



Guidelines for TB Blood Testing

**Minnesota Department of Health
TB Prevention and Control Program
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Outline

Interferon-Gamma Release Assays aka “TB blood tests”

- 1. What are they?**
- 2. What are the current recommendations?**

TB Morbidity

United States, 2006–2010

Year	No.	Rate*
2006	13,727	4.6
2007	13,288	4.4
2008	12,904	4.2
2009	11,545	3.8
2010#	11,181	3.6

*Cases per 100,000 # Provisional data

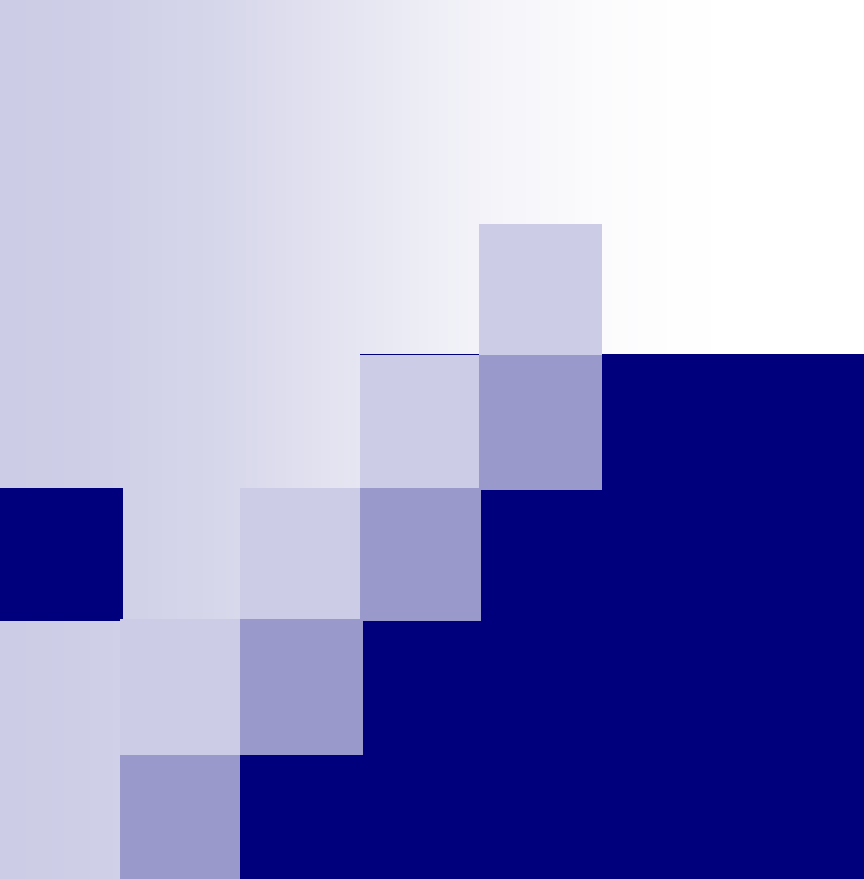


Interferon Gamma Release Assays

aka “TB blood tests”

Abbreviations

- *BCG* = Bacille Calmette-Guerin (vaccine)
- IGRA = Interferon- γ Release Assay
- LTBI = Latent TB Infection
- *MTB* or *M.tbc* = *Mycobacterium tuberculosis*
- TST = Tuberculin Skin Test (“Mantoux”, “PPD”)



**CDC
Guidelines
06/25/2010**



MMWRTM

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Recommendations and Reports

June 25, 2010 / Vol. 59 / No. RR-5

**Updated Guidelines for Using
Interferon Gamma Release Assays
to Detect *Mycobacterium tuberculosis*
Infection – United States, 2010**

Types of IGRAs

- QuantiFERON®-TB Gold
 - CDC guidelines: 2005
- QuantiFERON®-TB Gold In-Tube (QFT-GIT)
 - FDA-approved: 2007
- T-SPOT TB
 - FDA-approved: 2008



T-SPOT TB Test Materials
Image Credit: U.S. Food and Drug
Administration (FDA), 2009

Adapted from CDC Self Study Module 3 – Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease

How do IGRAs Work?

- Measure immune system's reaction to *M. tuberculosis*
- Blood mixed with antigens and incubated
- If infected with *M. tuberculosis*, blood cells will recognize antigens & respond by releasing interferon gamma (IFN- γ)
- IGRAs measure the (IFN- γ) released

Differences in Currently Available IGRAs

	QFT-G	QFT-GIT	T-Spot
Format	Process whole blood within 12 hours.	Process whole blood within 16 hours	Process peripheral blood mononuclear cells (PBMCs) within 8 hours.
<i>M. tuberculosis</i> Antigen	Separate mixtures of synthetic peptides representing ESAT-6 & CFP-10	Single mixture of synthetic peptides representing ESAT-6, CFP-10 & TB7.7.	Separate mixtures of synthetic peptides representing ESAT-6 & CFP-10
Measurement	IFN- γ concentration	IFN- γ concentration	# of IFN- γ producing cells (spots)
Possible Results	Positive, negative, indeterminate	Positive, negative, indeterminate	Positive, negative, indeterminate, borderline

Advantages of IGRAs

- Only one patient visit
- Results available in 24 hours
- No “boosting” effect
- Less likely to have incorrect reading of results as compared to TST
- More specific than TST: not affected by prior BCG vaccination or the presence of most non-tuberculous mycobacteria

Disadvantages of IGRAs

- Laboratory factors:
 - Must make prior arrangements with lab
 - Samples must be processed within 8-16 hrs
 - Potential errors in collecting/transporting blood or running/interpreting test
- Limited data on the use of IGRAs for:
 - Children < age 5
 - Persons recently exposed to *M. tuberculosis*
 - Immunocompromised persons
 - Serial testing (e.g., annual HCW testing)
- Cost (??)



