Diagnosis of TB Infection

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Definition

- Latent TB Infection (LTBI) is a state of:
  - Persistent bacterial viability
  - Immune control, and
  - No evidence of clinically manifested active tuberculosis
- Currently not possible to diagnose directly
- LTBI diagnosed by *in vivo* or *in vitro* stimulation by *M. tuberculosis* antigens
- Active tuberculosis will develop in 5 – 15% of persons with LTBI during their lifetimes

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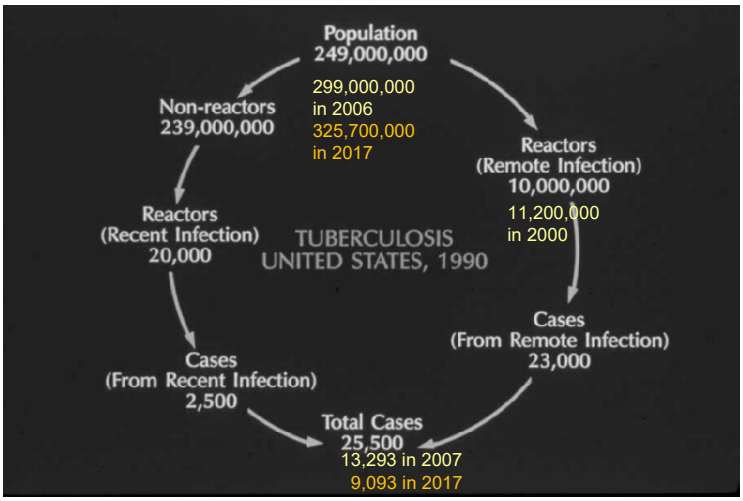
Mack, et al, TBNET Consensus Statement, Eur Rerspir J 2009;33:956-73
Getahun, et al, Latent *Mycobacterium tuberculosis* Infection, N Engl J Med 2015;372:2127-35



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Targeted Testing

- Targeted testing is an essential TB prevention and control strategy in the United States. Targeted testing is used to identify and treat persons who are at high risk for latent TB infection or at high risk of developing TB disease once infected with *M. tuberculosis*
- Identifying and treating persons who have latent TB infection is important because treatment can prevent these persons from developing TB disease in the future. This helps to stop the further spread of TB in communities
- All TB testing activities should be accompanied by a plan for follow-up care, medical evaluation, and treatment for persons diagnosed with latent TB infection or TB disease

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TB 101 for Health Care Workers, www.cdc.gov/tb

Targeted Testing cont.

- Targeted testing should be used to identify and treat persons who are at high risk for:
  - Infection with *M. tuberculosis*
  - Developing TB disease once infected with *M. tuberculosis*
- Because of differences in populations from one community to another, definitions of high-risk populations should be made at the local level according to local demographics and TB epidemiology

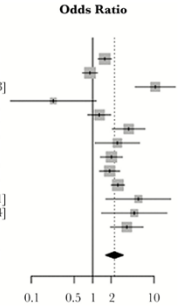
Groups at High Risk for TB Infection

- Contacts of persons known or suspected to have infectious TB disease
- People who have come to the United States within the last 5 years from areas of the world where TB is common
  - For example: Asia, Africa, Eastern Europe, Latin America, and Russia
- Persons who visit areas of the world where TB is common, especially if visits are frequent or prolonged
  - Redbook: Has your child traveled (had contact with resident populations) to a high-risk country for more than a week?
- People who live or work in congregate settings whose clients are at increased risk for TB disease
- Health care workers who serve clients who are at increased risk for TB disease
- Infants, children, and adolescents exposed to adults at increased risk for infection or disease

Forest Plot Showing Pooled Odds Ratio (OR) for Latent Tuberculosis Infection Among Healthcare Workers (HCWs)

Study	HCWs Events	HCWs Total	Control Events	Control Total	W(random)	OR	95% CI
Agaya et al 2015	534	898	160	332	10.1%	1.58	[1.22−2.03]
Corbett et al 2007	183	342	248	443	10.0%	0.90	[0.68−1.20]
Drobniewski et al 2007	107	262	8	130	7.1%	10.53	[4.94−22.43]
Durando et al 2013	3	585	3	136	3.2%	0.23	[0.05−1.14]
Franco et al 2006	101	169	88	164	9.2%	1.28	[0.83−1.98]
Maciel et al 2007	114	619	12	218	8.0%	3.88	[2.09−7.18]
Sawhney et al 2015	20	100	9	100	6.5%	2.53	[1.09−5.87]
Nikokar et al 2010	113	185	79	181	9.3%	2.03	[1.34−3.07]
Powell et al 2011	380	956	40	155	9.5%	1.90	[1.29−2.78]
Rutanga et al 2015	635	1023	135	348	10.2%	2.58	[2.01−3.32]
Storla et al 2009	42	155	3	48	4.5%	5.58	[1.64−18.91]
Zu et al 2014	6	20	7	85	4.5%	4.78	[1.40−16.34]
van Rie et al 2013	68	120	21	79	8.0%	3.61	[1.95−6.69]
Random effects model		5434		2419	100%	2.27	[1.61−3.20]

