Latent Tuberculosis Infection (LTBI) Investigation Guidance Document

Purpose

This guide is designed to aid in the investigation of cases LTBI. The materials in this guide may assist with education and communication efforts during the case investigation. Materials in this guide were created by Montana Department of Public Health and Human Services (MTDPHHS) Communicable Disease Epidemiology Section and represent the current guidance for LTBI investigations. The intended audience for this document is local health jurisdictions in Montana. Please do not distribute this document to any key surveillance partners.

Case Definition

The case definition for LTBI can be found in the Administrative Rules of Montana (ARM) under 37.114.1001.

(4) A case of latent tuberculosis infection exists if the case meets the laboratory and clinical criteria in (5) and (6).
(5) Laboratory criteria for latent tuberculosis infection:
(a) a positive tuberculin skin test (TST); or
(b) a positive interferon gamma release assay (IGRA).
(6) Clinical criteria for latent tuberculosis infection:
(a) no clinical evidence compatible with TB disease including no signs or symptoms consistent with TB disease; and
(b) chest imaging without abnormalities consistent with TB disease (chest radiograph or CT scan); or
(c) abnormal chest imaging that could be consistent with TB disease with microbiologic testing that is negative for abnormal chest imaging that could be consistent with TB disease with microbiologic testing that is negative for Mycobacterium Tuberculosis Complex and where TB disease has been clinically ruled out.

This outlines that you have a case of LTBI if you have: a positive skin or blood test, a clear chest x-ray, and no s/s consistent with active disease or active TB has been ruled out.

Montana is a low incidence state for TB. We only average 5 cases of active TB a year and our estimated burden of LTBI is around 7,000 to 9,000. Given that information, a lot of low-risk people get tested for TB. **It is recommended that if someone is tested that is low risk, that they get a confirmatory test either with an additional blood or skin test. They should only be considered positive if the second test also comes back positive.** They then can get a chest x-ray and be treated for LTBI if appropriate (which is most of the time).

Labs

Below are a couple examples of labs that you might see in MIDIS for TB blood tests or IGRAs.

Mycobacterium tuberculosis stimulated gamma interf:
Positive
Reference Range: (Negative) - (Final)

GAMMA INTERFERON BACKGROUND BLD IA-ACNC:
0.30 IU/mL - (Final)

M TB IFN-G BLD-IMP:
Positive (qualifier value)
Reference Range: (NEGATIVE) - (Final)

M TB IFN-G CD4+ BCKGRND COR BLD-ACNC:
1.33 IU/mL - (Final)

M TB IFN-G CD4+CD8+ BCKGRND COR BLD-ACNC:
2.33 IU/mL - (Final)

MITOGEN IGNF BCKGRD COR BLD-ACNC:
8.15 IU/mL - (Final)

QFT Mitogen-Nil: 5.25 IU/mL
Reference Range: (*) - (Final)

QFT TB1 - Nil: 0.38 IU/mL
Reference Range: (*) - (Final)

QFT TB2 - Nil: 0.54 IU/mL
Reference Range: (*) - (Final)

Quantiferon-Gold Plus (ELISA):
POSITIVE - (Final)
Reference Range: (Negative) - (Final)

QuantiFERON Mitogen minus NIL:
>10.00 IU/mL - (Final)
QuantiFERON NIL:
0.03 IU/mL - (Final)
Quantiferon Plus TB1 minus NIL:
0.50 IU/mL - (Final)
Reference Range: (0.00-0.34) - (Final)

Quantiferon Plus TB2 minus NIL:
0.43 IU/mL - (Final)
Reference Range: (0.00-0.34) - (Final)

Quantiferon TB Gold Plus:
Positive - (Final)
Reference Range: (Negative) - (Final)

The main thing to focus on with LTBI labs is the qualifying value and not the quantifying values. Is the lab positive or not? Base your investigation on this. The numbers can be helpful if you have a borderline positive (anything between 0.35 and 0.8 for TB – NIL) and the provider is wondering about retesting. Usually, I recommend to retest if there is any question about the results or the validity of the test and it's in the borderline zone. Remember that negative tests won't come into MIDIS, so if the provider retests and it's negative, you'll need to follow up for a result. The flow chart below can clarify how the result is made and Table 2.4 below can clarify how to interpret the results. You can always email if you have questions about a lab though.

