)	Hepatotoxicity, rash, hypersensitivity; administer pyridoxine to patients at risk for neuropathy; 6-mo isoniazid regimen may not be recommended by all state departments of public health

JAMA 2023

Window prophylaxis

- Once active TB disease has been ruled out, children who are younger than 5 years of age who have been exposed to TB should receive LTBI treatment, even if they have an initial negative immunologic test result.

- Children should be retested 8 to 10 weeks after they were last exposed to TB.

- Window prophylaxis can be stopped only if: the child is now older than 6 months, repeat TST is negative, *and* repeat TST was collected at least 8 weeks after last contact with the infectious person

- If treatment is not initiated, provide education to the patient about the signs and symptoms of TB
- Discuss the test results with the patient and document them clearly
- Continue to perform risk- benefit assessments in the future

In general, an "intention to test should be an intention to treat" so be sure to document the reason why treatment was not initiated

Monitoring while on LTBI treatment:

For healthy adults *without* underlying risk factors for hepatotoxicity, check in monthly to ask about

- adherence
- signs and symptoms of TB disease
- signs and symptoms of adverse medication reactions

For adults *with* risk factors for hepatotoxicity

- check a baseline AST, ALT, total bilirubin, alk phos, albumin; If starting a rifamycin also check CBC
- check in monthly for adherence and new signs and symptoms
- consider rechecking labs periodically if baseline was abnormal or new signs or symptoms appear

DOT for LTBI treatment:

- required for LTBI treatment if using an intermittent (twice weekly) INH regimen
- initially required for 12 dose INH + rifapentine weekly regimen, but now this is considered optional in the guidance depending on the setting and resources available
- recommended in any situation where the risk of progression to TB disease is very high if the preventive treatment is not taken (for example in children and adolescents).
- may also be considered if there is special concern for non-adherence to treatment

CDC 2020

After completion of treatment:

- Make sure the person is given documentation of their positive test and completion of treatment

- Educate them that they would be expected to have a positive test for TB in the future- this does not mean that their treatment didn't work

What if there is an interruption in treatment?

- Be sure to perform symptom review before restarting treatment for LTBI
- If the person is having any symptoms consistent with TB disease, repeat chest xray, perform physical exam, and collect sputum before considering restarting treatment

Today we…

- Reviewed the definition of LTBI
- Reviewed the currently available testing methods for LTBI, and how to best use each test depending on the circumstances
- Reviewed treatments for LTBI, and how to choose the option that will best fit an individuals' needs and give them the greatest likelihood of success

Thank you!

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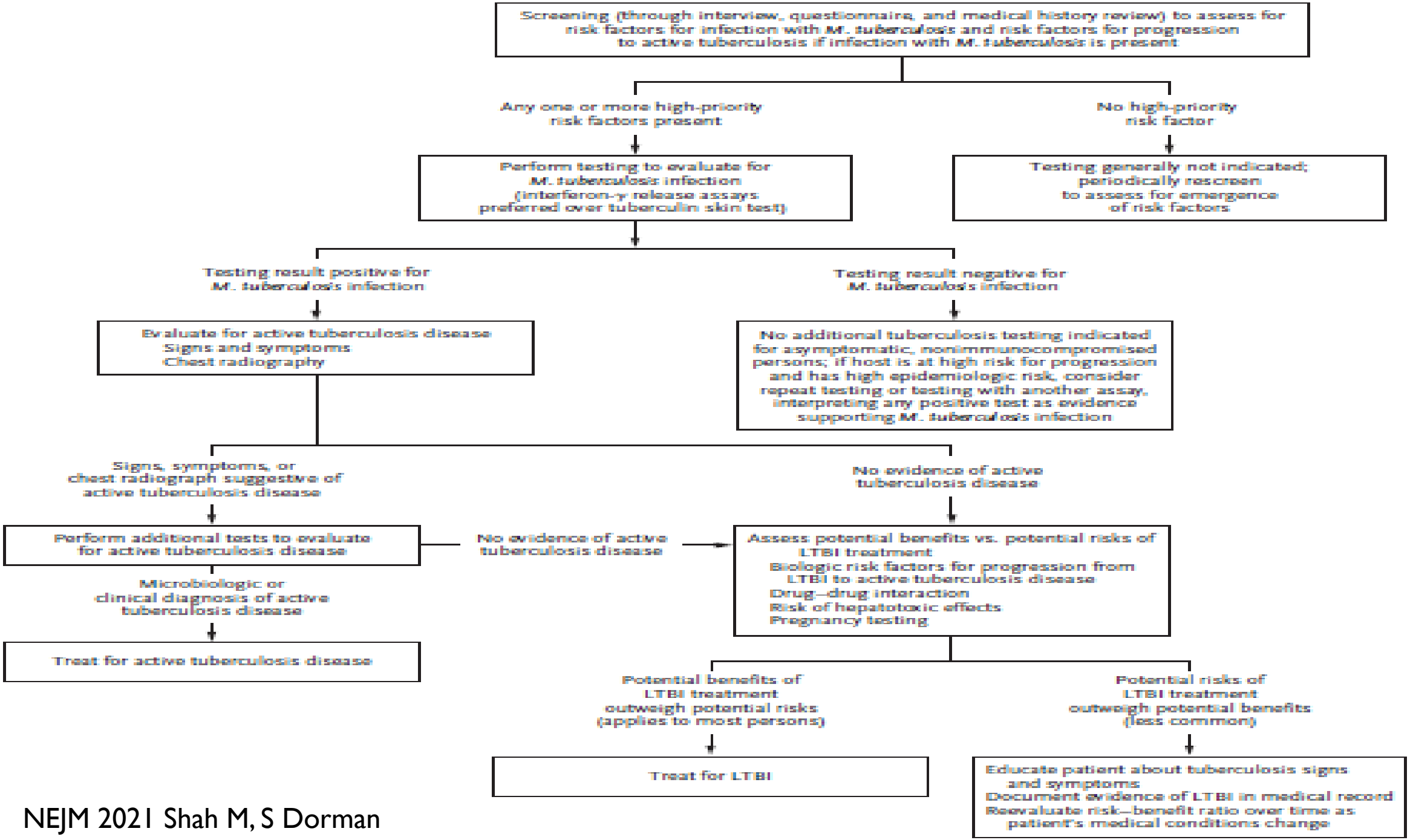