Heterogeneity: I-squared=84.8%, tau-squared=0.2849, p<0.0001



From: Risk of Tuberculosis Infection and Disease for Health Care Workers: An Updated Meta-Analysis
Open Forum Infect Dis. 2017;4(3). doi:10.1093/ofid/ofx137

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Groups at High Risk for Developing TB Disease

- People living with HIV/AIDS
- Children younger than 5 years of age
- Persons who are receiving immunosuppressive therapy
- Persons who were recently infected with *M. tuberculosis* (within the past 2 years)
- Persons with a history of untreated or inadequately treated TB disease
- Persons with silicosis, diabetes, chronic renal failure, leukemia, lymphoma, or cancer of the head, neck, or lung
- Persons who have had a gastrectomy or jejunoileal bypass
- Persons who weigh less than 90% of their ideal body weight (underweight)
- Cigarette smokers and persons who abuse drugs or alcohol

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Collaborative Framework for Care and Control of Tuberculosis and Diabetes

International Union Against Tuberculosis and Lung Disease

World Health Organization

Diabetes triples the risk of developing tuberculosis (TB)

Consequently, rates of TB are higher in people with diabetes than in the general population, and diabetes is a common comorbidity in people with TB

Diabetes can worsen the clinical course of TB, and TB can worsen glycaemic control in people with diabetes

Individuals with both conditions thus require careful clinical management

Strategies are needed to ensure that optimal care is provided to patients with both diseases

TB must be diagnosed early in people with diabetes, and diabetes must be diagnosed early in people with TB

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Groups at High Risk for BOTH:

--exposure to TB infection, and
--developing TB disease

- Populations defined locally as high risk for latent TB infection or TB disease, such as medically underserved, low-income persons, or persons who abuse drugs or alcohol
- Populations defined locally as having an increased incidence of TB disease, possibly including medically underserved or low-income populations
- Cigarette smokers*

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TB 101 for Health Care Workers, www.cdc.gov/tb

*Core Curriculum on Tuberculosis: What the Clinician Should Know

Poll Question

- Ms. Rose has a past medical history of hepatitis C, uncontrolled diabetes mellitus, and cigarette smoking
- Which of the following does NOT put Ms. Rose at risk for developing active TB disease?

  A. Having hepatitis C virus infection

  B. Cigarette smoking

  C. Having diabetes mellitus

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Poll Question

- Studies suggest that active tuberculosis will develop in what percentage of persons with latent *Mycobacterium tuberculosis* infection?

  A. Less than 5%

  B. 5 to 15%

  C. 25 to 30%

  D. 45 to 50%

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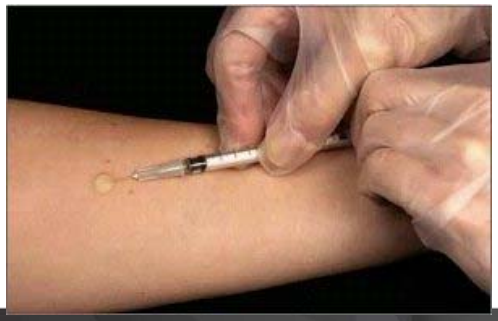
Testing for TB Infection

- Diagnostic tests that can be used to detect TB infection include:
  - The Mantoux tuberculin skin test (TST)
  - Interferon-gamma release assays (IGRAs)
- A positive TST or IGRA result only indicates if someone has been infected with *M. tuberculosis*
- These tests **cannot** identify whether or not a person has **TB disease**

Mantoux Tuberculin Skin Test

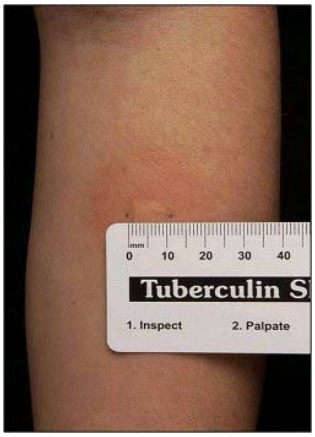
- PPD = Purified Protein Derivative
- Intradermal



PPD

- 5 TU Mantoux intradermal test
- Measure size in mm induration across arm
- Two bell shaped curves that overlap
- Size helps dx of latent MTB infection
  - vs. NTM infections, BCG vaccinated people
- Size doesn't provide any information RE: prognosis for reactivation of TB

PPD is a culture filtrate of *M. tuberculosis*, which contains >200 antigens also found in BCG and NTM



Measuring induration at 48 – 72 hours.
In this photograph, the induration is 11 mm