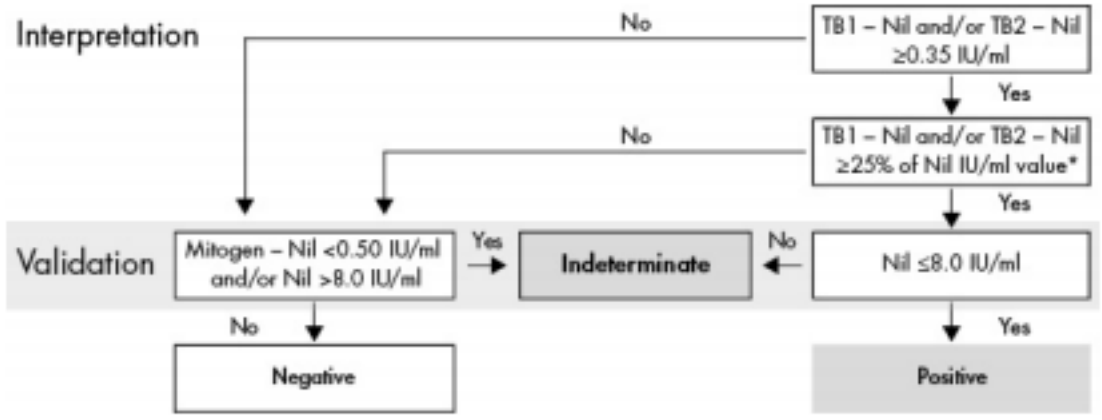


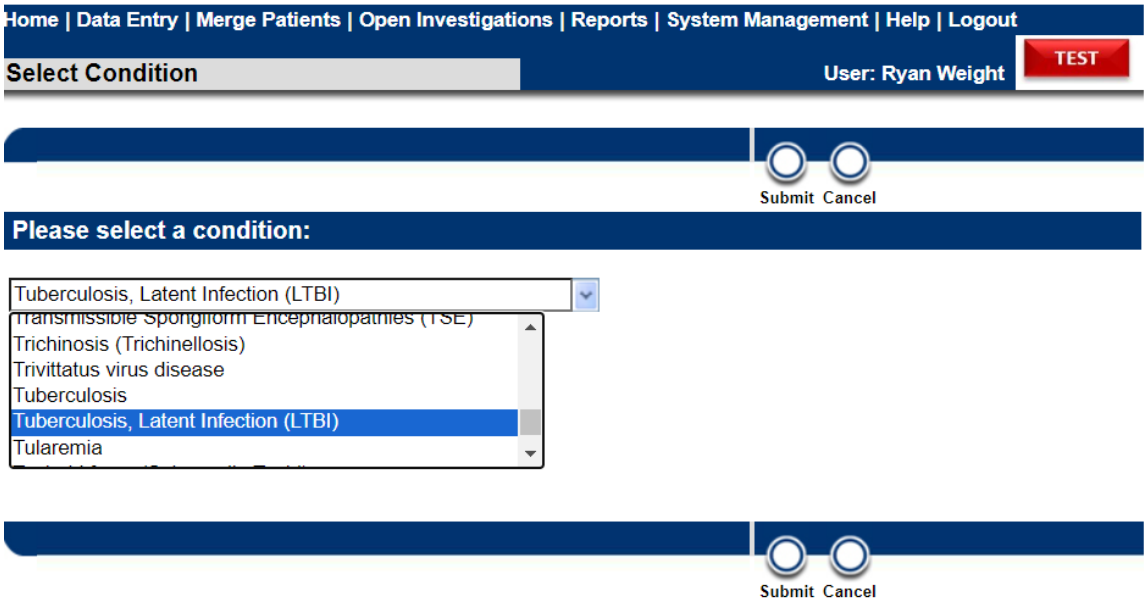
Figure 6. QFT-Plus test interpretation. *For TB1 minus Nil or TB2 minus Nil value to be valid, the ≥25% of Nil IU/ml value must be from the same tube as the original ≥0.35 IU/ml result.