NEJM 2021 Shah M, S Dorman

NEXT, ASSESS THE PERSON'S RISK FOR HAVING TB INFECTION AND PROGRESSION TO ACTIVE DISEASE

Clues in the person's history that predict high risk for infection with tuberculosis:

- Being a household or close contact of someone with active TB
- Birth, residence or prolonged travel (>1 month) in a setting in which TB disease is common (most countries in Africa, Asia, Eastern Europe, Latin America, and the Pacific Islands)
- Other circumstances based on local epidemiology (correctional facilities and homeless shelters)
- Immunosuppression

Biologic factors that can increase risk of progression to tuberculosis disease:

- Diabetes mellitus
- Silicosis
- Chronic kidney disease
- Chronic malabsorption, gastrectomy, or intestinal bypass
- Age less that 5 years
- A BMI of 20 or less
- Current or former smoker
- Leukemia/lymphoma, cancer of the head and neck

NEJM 2021

HIGH PRIORITY CANDIDATES FOR SCREENING:

HIGH RISK OF TUBERCULOSIS INFECTION:

- Persons who have spent time with someone who had TB disease
- Persons from a country in which TB is common
- Live or work in high risk settings like correctional facilities, nursing homes, shelters for people experiencing homelessness
- Healthcare workers who care for people at increased risk for TB disease
- Mycobacteriology lab personnel
- Infants, children and adolescents exposed to adults who are at increased risk for Tb infection or disease

MORE LIKELY TO DEVELOP TUBERCULOSIS DISEASE:

- Persons living with HIV
- Persons who became infected with TB bacteria in the last 2 years
- Babies and children
- Persons who use IV drugs
- Persons who have other conditions that weaken the immune system
- Persons with a history of inadequately treated TB
- Elderly persons
- Persons with renal failure, diabetes mellitus and silicosis

"Flexibility should be used in defining high-risk groups for testing…definitions should be made at the local level according to local demographics and TB epidemiology"

CDC Training Module 3

"TARGETED TESTING"

People at High Risk for Exposure to or Infection with *M. tuberculosis*	People at High Risk for Developing TB Disease after Infection with *M. tuberculosis*
• **Contacts** of people known or suspected to have TB disease • People born in or who frequently travel to countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, and Guatemala, or other countries with high rates of TB • People who live in, or have lived in, high-risk congregate settings (for example, homeless shelters or correctional facilities) • Employees of high-risk congregate settings • Health care workers who serve patients with TB disease • Populations defined locally as having an increased incidence of LTBI or TB disease, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol • Infants, children, and adolescents exposed to adults who are at increased risk for LTBI or TB disease	• People living with HIV • Children younger than 5 years of age • People recently infected with *M. tuberculosis* (within the past 2 years) • People with a history of untreated or inadequately treated TB disease • Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation • Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, or cancer of the head, neck, or lung • Persons who have had a gastrectomy or jejunoileal bypass • Low body weight • Cigarette smokers and persons who abuse drugs or alcohol • Populations defined locally as having an increased incidence of disease due to *M. tuberculosis*, including medically underserved, low-income populations