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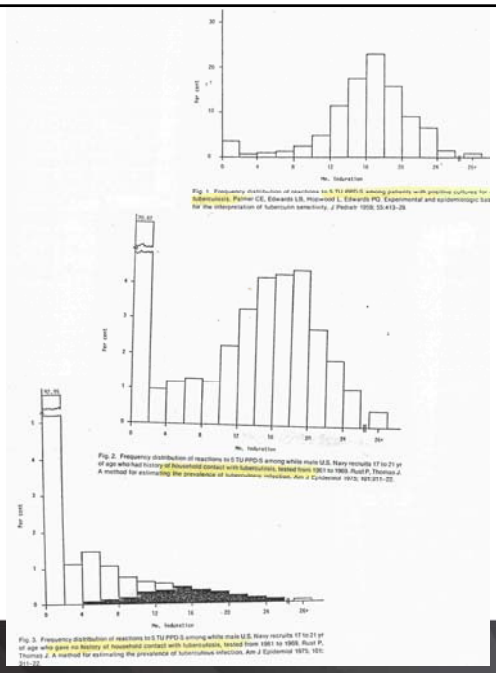
Al Zahrani, Al Jahdali, and Menzies, Am J Respir Crit Care Med 2000;162:1419-22



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The Tuberculin Skin Test, ATS, Am Rev Respir Dis 1981; 124:356-63

An Induration of **5 or More mm** is Considered Positive for:

- People living with HIV
- Recent contacts of persons with infectious TB disease
- Persons with chest x-ray findings suggestive of previous TB disease
- Patients with organ transplants and other immunosuppressed patients

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An Induration of **10 or More mm** is Considered Positive for:

- People who have come to the United States within the last 5 years from areas of the world where TB is common (for example, Asia, Africa, Eastern Europe, Latin America, and Russia)
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with conditions that increase risk for progressing to TB disease
- Children less than 4 years of age
- Infants, children, and adolescents exposed to adults in high-risk categories

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TB Skin Testing

- Placing a "screening" TST implies a commitment to administer TLTBI if latent TB infection is diagnosed
- Interpret results by mm induration AND risk of progression to disease
  - **Immunocompromised or recently exposed ≥ 5 mm**
  - **Otherwise healthy ≥ 15 mm**
  - **No age limitations in treatment decisions**
- Ignore h/o BCG vaccine in TST interpretation
- "Two-step" baseline for Health Care Workers, residents of Long Term Care facilities

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Reaction ≥ 5 mm Paradox

- 5 mm of induration is positive if:
  - HIV-infected
  - Recent contact of case
  - Fibrotic changes on CXR
  - Immunosuppressed
- CXR, HIV serology may not be obtained unless PPD is "positive"
- Medical evaluation indicated if induration ≥ 5 mm

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What Causes + TST?

- Delayed-type hypersensitivity (DTH) skin testing measures cellular immunity, which takes 2-3 days to manifest
- Initiated by T lymphocytes that are already specifically sensitized to locally deposited antigen
- Induration = edema and lymphocytic infiltrate
  - CD4 cells with memory phenotype (CD45RO)
  - Depends on Gamma interferon (IFN-γ) production by macrophages and antigen-specific CD4 T cells, also IL-2
- Anergy results from interruption in process

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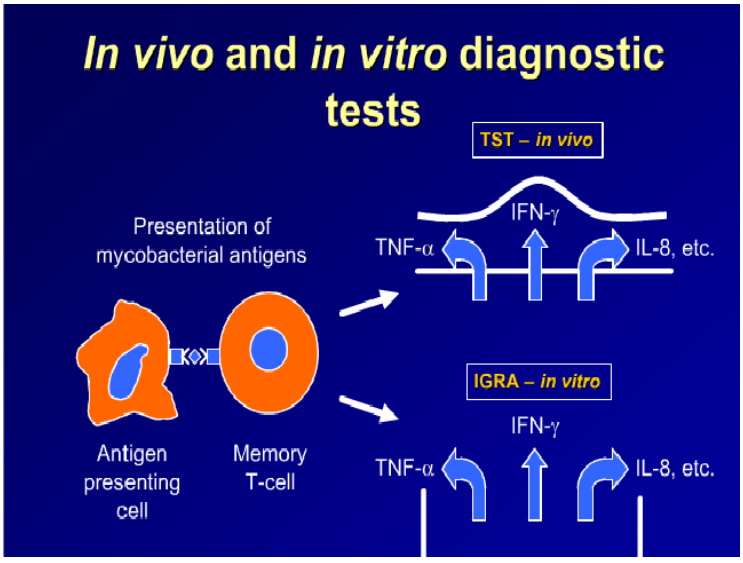