Table 2.4
Interpretation of TB Blood Test Results

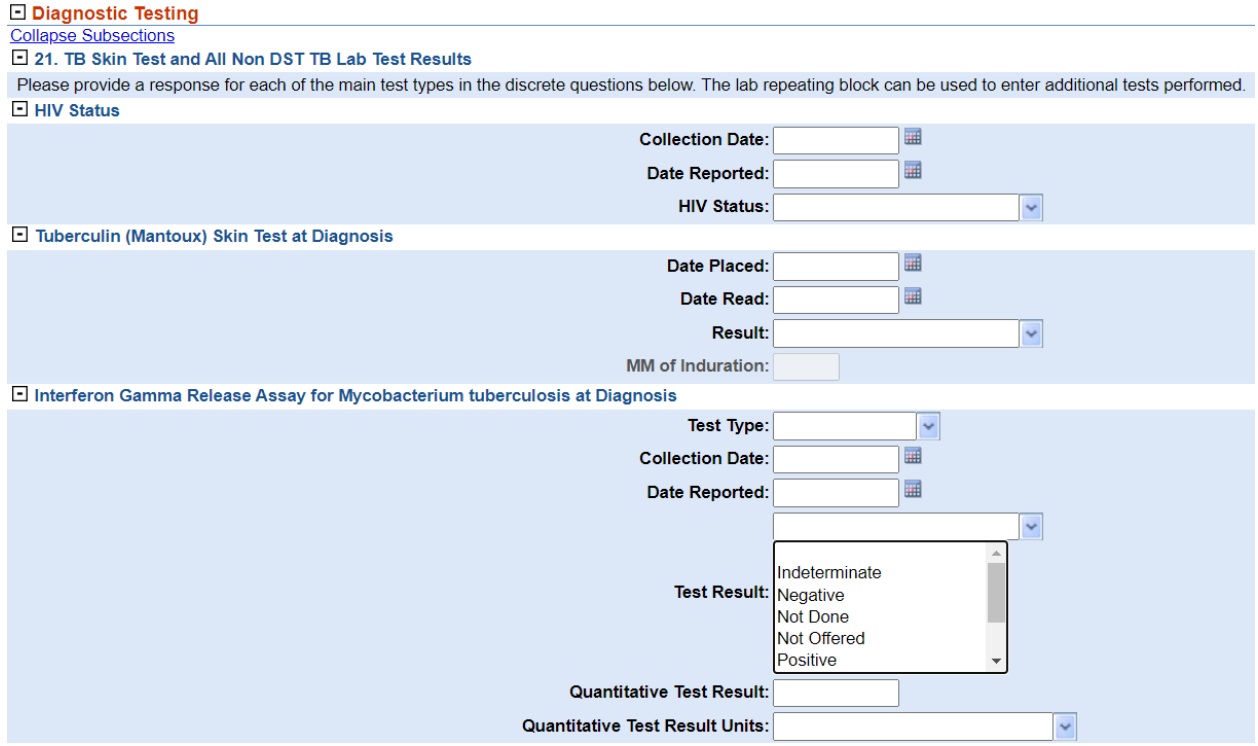
TB Blood Test Result	Interpretation
Positive	*M. tuberculosis* infection likely.
Negative	*M. tuberculosis* infection unlikely, but cannot be excluded, especially if • Patient has signs and symptoms of TB disease. • Patient has a high risk medical condition for developing TB disease once infected with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

MIDIS

There should only be one investigation in MIDIS per person for LTBI. If the patient has a history of testing, email me to make sure there isn't an investigation already. Once you receive a lab you can create an investigation right away. Remember that when you are dealing with a blood or skin test this is indicative of LTBI and not active TB. **Please choose the Tuberculosis, Latent Infection investigation NOT Tuberculosis!** Tuberculosis is for active TB not LTBI.



Once you get into the investigation, fill out any risk factor information and testing that has been done. If there is negative testing it won't go into MIDIS, please put any negative testing into the diagnostic testing section. This is especially helpful if the provider retests a low-risk individual, and it comes back negative. You can then call it not a case. If that test is not in the investigation, I might reject it as all I see is are positive labs.