Module 3, CDC TB training module

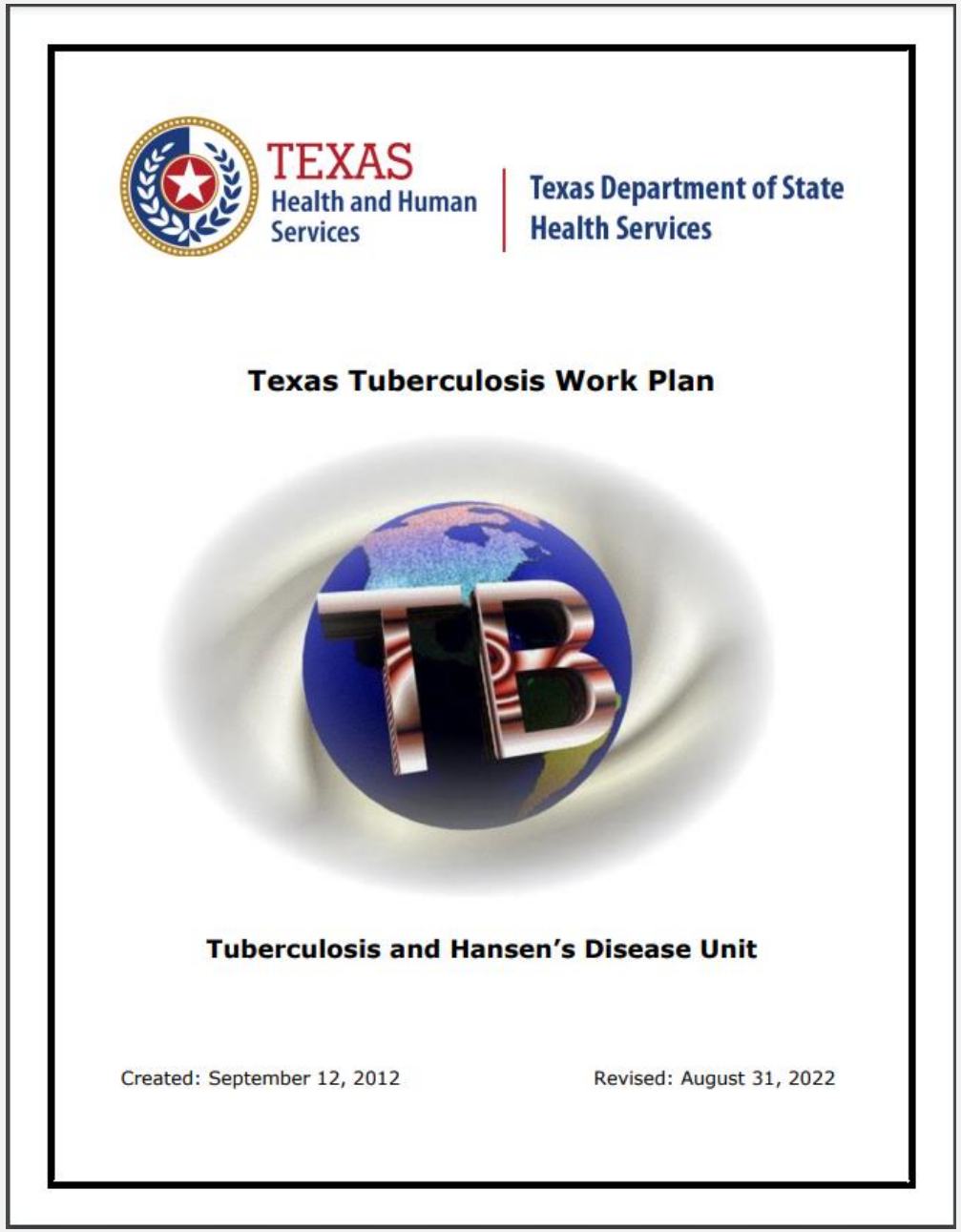
IF INTERFERON GAMMA RELEASE TEST OR TUBERCULIN SKIN TEST IS POSITIVE...

Review signs and symptoms again

and

Perform chest radiography

- Collect sputum for AFB smear, culture and MTB NAAT if there are signs and symptoms of TB and/or chest xray is abnormal



For patients age 12 years and older, screen for HIV infection using an approved laboratory-based HIV immunoassay.

For patients younger than 12 years old, screen for HIV infection using an approved laboratory-based HIV immunoassay if risk factors for HIV infection are present (including known or self-reporting of: mother with HIV infection and no documentation of child's status; history of blood transfusion outside the United States; history of sexually transmitted infection (STI), sexual activity, pregnancy, intravenous drug abuse).

https://www.dshs.texas.gov/sites/default/files/LIDS-TB/policies/TBWorkPlan.pdf

SCREENING FOR TUBERCULOSIS FOR PEOPLE WITH HIV

- All persons with HIV should be evaluated for LTBI at the time of HIV diagnosis, regardless of their epidemiological risk of TB exposure **(AII)**

- Persons with advanced HIV infection (CD4 count <200 cells/mm^3) and negative diagnostic tests for LTBI, without indications for initiating empiric LTBI treatment (i.e., no recent exposure to a culture-confirmed TB case), should be retested for LTBI once they start ART and attain a CD4 count ≥200 cells/mm^3 to ensure that the initial test result was a true negative result.