Lancet 2000; 356:1099

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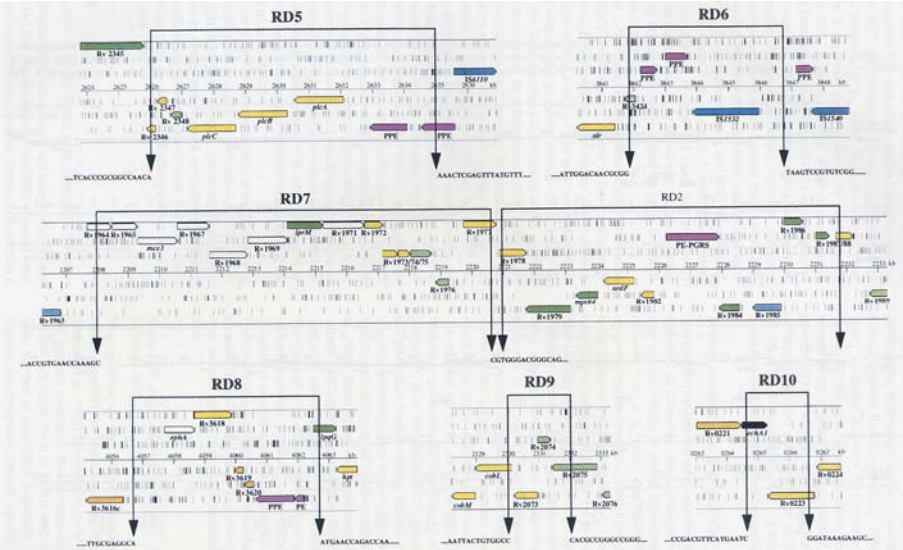

Fig. 2. Overview of the RD5–RD10 deleted regions. The regions deleted from the *M. tuberculosis* genome are shown delimited by arrows with the sequence flanking each deletion. ORFs are represented as pointed boxes showing the direction of transcription, with colours reflecting the functional classification of the ORFs as described previously (Cole *et al.*, 1998). Putative functions and families of the ORFs are described in Table 1. Stop codons are shown as small vertical bars.

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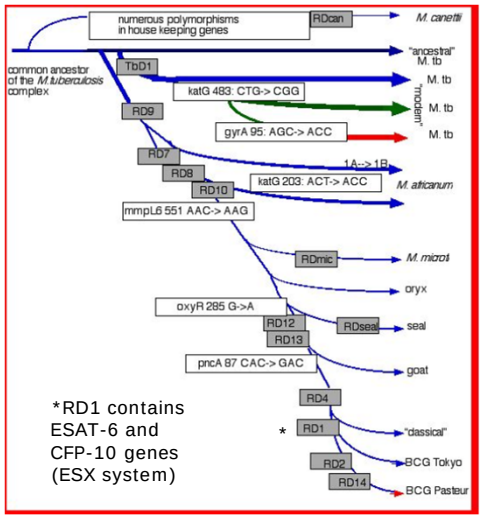
Molecular Microbiology (1999) 32(3), 643–655



Scheme of the proposed evolutionary pathway of the *M. tuberculosis* bacilli illustrating successive loss of DNA in certain lineages. Brosch R, et al, Proc Nat Acad Sci USA, 2002;99:3684-9.

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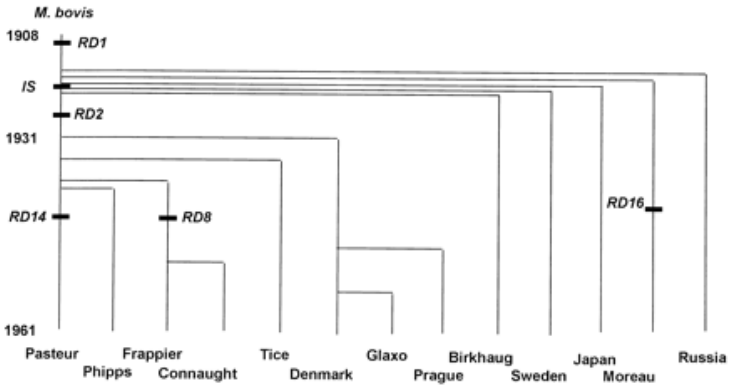

Behr MA, Wilson MA, Gill WP, et al. Comparative genomics of BCG vaccines by whole genome DNA microarray. 1999 Science: 284;1520-23.

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In Summary . . .

- The absence of RD1 resulted in attenuation of virulence in *M. bovis*, i.e., the BCG vaccine
- BCG is live bacterial vaccine, given on ~day 7 of life
  - Most commonly used vaccine in the world
- RD1 comprises nine genes, two of which are the secreted proteins **ESAT-6** (early secreted antigenic target - 6 kDa) and **CFP-10** (culture filtrate protein - 10 kDa)
  - Both of these proteins are immunodominant antigens and major virulence factors of *M. tuberculosis*
  - **BCG-vaccinated people who are not also TB-infected should not have a specific immunologic reaction to ESAT-6 or CFP-10**
- ESAT-6 and CFP-10 are useful antigens in testing for TB infection

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Wong K. 2017. The role of esx-1 in mycobacterium tuberculosis pathogenesis. microbiolspec 5(3): doi:10.1128/microbiolspec.TBTB2-0001-2015

Interferon-γ Release Assays for TB
IGRA's

- In vitro blood tests that measure T-cell mediated interferon-γ release in response to specific *M. tuberculosis* antigens ESAT-6 and CFP-10
- QuantiFERON®-TB Gold In-Tube assay and T-SPOT®.*TB* test commercially available
  - Need special handling, rapid processing
  - Results from lab easy to locate in chart
  - Cost more than TST
- Benefits: single visit, fewer false + (NTM, BCG)
- **Neither TST or IGRA can distinguish between latent and active tuberculosis**

