LTBI Diagnosis: Advances and Prospects

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McGill

Stop TB Partnership

Working Group on New Diagnostics

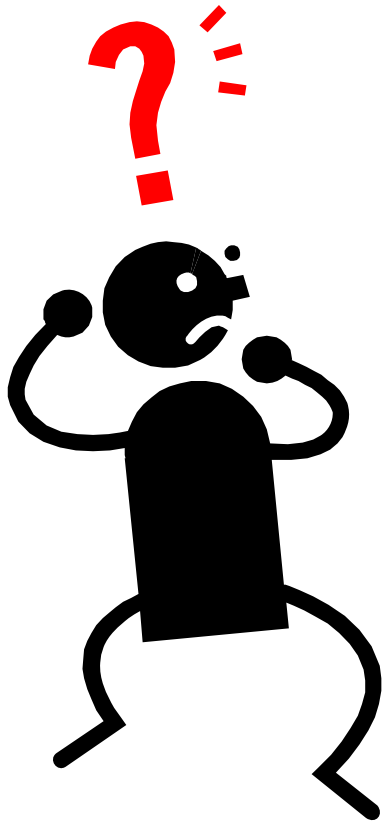
ANNUAL MEETING

Why focus on LTBI diagnosis?

- Global Plan to Stop TB: by 2012, a test that will accurately identify people with LTBI and those at high risk of progression to active disease
- As active TB case rates decrease over time, LTBI Dx and Rx will become important to eliminate TB
- Even in resource-limited settings, high-risk populations may benefit from IPT (immunocompromised, children, and contacts)
- New LTBI tests are giving us a fresh perspective on LTBI, a poorly understood entity shrouded in fuzzy terminology!

How many ways to say TB infection???

- Latent infection
- Active infection
- Inactive infection
- Subclinical infection
- Acute infection
- Chronic infection
- Persistent infection
- Dormant infection
- Recent infection
- Remote infection
- Quiescent infection
- Incipient disease



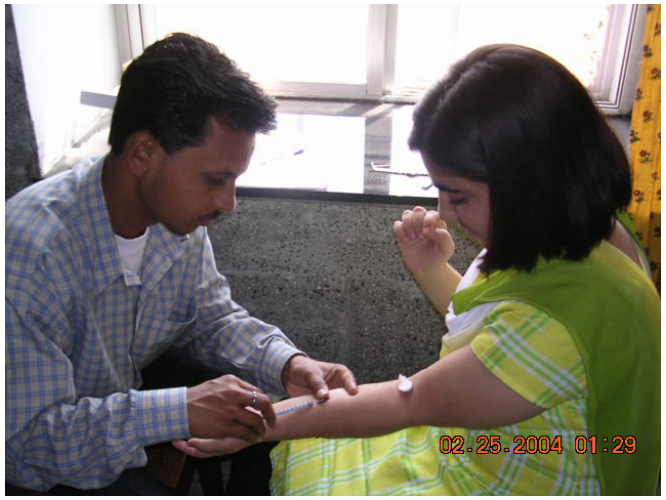
Advances in Latent TB diagnosis

- Improving the interpretation of TST
- Improving the TST reagent
- Replacing the TST with in-vitro assays (IGRAs)

The end of tuberculin skin testing?

Tuberculin skin test (TST)

- TST
  - Measures cell-mediated immune response (CMI)
    - Uses PPD: a crude antigenic mixture
- Limitations of TST:
  - fairly high proportion of false positives and false negatives
  - technical problems in administration and interpretation
  - difficulty in separating true infection from the effects of BCG and non-tuberculous mycobacteria (NTM)
  - repeated TST boosts the immune response
  - requires a 3-dimensional interpretation



Effect of BCG on TST results

INT J TUBERC LUNG DIS 10(11):1192–1204

REVIEW ARTICLE

False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria?

M. Farhat,*† C. Greenaway,*‡ M. Pai,*§ D. Menzies*

* Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, McGill University, Montreal, Quebec, Canada; † Massachusetts General Hospital, Harvard University, Boston, Massachusetts, USA; ‡ Division of Infectious Disease and Microbiology, SMBD-Jewish General Hospital, McGill University, Montreal, § Joint Departments of Epidemiology & Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada

- Analysis of 24 studies with N = 240,243 subjects
- When BCG is given in infancy, false-positive TST results due to BCG occur in 6% of vaccinated subjects
- When BCG is given after infancy, false-positive TST results due to BCG occur in 40% of vaccinated subjects

World Atlas of BCG Policies and Practices (Beta)

WWW.BCGATLAS.ORG

Authors: Alice Zwerling, Marcel Behr, Timothy Brewer, Dick Menzies & Madhukar Pai
Affiliations: McGill University & McGill University Health Center Montreal Quebec, Canada
Supported in part by the Public Health Agency of Canada

Home | Query | References | Questionnaire | Contact Us

The following tool is a World Atlas of BCG Policies and Practices.