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023) [pp X-1]

GUIDANCE FOR LTBI TREATMENT FOR PEOPLE LIVING WITH HIV

Treating LTBI to Prevent TB Disease in People with HIV

Indications

- Positive screening test[a] for LTBI, no evidence of active TB disease, and no prior history of treatment for active disease or latent TB infection **(AI)**
- Close contact with a person with infectious TB, regardless of screening test result **(AII)**

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023) [pp X-1]

PREFERRED THERAPY FOR LTBI FOR PEOPLE WITH HIV

Preferred Therapy

- Rifapentine (see weight-based dosing below) PO once weekly plus isoniazid 15 mg/kg PO once weekly (900 mg maximum) plus pyridoxine 50 mg PO once weekly for 12 weeks **(AI).** Note: Rifapentine is recommended only for virally-suppressed patients receiving an efavirenz-, raltegravir-, or once-daily dolutegravir-based ARV regimen **(AI).**
  - Rifapentine Weekly Dose (maximum 900 mg)
    - *Weighing 32.1–49.9 kg*: 750 mg
    - *Weighing ≥50.0 kg*: 900 mg
- Isoniazid 300 mg PO daily plus rifampin 600 mg PO daily plus pyridoxine 25–50 mg PO daily **(AI)** for 3 months. See the Dosing Recommendations for Anti-TB Drugs table for the list of ARV drugs not recommended for use with rifampin and those which require dosage adjustment (i.e., raltegravir, dolutegravir, or maraviroc).

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023)

SUMMARY OF THE CURRENT TREATMENTS FOR LTBI:

- Encourage people with who are at increased risk for TB infection and/or progression to TB disease and are found to have LTBI to take a course of preventative treatment.

- The shorter the regimen, the great the likelihood that they will complete the treatment.

- The current preferred treatments for TB infection is weekly Isoniazid and Rifapentine (12 doses), which can be completed in 3 months, Rifampin daily for 4 months, and Rifampin and INH daily for three months.

  Note some exceptions for special groups:

  - people younger than 2 years old
  - pregnant people
  - people who are thought to be infected with INH or rifampin resistant TB
  - people with HIV whose ART regimen is not compatible with rifapentine

TREATMENT OF CONTACTS EXPOSED TO MDR TB:

May offer treatment for LTBI vs following with observation alone

For treatment of MTB LTBI, we suggest 6 to 12 months treatment with a fluoroquinolone alone or with a second drug, on the basis of sourse-case isolate DST.

Randomized, clinical trials on the effectiveness of shorter, safer, more effective regimens for MDR LTBI are underway.

Am J Respir Crit Care Med 2015

ALTERNATIVE REGIMENS FOR LTBI TREATMENT FOR PEOPLE WITH HIV

Alternative Therapies

- Isoniazid 300 mg PO daily plus pyridoxine 25–50 mg PO daily for 6–9 months **(AII)** *or*
- Rifampin 600 mg PO daily for 4 months **(BI)** See the Dosing Recommendations for Anti-TB Drugs table (above) for the list of ARV drugs not recommended for use with rifampin and those which require dosage adjustment (i.e., raltegravir, dolutegravir, or maraviroc) *or*
- Isoniazid 300 mg PO daily plus rifapentine PO daily plus pyridoxine 25–50 mg PO daily for 4 weeks **(BI)** Note: Rifapentine is recommended only for patients receiving an efavirenz-based ARV regimen **(AI).**
  - Rifapentine Daily Dose (maximum 600 mg)
    - *Weighing <35 kg*: 300 mg
    - *Weighing 35–45 kg*: 450 mg
    - *Weighing >45 kg*: 600 mg

For persons exposed to drug-resistant TB, select drugs for prevention of TB after consultation with experts and with public health authorities **(AIII).**

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023)

TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Priority rank*	Regimen	Recommendation (strong or conditional)	Evidence (high, moderate, low, or very low)
Preferred	3 mos isoniazid plus rifapentine given once weekly	Strong	Moderate
Preferred	4 mos rifampin given daily	Strong	Moderate (HIV negative)[†]
Preferred	3 mos isoniazid plus rifampin given daily	Conditional	Very low (HIV negative)
		Conditional	Low (HIV positive)
Alternative	6 mos isoniazid given daily	Strong[§]	Moderate (HIV negative)
		Conditional	Moderate (HIV positive)
Alternative	9 mos isoniazid given daily	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus.

* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.

† No evidence reported in HIV-positive persons.

§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

MMWR 2020