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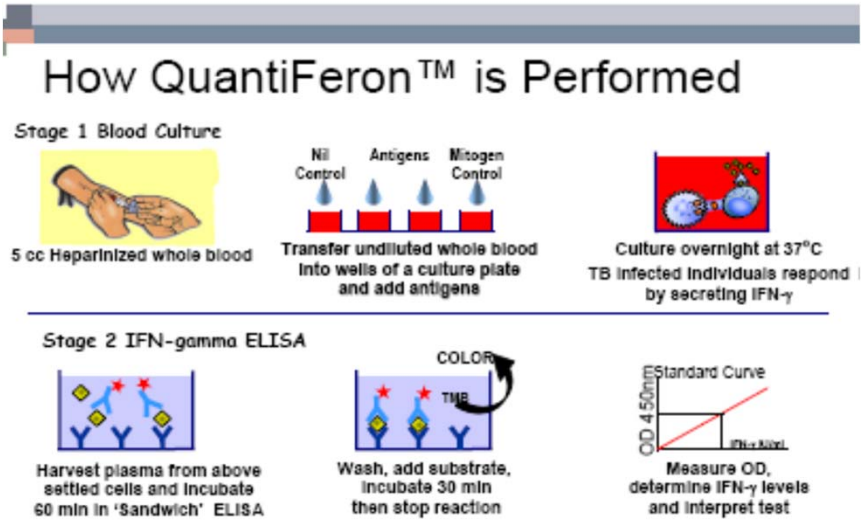

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QuantiFERON®-TB Gold In-Tube Assay

- Single blood draw
- 3 x 1 mL tubes
- Incubate whole blood in tube with antigens for ≤ 16 h (overnight)
- Standard ELISA
- Report TB Ag, Mitogen (positive control), Nil (saline, negative control), and TB Ag minus Nil in IU/mL
- Ask for quantitative report

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"Gold Standard"

- The primary test cut-off for QFT is
  - TB antigen response – Nil ≥0.35 IU/ml
- This was established through Receiver Operator Characteristic (ROC) curve analysis of data from
  - low risk BCG-vaccinated individuals for specificity,
  - patients with culture confirmed *M. tuberculosis* infection for sensitivity.

www.quantiferon.com FAQs-Health-Professionals

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T-SPOT®.*TB*

- 4 well microtiter plates coated with a mouse monoclonal antibody to interferon gamma (IFN-g)
- ESAT-6 and CFP-10 antigens, phytohemagglutinin (PHA)
- Use monoclonal antibody to IFN-g conjugated to alkaline phosphatase
- Ficoll or alternative PBMC separation materials
- Equipment and reagents to enable counting of PBMCs; either manually using Trypan Blue and a hemocytometer on a microscope or automatically using a suitable hematology analyzer
- A means of reading the plate such as a microscope, magnifying glass or plate reader
- Report number of spots caused by ESAT-6 and CFP-10

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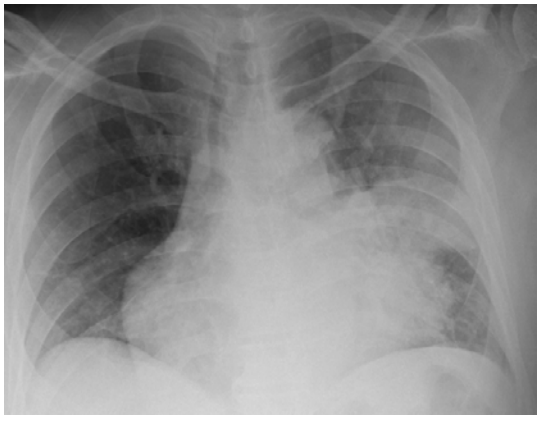

QuantiFERON TB Gold	POSITIVE	
QFT TB Ag minus Nil	9.062*	
QuantifFERON Mitogen	4.488	
QuantiFERON Nil	0.955	
QuantiFERON TB Ag	>10	Units: IU/mL

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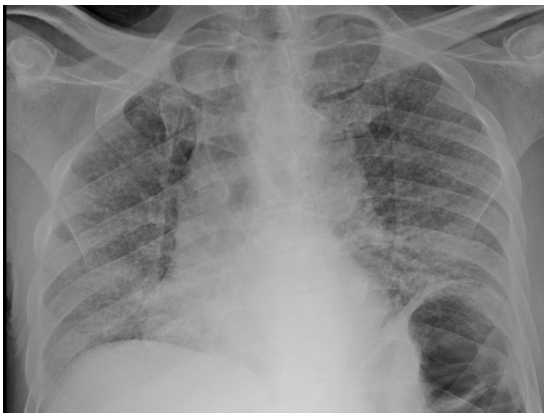