After filling out the investigation with the information that you have, reach out to the provider, or look at the medical notes to see why the patient was tested if unknown and collect the remaining information for the investigation. Understanding why the patient was tested can help in determining if the patient is low risk or not. If the patient is low risk, you may need to suggest retesting to the provider and educate them. The testing flowchart, investigation form, and other resources can be found on the DPHHS TB webpage under the LTBI Toolkit.

For assigning a state case number, this will be specific for your county. Format is year, state, first 4 letters of jurisdiction, and then 0010_ with the blank being the count for LTBI case for the current year. For example Lewis and Clark Counties 12th case would be 2024-MT-LEWI00112.

Case Status

If all you have is a positive lab and no additional information, please make it a Suspect Case. If you have some risk factor information that would increase this person's risk of having LTBI you can make it a Probable Case. If they retested and the second test was positive you can make it a Confirmed Case. If there is any treatment information past or present, you can make it a Confirmed Case. Additionally, you can make it confirmed if the patient refuses treatment or the provider decides not to treat.

If the patient was ever treated in the past for LTBI and the provider is not considering treatment because of this, please back date the MMWR week and year to roughly when that occurred. Also, back date any investigation where a patient received a definitive diagnosis. This helps avoid artificially inflating numbers now that LTBI is reportable.

Once you've completed the investigation you can either leave it open until the patient completes therapy so you can update that in the investigation, or you can close it and use the tracker on the CDEpi Resource Page. Either method is fine as long as the treatment information is recorded. This is very important if the patient moves or if providers are looking for treatment information for the patient.

FAQ

The provider tested and the IGRA was positive. They then ordered a chest x-ray that was negative or normal. Does this mean that they don't have LTBI?

NO! The blood or skin test checks for infection. If they are positive with either, they have LTBI. The chest x-ray only looks for progression of disease. We want a clear x-ray. That means that they haven't progressed in disease and the LTBI regimen will be sufficient to treat their TB bacterial burden. Some providers might need to be educated about this.

A patient came back with an abnormal x-ray. What should we do?

The next step would be to rule out active TB disease. This would require getting 3 sputum samples collected 8 hours apart sent to the state lab. These would be set up for AFB testing and culture. We would want to order NAAT PCR testing on 2 of those samples for rapid diagnostic testing. If those come back negative, then we can treat with LTBI unless the provider still has a suspicion for active TB. If the results are positive, we have a case of active TB.

My provider has questions about materials for their LTBI patient or about what regimen/dosing/monitoring to use. Where can I find this info?

All of this and more can be found on the MT DPHHS Tuberculosis page. Right at the top of that page is a link to the LTBI Toolkit. This has forms, one pagers, and links to everything you or the provider could need. There is a link to the LTBI Treatment Guide for Primary Providers there as well. This guide has everything regarding regimens, dosing, monitoring, and special considerations. If you or the provider have more questions you can reach out to the State TB Program.

I have a patient that is underinsured or not insured but wants to get treatment. How can I help?

On the bottom of MT DPHHS Tuberculosis page, you can find a drop down for the LTBI Treatment Program. This is designed to provide LTBI meds to those that are underinsured or who don't have insurance. The Policy and form are right there. All you need to do is fill out the form and send it to the TB Program with a script and I'll send you the meds. We can not send meds directly to patients.

I was notified that a health care worker tested positive with an IGRA on baseline testing. Can they work?

Health care personnel with a positive TB test result should receive a symptom evaluation and chest x-ray to rule out TB disease. Additional workup may be needed based on these results. If the health care worker is not symptomatic and has a clear x-ray they should not be excluded from work. Treatment is recommended for all health care workers.

References

https://www.cdc.gov/tb/education/corecurr/index.htm#Anchor_Interactive

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8016318/

https://rules.mt.gov/gateway/RuleNo.asp?RN=37%2E114%2E1001

https://dphhs.mt.gov/publichealth/cdepi/diseases/Tuberculosis/index

https://www.cdc.gov/mmwr/volumes/68/wr/mm6819a3.htm?s_cid=mm6819a3_x