

TB or Latent TB? That Is the Question

Next steps after the IGRA

Yvonne Boire, BSN, RN

Nurse Program Coordinator Vermont Department of Health Division of Laboratory Sciences and Infectious Disease Yvonne.Boire@vermont.gov

May 21, 2025 Vermont Immunization and Infectious Disease Conference



Vermont Immunization & Infectious Disease Conference Hotel Champlain, Burlington, VT May 21, 2025 Session I – Tracking Trouble: Innovations in Infectious Disease Surveillance from Sewers to Syndemics Speakers: Yvonne Boire, BSN, RN, Lynn Blevins, MD, MPH, and Daniel Daltry, MSW

All those with control of content (speakers, planners, moderators, reviewers, staff) who have relevant financial relationships with "ineligible companies" are listed below (name of company only/no logos, trade names, or product group messages). (*An "ineligible company" is defined as those whose primary business is producing, marketing, selling, reselling or distributing healthcare products used by or on patients.*)

No speakers, planners or CMIE reviewers have any financial relationships with ineligible companies.

This activity did not receive any support from ineligible companies (grants or in-kind).

<u>Meeting Disclaimer:</u> Regarding materials and information received, written or otherwise, during this Conference, the scientific views, statements, and recommendations expressed during this activity represent those of the authors and speakers and do not necessarily represent the views of the University of Vermont.

Vermont Immunization & Infectious Disease Conference Hotel Champlain, Burlington, VT May 21, 2025



In support of improving patient care, this activity has been planned and implemented by The Robert Larner College of Medicine at the University of Vermont is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME) and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The University of Vermont designates this live activity for a maximum of 5.0 AMA PRA Category 1 Credit(s)[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This program has been reviewed and is acceptable for up to 5.0 Nursing Contact Hours.

As a Jointly Accredited Organization, The Robert Larner College of Medicine at the University of Vermont is approved to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Organizations, not individual courses, are approved under this program. State and provincial regulatory boards have the final authority to determine whether an individual course may be accepted for continuing education credit. The University of Vermont maintains responsibility for this course. Social workers completing this course receive 5.0 ethics continuing education credits.

This activity was planned by and for the healthcare team, and learners will receive 5.0 Interprofessional Continuing Education (IPCE) credit for learning and change.

Objectives

At the conclusion of this presentation attendees should be able to:

- 1. Describe who is being tested for TB infection in Vermont
- 2. Identify who should be screened for TB infection in Vermont
- 3. Understand considerations in interpreting IGRA results
- 4. Identify the components of a TB assessment
- 5. Identify TB and LTBI resources available to providers

TB incidence: Worldwide, Nationally, and in Vermont

The estimated worldwide TB incidence rate in 2023 was 134 per 100,000 population, representing estimated 10.8 million cases worldwide (WHO)



The national TB incidence in 2023 was 2.9 per 100,000 population, representing 9,615 cases nationally (CDC)

Vermont has one of the lowest TB incidence rates in the country. The 2023 incidence rate was 0.46 per 100,000 population, representing 3 cases in Vermont (VDH)

Who is getting tested for TB infection in Vermont?



Most people being tested for TB infection in Vermont fit into 1 of 3 buckets:

- 1. Screening for an immigration or refugee health exam
- 2. Screening before starting immunosuppressive therapy
- 3. Screening for employment in the health care setting

Tests used to screen for TB infection

1) TB blood test (IGRA)

- T-Spot
- QuantiFERON Gold
- 2) TB skin test





Things to understand about BOTH tests:

- Neither can distinguish between TB infection and TB disease
- Neither can be used to test for cure
- Both must be interpreted with consideration of the individual's risk factors
- Neither should be used as a sole test when TB disease is suspected

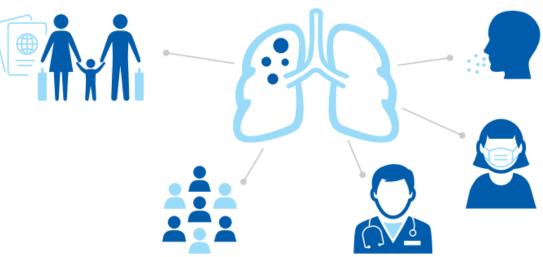
Questions to ask before you screen for TB

- 1. Has this person ever tested positive for TB infection before?
- 2. Has this person ever had BCG vaccination?
- 3. Does this person have risk factors for TB infection or progression to TB disease if infected?
- 4. Does this person have signs or symptoms consistent with TB disease?