QuantiFERON TB Gold	INDETERMINATE	
QFT TB Ag minus Nil	0.850	
QuantifFERON Mitogen	>10	
QuantiFERON Nil	8.205	
QuantiFERON TB Ag	9.056	Units: IU/mL

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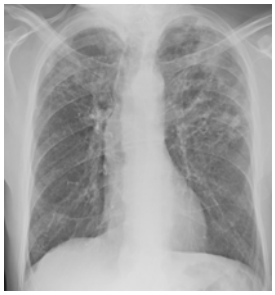
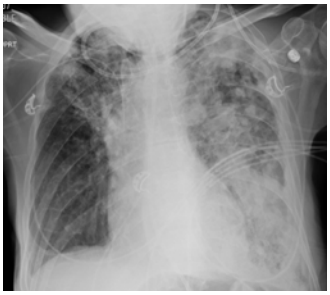
	3/14/2017	8/1/2017
QuantiFERON TB Gold	positive	negative
QFT TB Ag minus Nil in IU/mL	0.818	0.028
QuantifFERON Mitogen	>10	1.462
QuantiFERON Nil	0.055	0.107
QuantiFERON TB Ag	0.873	0.135





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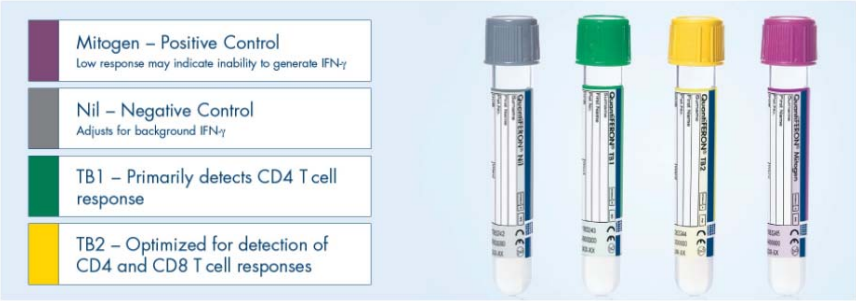
IGRA Update

QuantiFERON® TB Gold-Plus



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Differences Between QFT-GIT and QFT-Plus

- Number of tubes used and volume (ideal volume)
  - QFT-GIT = 3 tubes (CD4+) = 2.4 mL
  - QFT-Plus = 4 tubes (CD4+ / CD8+) = 3.2 mL
- Polypeptides used in assays:
  - QFT-GIT (ESAT-6Rv3874, CFP-10Rv3875, TB 7.7Rv3875c)
  - QFT-Plus (ESAT-6Rv3874, CFP-10Rv3875)
- Size of polypeptides
  - QFT-GIT: 20-mer (18pp with 10aa overlap)
  - QFT-Plus: 20-mer in TB1; 20-mer and smaller in TB2
- ELISA Standards: Used for standard curves
  - QFT-GIT: 26 pts with 2 sets of 8-standards
  - QFT-Plus: 22 pts with 2 sets of 4-standards

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Value of QFT-Plus Being Evaluated . . .

- TB-specific CD8+ T cells that produce IFN-ɣ have been more frequently detected in those with active vs. latent TB
- ΔTB2>TB1 associated with recent exposure to TB
- In high-risk/active TB patients, TB2 tube may be the only positive
- ΔTB2>TB1 may decrease with response to Rx of active TB
- In low-risk populations, sensitivity increases if you require both TB2 and TB1 +

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Comparative verification study in 16 clinical laboratories in the Netherlands and Belgium from May 2015 - December 2016
N = 1031 tested, n = 131 (12.7%) + by both QFT-GIT and QFT-Plus

E.D. Pieterman et al.

Table 4
Difference in IFN-γ between TB1 and TB2 > 0.6 IU/mL in positive results.

Test indication	IFN-γ > 0.6 IU/mL (% within positive results)
Tuberculosis infection in differential diagnosis	7 (17%)
Contact investigation	18 (33%)
Screening before immunotherapy	2 (11%)
Periodic check by occupational health services	3 (33%)
Other[a]	2 (15%)
Unknown	4 (33%)
Total	36

[a] Screening of immigrants, screening of homeless, employment medical examination, other.

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Tuberculosis 108 (2018) 136–142

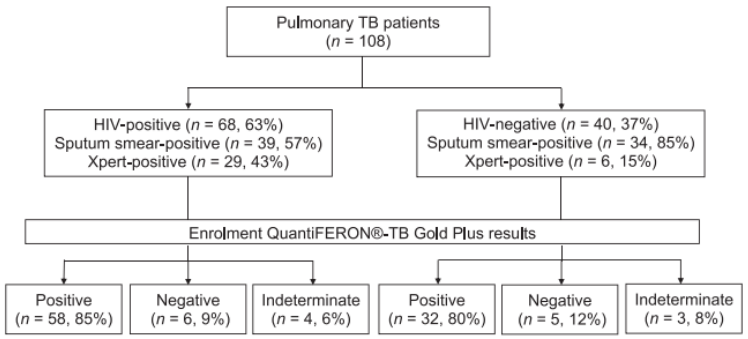

Figure 1 Patients with pulmonary TB enrolled in the study: HIV status, microbiology results and QuantiFERON®-TB Gold Plus results. TB = tuberculosis; HIV = human immunodeficiency virus.