Currently the atlas includes information for over 140 countries from around the world. We have endeavoured to collect data on each country's current and past Bacille Calmette-Guerin (BCG) vaccination policies and practices.

As you know, variations in BCG vaccination practices impact the interpretation of TB diagnostics, such as the widely used Tuberculin Skin Test (TST). The World Atlas of BCG Policies and Practices will help clinicians in your country and around the world make better diagnostic decisions concerning TB infection. We have made the data available, for use as a searchable online tool for physicians and researchers alike.

If information for your country is missing, we encourage you to complete a very short questionnaire (should take only about 5 minutes to complete) concerning your country's BCG vaccination policy. The questionnaire is available on the website as a word form document. Please take the time to complete the questionnaire and contribute to the creation of a valuable resource for physicians and patients in your country.

India

Country: India
Code: IND
Region: South Asia
Income group (World Bank): Low income
Category: A, B or C: A
First BCG_who: birth
Second BCG_who:
Third BCG_who:
Fourth BCG_who:
Current BCG vaccination?: Yes
Q2: A, B, C: A
Which year was vaccination introduced?: 1948
Year BCG stopped: N/A
Age of 1st BCG?: At birth
Multiple BCG?: No
Age BCG #2: N/A
Age BCG #3: N/A
Age of BCG #4: N/A
Multiple BCG in the past?: No
Age Past BCG #2: N/A
Age past BCG #3: N/A
Year booster BCG stopped: N/A
BCG Strain: BCGVL Chennai strain, BCG laboratory Guindy, Chennai, India
TST done post BCG?: No
BCG coverage year: 2006
BCG coverage: 99
Year of changes: 1948: BCG intro as pilot project, 1949: Immunization program in schools, 51-59 Mass immunization campaigns
Explain changes: 1978: extended program of immunization to be given at birth or within 1st mo, 1985: universal immunization program BCG vaccine policy cotinued as earlier
Special groups: No
Explain: N/A
Summary : A

Alice Zwerling et al.

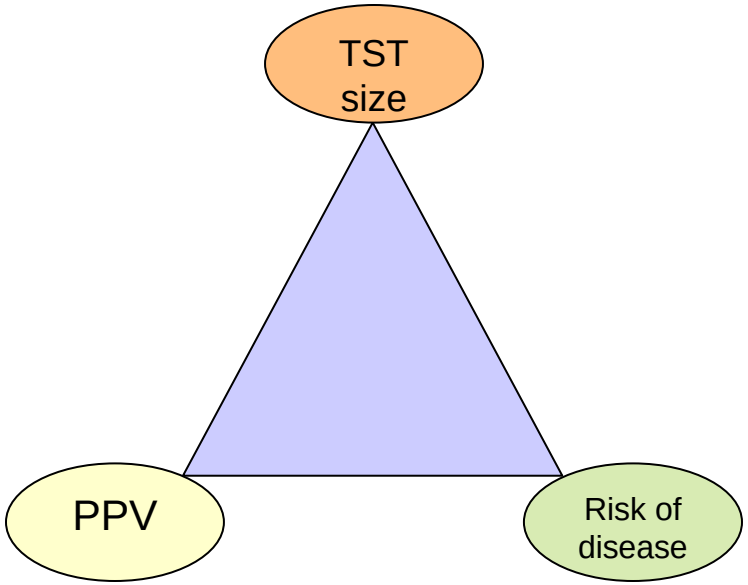
Funded by: Public Health Agency of Canada

INT J TUBERC LUNG DIS 12(5):498–505

Thinking in three dimensions: a web-based algorithm to aid the interpretation of tuberculin skin test results

D. Menzies,* G. Gardiner,*† M. Farhat,*† C. Greenaway,*‡ M. Pai*§

* Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, McGill University, Montreal,
† Massachusetts General Hospital, Harvard University, Boston, Massachusetts, USA; ‡ Division of Infectious Di
Microbiology, Sir Mortimer B Davis Jewish General Hospital, McGill University, Montreal, § Department of Epid
and Biostatistics, McGill University, Montreal, Canada