Consider risk when screening for TB infection

TB experts suggest that only people who have TB risk factors should be screened for TB infection.



Current guidance encourages providers to consider TB risk factors when interpreting TB test results.

TB risk factors

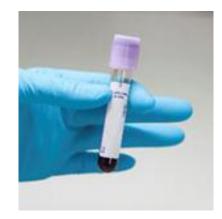
Risk of TB Infection	Risk of Progression to TB
Had contact with a person with active infectious TB	Have recently been infected with TB (in the past 2 years)
Were born in, lived in, or frequently traveled to countries where TB is common	Have certain health conditions that compromise the immune system
Live or used to live in large group settings where TB is more common	History of untreated or inadequately treated TB disease
Work or used to work in places where TB is more common or more likely to spread	Take medications or receive treatments that weaken the immune system
	Under age 5

Considerations for people at low risk

When a person with low risk factors has a positive TB test, repeat testing may be indicated to confirm the result.

This can be considered for people who have:

- No signs or symptoms of TB disease
 Low risk factors for exposure to TB
 Low risk factors for program to TB disease
- ✓ Low risk factors for progression to TB disease



These individuals would only be considered infected with TB if the second test is also positive. If the second test is negative, the person is not considered infected with TB.

Considerations for people at risk for TB infection

Performing a second TB test on someone with risk factors for TB infection is not generally recommended.



Discordant results in this population are more difficult to interpret because there is a high pre-test probability for infection.

If someone with risk factors for TB exposure has discordant TB test results, consider consultation with a TB expert.

Considerations for people at risk for progression to TB

Some people have low risk for having been exposed to TB but have high risk for progression to TB disease if infected.

Deciding whether to perform a second test to confirm the first result is not an easy choice.

The consequence of getting it wrong can be high.

Consider consultation with a TB expert.



"Low level" QuantiFERON results

The QuantiFERON is meant to be reported as a qualitative value: positive, negative, or indeterminate.

The manufacturer of this product does not define a "low level" result or provide special guidance for how to interpret results just above the threshold for positivity.

If using the quantitative values to interpret the QuantiFERON result, be sure to also consider the patient's risk factors, as guided by national TB experts and the product manufacturer.





The QuantiFERON Gold

Table 2. Interpretation of QFT-Plus results

Nil (IU/ml)	TB1 minus Nil (IU/ml)	TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)*	QFT-Plus Result	Report/Interpretation
≤8.0	≥0.35 and ≥ 25% of Nil value	Any	Any	Positive†	<i>M. tuberculosis</i> infection likely
	Any	≥0.35 and ≥ 25% of Nil value			
	<0.35 or ≥0.35 and <25% of Nil value	<0.35 or ≥0.35 and <25% of Nil value	≥0.5	Negative	<i>M. tuberculosis</i> infection NOT likely
	<0.35 or ≥0.35 and <25% of Nil value	<0.35 or ≥0.35 and <25% of Nil value	<0.5	Indeterminate [‡]	Likelihood of <i>M. tuberculosis</i> infection cannot be determined
>8.0 [§]	Any				cannor be determined

QFT-Plus results are based on the amount of IFN- γ that is released in response to the M. tuberculosis antigens and control substances.

The result should include qualitative value (positive, negative, indeterminate) and quantitative values (Nil, Mitogen, TB1-Nil, TB2-Nil).

https://www.quantiferon.com/wp-content/uploads/2017/04/English_QFTPlus_ELISA_R04_022016.pdf

Okay, so the IGRA is positive, now what?

Active TB disease **must** be ruled out before diagnosing and treating LTBI.

Components of a TB assessment:

- Medical history
- TB test (TB blood test or a tuberculin skin test)
- Chest radiograph
- Physical examination
- Sputum examinations if indicated
- Microscopy performed on non-pulmonary specimen if indicated

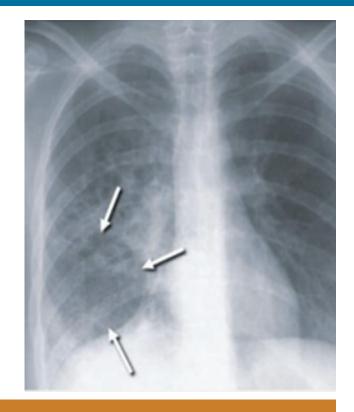


The chest x-ray

The chest x-ray should be performed promptly after a positive TB test to rule out active pulmonary TB.