CDC Recommendations (1)

- Can be used in place of TST in all situations in which CDC currently recommends testing
- Routine testing with both TST and IGRA is **not** recommended.
- Despite the indication of a preference in certain situations, use of either test is acceptable medical and public health practice.
- Caution in interpretation should be used when testing certain populations because of limited data on the use of IGRAs

CDC Recommendations (2)

- Decisions on which test (or combination of tests) to use should be based on the reasons and the context for testing, test availability, and overall cost of testing
- Multiple negative results from any combination of these tests does not rule out *M. tuberculosis* infection.



CDC Recommendations (3)

- As with TST, minimize unnecessary and misleading testing of persons at low risk of infection and a low risk of disease due to *M. tuberculosis*.
- Each institution and TB control program should evaluate the availability and benefits of using IGRAs.



IGRA Preferred

- 1. Persons who have received BCG (either as a vaccine or for cancer therapy); and**
- 2. Persons from groups that historically have low rates of return for TST reading (e.g., homeless persons, drug-users.)**



TST Preferred

- **Children aged <5 years**



Use Either TST or IGRA

- TB contact investigations
- Periodic screening of persons at risk for occupational exposure to *M. tuberculosis* (e.g., surveillance programs for health-care workers)
 - special considerations regarding test conversions and reversions

Using Both TST and IGRA might be useful in the following situations (1):

- When the initial test is **negative** and:
 - The risk for infection, the risk for progression to disease, and the risk for a poor outcome are high (e.g., HIV infected persons or children under 5 years of age who are exposed to a person with infectious TB).
 - There is clinical suspicion for TB disease

Using Both TST and IGRA might be useful in the following situations (2):

- When the initial test is **positive** and:
 - Additional evidence of infection is required to encourage acceptance and adherence
 - The person has a low risk of both infection and progression from infection to TB disease. An alternative is to assume, without additional testing, that the initial result is a false positive or that the risk for disease does not warrant additional evaluation or treatment, regardless of test results.



Using Both TST and IGRA might be useful in the following situations (3):

- When the initial IGRA result is indeterminate, borderline, or invalid and a reason for testing persists.



Medical Management After IGRA Testing

- Don't rely only on IGRA or TST results to determine follow-up
- Consider epidemiologic and medical history and other clinical information.
- If risks, symptoms, or signs are present, need additional evaluation to determine if the person has LTBI or active tuberculosis.



Medical Management After IGRA Testing

- Neither IGRA nor TST can distinguish LTBI from active TB.



Healthy Persons at Low Risk for TB

- **A single positive IGRA or TST result should not be taken as reliable evidence of *M. tuberculosis* infection.**
- **It is reasonable to discount an isolated positive result as a false positive.**

Medical Management After IGRA Testing

- It is reasonable to consider a positive result from either of two tests as evidence of infection when
 - clinical suspicion exists for active tuberculosis (i.e., in persons with symptoms, signs, and/or radiographic evidence of active tuberculosis) or
 - the risks for infection, progression, and a poor outcome are increased (e.g., when persons with HIV infection or children aged <5 years are at increased risk for *M. tuberculosis* infection).



Medical Management After IGRA Testing: BCG-vaccinated

- If the person is not at increased risk for a poor outcome if infected (e.g., HIV+), it is reasonable to discount TST reactions <15 mm in size as false positives when an IGRA is clearly negative.



Medical Management After IGRA Testing: Other Situations

- Inadequate evidence exists on which to base recommendations for dealing with discordant results.
- However, in the absence of convincing evidence of infection, diagnostic decisions may reasonably be deferred unless there is an increased risk for progression to disease if infected and/or a high risk exists for a poor outcome if disease develops.



Summary/Key Points: IGRAs

- There are several advantages compared to TST
- A major advantage is that IGRA results are NOT affected by prior BCG vaccination
- Can be used in place of TST in all situations in which CDC currently recommends testing
- More research needed regarding the performance of IGRAs in certain situations
- Routine testing with both TST and IGRA is **not** recommended.
- Minimize testing low-risk persons with either IRGA or TST

References

- Surveillance data:
 - CDC's Division of TB Elimination www.cdc.gov/tb
 - MDH TB Program
- [Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010](#)
MMWR 2010; 59 (RR-5); 1-25
- Interferon-Gamma Release Assays (IGRAs) - Blood Tests for TB Infection (Fact Sheet)
<http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.pdf>



Common Questions & Answers



Are IGRAs more reliable than TSTs?

- IGRAs and TSTs are equally sensitive
- IGRAs are more specific in most situations



Can IGRA be used for children?

What's the age cut-off ?

- TST is preferred for children under age 5 years
- This is because there are not sufficient data on how IGRA tests perform in children



Where can I send blood samples?

- Health care facilities should make prior arrangements with a qualified laboratory (i.e., compliant with CLIA and uses FDA-approved methods).
- Arrange for delivery of the blood sample to the laboratory within the correct time frame.

Can IGRAs Be Given To Persons Receiving Vaccinations?

- As with TST, live virus vaccines might affect IGRA test results. This has not been well studied.
- Until additional information is available, IGRA testing should be done as follows:
 - Either on the same day as vaccination with live-virus vaccine or 4-6 weeks after the administration of the live-virus vaccine
 - At least one month after smallpox vaccination