McGill

Thinking in three dimensions:
An algorithm to aid interpretation of the tuberculin skin test
(Version 1.0 January 19,2006)

Initial design: Maha Farhat, MD; Christina Greenaway, MD and Dick Menzies, MD;
Revisions and updates Dick Menzies, MD and Madhukar Pai MDPhD
Programming: Irena Sesartic

|| Disclaimer || References ||

The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of 10+mm, based on his/her clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPDS, or 2 TU RT-23). Prevalence of tuberculosis infection is derived using the Styblo formula and incidence of smear positive TB in the country of origin (from WHO). The effects of NTM and BCG on TST positivity were compiled from a literature review as were the relative risks of various health conditions. For further information see references, or contact the authors.

Select:

1.TST reaction size: 10-14 mm

2.Age: 0 **Age at immigration if applicable:** 0

3.Countrybirth: of Albania **If Country of birth is the USA:** Alabama

4.BCG status:
- ○ Never vaccinated or unknown
- ○ Vaccinated age < 2 years
- ◉ Vaccinated age >= 2 years

5.Contact with active TB:
- ○ None
- ○ Close Contact
- ◉ Casual

6.Please select all the conditions that currently apply to the patient:
- ☐ Diabetes Mellitus
- ☐ Chronic renal failure/hemodialysis

http://meakins.mcgill.ca/respepi/homeE.htm

OPEN ACCESS Freely available online

PLoS one

ESAT-6/CFP10 Skin Test Predicts Disease in *M. tuberculosis*-Infected Guinea Pigs

Karin Weldingh*, Peter Andersen

Department of Infectious Disease Immunology, Statens Serum Institut, Copenhagen, Denmark

Abstract

Background: Targeted preventive chemotherapy of individuals with progressive subclinical (incipient) disease before it becomes contagious would break the chain of tuberculosis transmission in high endemic regions. We have studied the ability of a skin test response to ESAT-6 and CFP10 (E6/C10) to predict later development of tuberculosis disease in the guinea pig model.

Methods and Findings: Guinea pigs, either vaccinated with BCG or unvaccinated, were infected with a low dose of *Mycobacterium tuberculosis* by the aerosol route and the development of delayed type hypersensitivity responses to E6/C10 and to purified protein derivative (PPD) were followed until the onset of clinical disease. We demonstrated a negative correlation between the size of the skin test response and the time to the onset of clinical disease; a large E6/C10 skin test response correlated to a shorter survival time post skin testing, while a small E6/C10 skin test reaction correlated with a longer survival time ($r = -0.6$ and $P < 0.0001$). No correlation was found using PPD.

Conclusions: Our data suggest that it may be possible to develop a prognostic skin test based on E6/C10 that will allow the identification of individuals with incipient disease, who have the highest risk of developing active tuberculosis in the near future.

Tuberculosis (2006) **86**, 363–373

ELSEVIER

Tuberculosis

http://intl.elsevierhealth.com/journals/tube

Safety of ESAT-6

Henrik Aggerbeck[a,*], Søren M. Madsen[b]

Improved rdESAT-6 skin test

Clinical and Experimental Immunology ORIGINAL ARTICLE doi:10.1111/j.1365-2249.2008.03605.x

Recombinant early secreted antigen target 6 protein as a skin test antigen for the specific detection of *Mycobacterium tuberculosis* infection

X. Wu, L. Zhang, J. Zhang, C. Zhang, L. Zhu and Y. Shi
Institute for Tuberculosis Research, the Second Affiliated Hospital of Chinese PLA General Hospital, Beijing, China