Any abnormality on the chest radiograph that might represent TB disease should trigger immediate action.

Young children should have both posterior-anterior and lateral views (assess for presence of hilar adenopathy).



When initiating LTBI treatment in someone with a remote diagnosis, ensure there is a recent negative chest x-ray before starting therapy.

What if I can't rule out TB disease?

If active TB disease is suspected, notify the Vermont Department of Health by calling 802-863-7240, option 2. Ask to speak with someone about TB.

The VDH TB Program can help with:

- Providing testing guidance
- Assisting with sputum collection
- Testing specimen for TB at the state public health lab
- Accessing clinical support from TB experts



Establishing an LTBI diagnosis

A diagnosis of LTBI can be made if:

- 1. There is a positive TB test result (TST or TB blood test)
- 2. The patient has no signs, symptoms, or clinical evidence of TB
- 3. Or, if any abnormalities are present, TB has been clinically ruled out in favor of another diagnosis
- 4. The patient does not have prior history of appropriately treated TB disease or TB infection

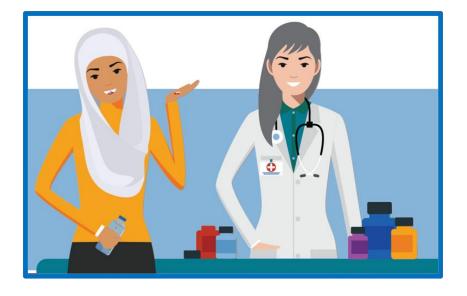


LTB-I-don't know what to do next

People with LTBI, especially those with risk factors, should be treated to prevent progression to active disease.

In Vermont, LTBI treatment and case management occurs in the community provider setting.

There are many great resources available to providers treating LTBI.



What do patients need to know about LTBI?

- \succ They have TB germs in their body that are inactive.
- Their immune system is keeping those germs controlled and preventing them from getting sick.
- If their immune system becomes weak, the TB germs could become active and make them sick.
- > If they become sick with TB, they might infect their family and friends.
- There is treatment available that can help prevent them from ever becoming sick with TB disease.
- If they develop signs or symptoms of TB disease, they should seek care.

LTBI education resources for patients

<u>CDC's Questions and Answers About Tuberculosis</u> provides a lot of information about both TB and LTBI and is translated into 11 languages. This resource can be given to clients as a full booklet or in relevant sections. Pages 9-15 are especially relevant and useful for folks being educated about LTBI and LTBI treatment.

<u>CDC's Think.Test.Treat TB Campaign Patient Education Resources</u> a webpage that has many patient education resources available. Most are translated into a variety of languages.

<u>Southeastern National Tuberculosis Center</u> a TB Center of Excellence product list that has a handout differentiating LTBI from TB and explaining why LTBI treatment is important. Translated into many languages. Find by going to the products page and typing, "prevent tuberculosis".

<u>GTBI's Patient Education Videos</u> products from a TB Center of Excellence which explain how TB is spread and the difference between latent TB and TB disease.

LTBI treatment regimens

Latent

Infection

Treatment

Regimens

Tuberculosis

There are several options available for LTBI treatment.

Preferential recommendation is given to the short course rifamycin based therapies, unless contraindicated. 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 wr
					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 ⁵ (3HR)	3 months Daily	Daily	90	Adults INH [†] : 5 mg/kg; 300 mg maximum RIF ^{\$} : 10 mg/kg; 600 mg maximum
			Daily		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	

Guidance resources for providers (general & adult)

CDC's Core Curriculum on Tuberculosis: What the Clinician Should Know

CDC's Latent Tuberculosis Infection: A Guide for Primary Health Care Providers

NTCA's Testing and Treatment of Latent Tuberculosis Infection in the United States: A Clinical Guide for Health Care Providers and Public Health Programs

GTBI's Pocket Guide: Diagnosis and Treatment of Latent Tuberculosis Infection (adults)

CDC's Treatment Regimens for Latent TB Infection (webpage)

<u>GTBI's Rifamycin Drug-Drug Interactions: A Guide for Primary Care Providers Treating Latent</u> <u>Tuberculosis Infection</u>

GTBI's Interactive Online Tool: LTBI Assist

Guidance resources for providers (pediatric specific)

GTBI's Pediatric Tuberculosis (TB) Risk Assessment Tool

<u>GTBI's Pocket Guide: Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) in Children</u> and Adolescents Pocket Card

GTBI's Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider

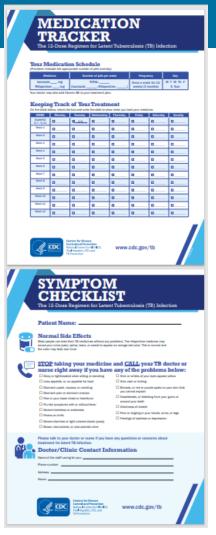
Heartland National TB Centers's Tips for Treating Latent TB Infection in Children

What do patients need to know about LTBI treatment?