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Telisinghe et al 2017
The sensitivity of the QuantiFERON-TB Gold Plus assay in Zambian adults with active tuberculosis

2018 Red Book

- TST has been favored over IGRA in children <5 years
  - Very young have higher risk of progression to disease, so increased sensitivity is deemed more important than specificity
- **NEW:** Can use IGRA's in immunocompetent >= 2 years of age in all situations where a TST would be used
  - Some experts use in children >= 1 year of age
  - IGRA preferred if prior BCG recipient
- If contact to active TB case, do both and start TLTBI if either +
  - "Window" prophylaxis

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American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

FROM THE AMERICAN ACADEMY OF PEDIATRICS

TECHNICAL REPORT

Interferon-γ Release Assays for Diagnosis of Tuberculosis Infection and Disease in Children

TABLE 1 Comparison of the TST and IGRAs

Characteristic	TST	IGRA
Antigens used	Many; PPD	3 (QFT) or 2 (T-SPOT)
Sample	Intradermal injection	Blood draw
Patient visits required	2	1
Distinguish between LTBI and TB disease	No	No
Cross-reactivity with BCG	Yes	No
Cross-reactivity with NTM	Yes	Only rare species[a]
Differing positive values by risk	Yes (5-10-15)	No
Causes boosting	Yes	No
Subject to boosting by previous TST	Yes	Possible
Durability over time (stays positive with or without treatment)	Yes	Unknown
Difficulties with test reproducibility	Yes	Yes
Relative cost	Lower	Higher
Location of need for trained staff	"Bedside"	Laboratory
Estimated specificity in BCG-unvaccinated children	95% to 100%	90% to 95%
Estimated specificity in BCG-vaccinated children	49% to 65%	89% to 100%
Estimated sensitivity (confirmed TB disease)	75% to 85%	80% to 85%
Estimated sensitivity (clinical TB disease)	50% to 70%	60% to 80%

[a] *M marinum, M kansasii, M szulgai,* and *M flavescens.*

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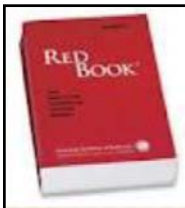

IGRAs AND THE 2018 AAP "RED BOOK"

- Can use IGRAs in immunocompetent children ≥ 2 years of age [previously ≥ 5 years of age] in all situations when a TST would be used; some experts down to 1 year of age
- Particularly useful/preferred for children who have received a BCG vaccination
- Same recommendations as TST for risk factors and frequency of testing
- Use with caution in immunocompromised children
- Neither IGRAs nor the TST are perfect; always need clinical judgment!

Texas Children's Hospital

BCM Baylor College of Medicine

Jeffrey R. Starke MD
Professor of Pediatrics
Baylor College of Medicine

IGRAs IN CHILDREN – SOME CLINICAL ISSUES

BCG-vaccinated child

- **Strategy 1**: TST: if negative, no more testing; if positive, follow with an IGRA
- **Strategy 2**: Do only the IGRA
- **Note**: If TB exposure, child should be considered infected if either test is positive

Child about to be immune compromised

- No TB risk factor: do either a TST or an IGRA
- TB risk factor: do both a TST and an IGRA and evaluate and treat if either test result is positive [RISK and BENEFIT]

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	5 TU Mantoux intradermal test	QuantiFERON Gold in-tube assay	T-spot TB
Preparation	--10- or 50-test multiple dose vials --Stored at 2°–8°C (36°–46°F) and protected from light. --Vials in use more than 30 days should be discarded due to possible oxidation and degradation which may affect potency.	--blood collection tubes with colored caps from manufacturer --tubes must be transferred to a 37°C ± 1°C incubator as soon as possible, and within 16 hours of collection.	--sodium citrate or sodium heparin Vacutainer CPT tubes --process within 8 hours of collection at room temperature --use of T-Cell *Xtend* reagent allows processing up to 32 hours -- 250,000± 50,000 PBMCs per well
Measure	Size in mm of induration	Interferon γ level in IU/mL	Spots of captured Interferon γ from individual T cells per well
Antigens tested	PPD, >200 antigen mixture, cross reactions with BCG and NTM	ESAT-6 and CFP-10	ESAT-6 and CFP-10
Does the magnitude of the result add any information?	Larger size helps diagnosis of latent MTB infection vs. NTM, BCG-vaccinated people	QFT is a *qualitative* (not quantitative) test of TB infection. With current knowledge, the magnitude of IFN-γ response cannot be correlated to stage or degree of infection, level of immune responsiveness, or likelihood for progression to active disease.	
How soon after infection does result turn positive?	8 – 12 weeks	No later than PPD	No later than PPD
Does a positive result turn negative after successful treatment of TB (latent or active)?	Will remain + ?forever	Responses comparable up to 15 months after treatment	Can remain + for decades after TB Rx, even in areas of low TB prevalence where reinfection unlikely