Summary

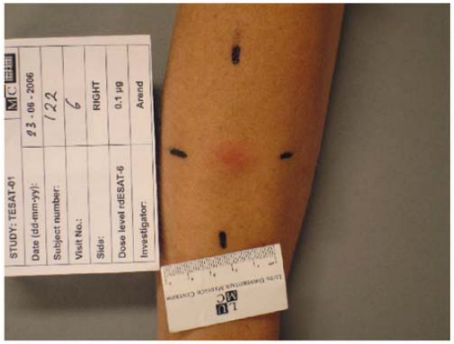
Although the delayed-type hypersensitivity skin test reaction to tuberculin purified protein derivative (PPD) is used worldwide for tuberculosis (TB) detection, it is incapable of distinguishing *Mycobacterium tuberculosis* (MTB) infection from bacille Calmette–Guérin (BCG) vaccination or infection with non-tuberculous *Mycobacteria*. As a result, there is an urgent need for a more specific diagnostic tool for TB. This study reports the skin reactions of guinea pigs and human volunteers to recombinant early secreted antigen target 6 (rESAT6), a secretory protein found only in MTB, *M. bovis* and few other mycobacterial species. These volunteers had varying histories of BCG vaccination and exposure to MTB, allowing us to determine the specificity of their response to TB exposure. Our results show that 1·0 μg of the purified MTB rESAT6 antigen elicited a positive skin response in both animals and humans exposed to MTB, as well as in animals exposed to *M. bovis* and *M. marinum*, all species of *Mycobacteria* that contain the gene for early secreted antigen target 6 (ESAT6). ESAT6 appears to be more specific to MTB infection than PPD, as demonstrated by the fact that we saw no skin responses in the BCG-vaccinated volunteers, nor in the guinea pigs sensitized with BCG vaccine, or with *Mycobacteria* that do not contain the gene encoding ESAT6. We believe that this is the first report of the use of a rESAT6 protein in a skin test in human volunteers, and that these data support its use in the specific detection of MTB infection.

Accepted for publication 7 January 2008
Correspondence: X. Wu, Mailing address: The Institute for Tuberculosis Research, the Second

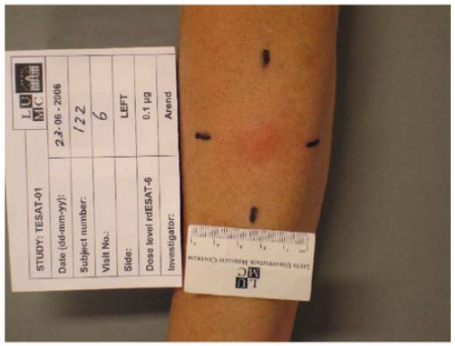
Double-blind randomized Phase I study comparing rdESAT-6 to tuberculin as skin test reagent in the diagnosis of tuberculosis infection

Sandra M. Arend[a,*], Willeke P.J. Franken[a], Henrik Aggerbeck[b], Corine Prins[a], Jaap T. van Dissel[a], Birgit Thierry-Carstensen[b], Pernille Nyholm Tingskov[b], Karin Weldingh[b], Peter Andersen[b]