Make sure your patients know how to safely take their medications.

Educate your patients to stop taking their medication and call the office if they experience symptoms of adverse drug reactions.

There are tools to help patients keep on track with their medications and monitor for symptoms.



Medication tracking tools for patients

<u>4R (Rifampin daily x4 months) Medication Tracker</u> Available from CDC in English and Spanish

<u>3HP (Isoniazid and Rifapentine once a week x12 weeks) Medication Tracker</u> Available from CDC in 6 languages

<u>3HR (Isoniazid and Rifampin daily x 3 months) Medication Tracker</u> Available from CDC only in English

Southeastern National Tuberculosis Center provides the 4R, 3HP, and 3HR trackers available in several other languages. Find by going to the products page and typing "tracker" into the search tab

Southeastern National Tuberculosis Center also has great fact sheets on Isoniazid, Rifapentine and Rifampin in many languages. Find by going to the products page and typing "patient fact sheet"

LTBI treatment monitoring

Schedule monthly visits to assess for:

- ✓ S/S of active TB
- ✓ Medication adherence
- ✓ Adverse effects



Some patients may need enhanced monitoring, such as routine lab work, if they have underlying health conditions or take certain medications.

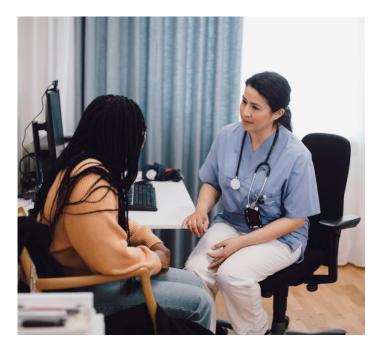
What do patients need to know after LTBI treatment?

- Their TB test (blood test/skin test) will likely always be positive.
- They should keep a record of their TB test, chest x-ray, and treatment completion to share with providers or employers as needed.
- Completing LTBI treatment greatly decreases their chance of developing TB disease, but it is not impossible to progress to TB disease.
- They should know the signs and symptoms of TB disease and when to seek assessment.
- They should understand that if they are exposed to TB again, they can become infected again.

What if I want to refer my patient to another provider?

Some care providers choose to refer their clients with LTBI to another provider. This might be due to a complexity in the patient's health status or because of the provider's unfamiliarity with LTBI treatment.

Even if you will not be treating the patient, be sure they have education about their diagnosis.



How does VDH help with LTBI assessment & treatment?

- 1. Direct providers to clinical guidance, educational resources, and clinical consultation.
- 2. Help providers access state supplied TB medication for their patients with financial barriers.
- 3. Provide in person or virtual LTBI trainings for practices.
- 4. Perform nurse case management for patients who are high risk*.
- 5. Help prevent disruption in treatment for clients moving out of state during therapy.

LTBI surveillance

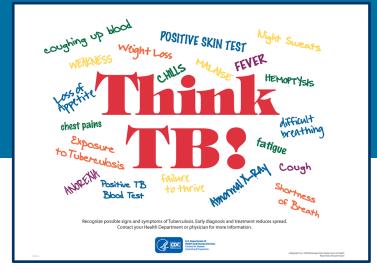
LTBI is reportable to the Vermont Department of Health.

LTBI surveillance has helped the Vermont TB Program:

- Understand why people are being tested in Vermont
- Learn more about the continuum of care after testing
- Identify gaps in knowledge
- Provide enhanced support for our area providers
- Prompt earlier VDH involvement in rule out active TB cases

Providers can find the LTBI case report form online.





It's up to you to "Think TB"

TREAT

Did you know?

Approximately 80% of TB cases in the U.S. are the result of untreated latent TB infection.



Find resources at: Think. Test. Treat TB | Think. Test. Treat TB. | CDC



Please reach out with any questions, comments, or concerns.

The Vermont Department of Health TB Program

802-863-7240, option 2 Ask to speak with someone about TB