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BMC ID 2010;10:57
IJTLD 2010;14:347

Groups Who Should be Given High Priority for Latent TB Infection Treatment

- People with a positive IGRA result or a TST reaction of 5 or more millimeters
  - HIV-infected persons
  - Recent contacts of a TB case
  - Persons with fibrotic changes on chest radiograph consistent with old TB
  - Organ transplant recipients
  - Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists)
- People with a positive IGRA result or a TST reaction of 10 or more millimeters
  - Recent immigrants (< 5 years) from high-prevalence countries
  - Injection drug users
  - Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
  - Mycobacteriology laboratory personnel
  - Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories
- Persons with no known risk factors for TB may be considered for treatment of LTBI if they have either a positive IGRA result or if their reaction to the TST is 15 mm or larger. However, targeted TB testing programs should only be conducted among high-risk groups. All testing activities should be accompanied by a plan for follow-up care for persons with TB infection or disease.

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Figure 2. Screening for Latent Tuberculosis Infection in Adults: Clinical Summary

Population	Asymptomatic adults at increased risk for infection
Recommendation	Screen for latent tuberculosis infection (LTBI). Grade: B

Risk Assessment	Populations at increased risk for LTBI include persons who were born in, or are former residents of, countries with increased tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (eg, homeless shelters and correctional facilities). Local demographic patterns may vary across the United States; clinicians can consult their local or state health departments for more information about populations at risk in their community.
Screening Tests	Screening tests include the Mantoux tuberculin skin test and interferon-gamma release assays; both are moderately sensitive and highly specific for the detection of LTBI.
Treatment and Interventions	The CDC provides recommendations for the treatment of LTBI at http://www.cdc.gov/tb/topic/treatment/ltbi.htm.
Balance of Benefits and Harms	The USPSTF concludes with moderate certainty that the net benefit of screening for LTBI in persons who are at increased risk for tuberculosis is moderate.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to http://www.uspreventiveservicestaskforce.org.

U.S. Preventive Services TASK FORCE

JAMA

CDC indicates Centers for Disease Control and Prevention; USPSTF, US Preventive Services Task Force.

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JAMA. 2016;316(9):962-969

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Groups with Increased Likelihood of Infection with Mtb	Benefit of Therapy	LTBI Testing Strategy	
Household contact or recent exposure of an active case	Yes	Likely to be Infected Low to Intermediate Risk of Progression (TST ≥ 10mM)	Likely to be Infected High Risk of Progression (TST ≥ 5mM)
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	Unlikely to be Infected (TST > 15mM)	

Risk of Infection

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

ATS/IDSA/CDC Guidelines: Diagnosis of Tuberculosis in Adults and Children, 2017

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Latent TB Cascade of Care:

- Identify TB infection
  - Place and read PPDs accurately
    - IGRA alternative to identify TB infection
- **PMH: prior TB exposure, infection, or disease**
  - Demographic factors (e.g., country of origin, age, ethnic or racial group, occupation) that may increase risk for exposure to TB or to drug-resistant TB
  - ROS: Unexplained weight loss, loss of appetite, night sweats, fever, fatigue, coughing for longer than 3 weeks, hemoptysis, chest pain
  - CXR
  - Screen for medical conditions that would increase risk of latent TB infection progressing to TB disease (h/o DM, HIV Ab), HepBsAg, Hep C Ab
  - Accurate medication list
    - Rifamycins have many drug interactions (OCA's)
- Administrate TLTBI

Latent TB diagnosed
Offered TLTBI
Accepted TLTBI
Completed TLTBI

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Poll Question

- Which of the following statements is true regarding latent *M. tuberculosis*?

  A. Currently available diagnostic tests cannot reliably predict the risk of future disease among persons who test positive

  B. Reversion from a positive to a negative test is more common with tuberculin skin tests than with interferon-ɣ release assays

  C. The risk of progression to active clinical disease depends on the strain of *M. tuberculosis* involved

  D. More than 50% of persons who are household contacts of someone with untreated tuberculosis will become infected

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Poll Question

- Mr. Smith is currently homeless and presents with 4 weeks of a productive cough and fevers. He is febrile to 38.0. A chest x-ray shows an infiltrate in the right lower lobe. An IGRA test is negative.
- What is the next best step in caring for Mr. Smith?
  A. Begin levofloxacin
  B. Obtain sputum for AFB smear/culture
  C. Repeat the IGRA
  D. Obtain a tuberculin skin test

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Poll Question

- Mr. Rai recently emigrated from Nepal and presents to your office due to a positive TST. His chest x-ray shows a left-sided pleural effusion. He reports BCG vaccination. He is feeling well.
- What is the next best step in caring for Mr. Rai?
  A. No further follow-up is needed
  B. Obtain an IGRA test to confirm the TST
  C. Treat for latent tuberculosis infection
  D. Obtain a thoracentesis for AFB smear and culture

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