Tuberculosis 2008

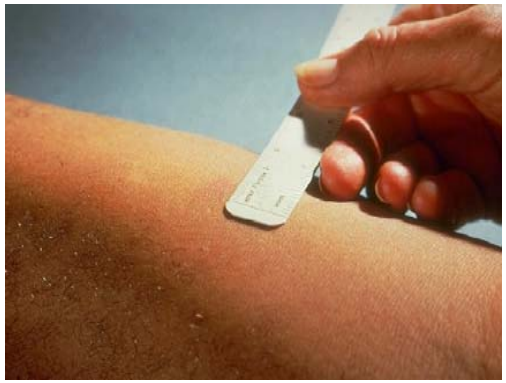


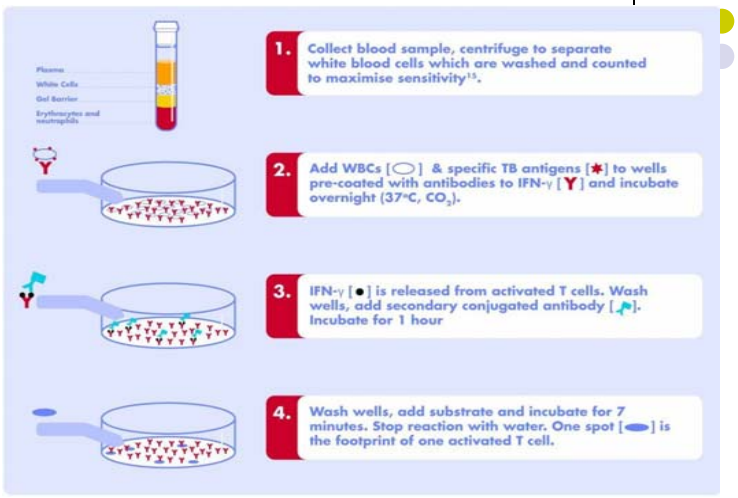
2 TU RT23



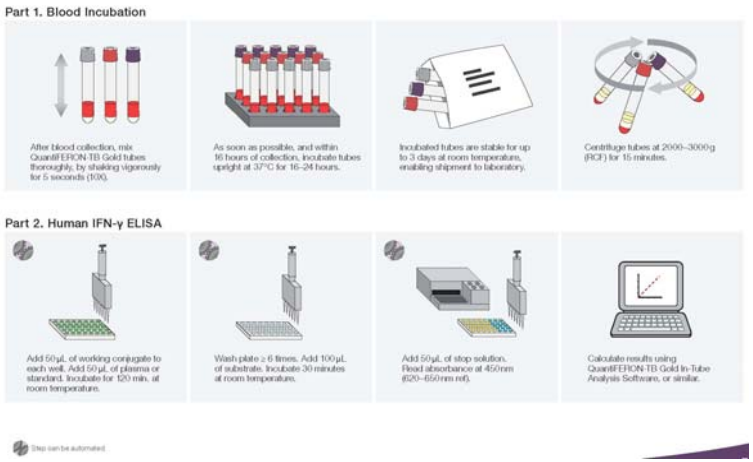
rdESAT-6

Interferon-gamma release assays (IGRA)



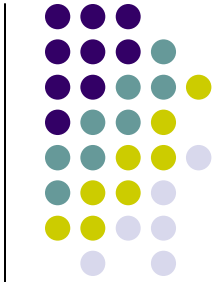


T-SPOT.*TB*® [Oxford Immunotec, UK]



QuantiFERON-TB Gold® In Tube [Cellestis Ltd, Australia]

Meta-analyses on IGRAs



Annals of Internal Medicine | ARTICLE

Meta-analysis: New Tests for the Diagnosis of Latent Tuberculosis Infection: Areas of Uncertainty and Recommendations for Research

Dick Menzies, MD, MSc; Madhukar Pai, MD, PhD; and George Comstock, MD, DrPH

Background: Until recently, the tuberculin skin test was the only test for detecting latent tuberculosis (TB) infection, but 2 ex vivo interferon-γ release assays (IGRAs) are now commercially licensed.

Purpose: To estimate sensitivity, specificity, and reproducibility of IGRAs (commercial or research versions of QuantiFERON [QFT] and Elispot) for diagnosing latent TB infection in healthy and immune-suppressed persons.

Data Sources: The authors searched MEDLINE and reviewed citations of all original articles and reviews for studies published in English.

Study Selection: Studies had evaluated IGRAs using *Mycobacterium tuberculosis*–specific antigens (RD1 antigens) and overnight (16- to 24-h) incubation times. Reference standards had to be clearly defined without knowledge of test results.

Data Extraction and Quality Assessment: Specific criteria for quality assessment were developed for sensitivity, specificity, and reproducibility.

Data Synthesis: When newly diagnosed active TB was used as a surrogate for latent TB infection, sensitivity of all tests was suboptimal, although it was higher with Elispot. No test distinguishes active TB from latent TB. Sensitivity of the tuberculin skin test and IGRAs was similar in persons who were categorized into clinical gradients of exposure. Pooled specificity was 97.7% (95% CI, 96% to 99%) and 92.5% (CI, 86% to 99%) for QFT and for Elispot, respectively. Both assays were more specific than the tuberculin skin test in samples vaccinated with bacille Calmette–Guérin. Elispot was more sensitive than the tuberculin skin test in 3 studies of immune-compromised samples. Discordant tuberculin skin test and IGRA reactions were frequent and largely unexplained, although some may be related to varied definitions of positive test results. Reversion of IGRA results from positive to negative was common in 2 studies in which it was assessed.

Limitations: Most studies used cross-sectional designs with the inherent limitation of no gold standard for latent TB infection, and most involved small samples with a widely varying likelihood of true-positive and false-positive test results. There is insufficient evidence on IGRA performance in children, immune-compromised persons, and the elderly.

Conclusions: New IGRAs show considerable promise and have excellent specificity. Additional studies are needed to better define their performance in high-risk populations and in serial testing. Longitudinal studies are needed to define the predictive value of IGRAs.

Ann Intern Med. 2007;146:340-354. www.annals.org

For author affiliations, see end of text.

Annals of Internal Medicine | REVIEW

Systematic Review: T-Cell–based Assays for the Diagnosis of Latent Tuberculosis Infection: An Update

Madhukar Pai, MD, PhD; Alice Zwerling, MSc; and Dick Menzies, MD, MSc

Background: Interferon-γ–release assays (IGRAs) are alternatives to the tuberculin skin test (TST). A recent meta-analysis showed that IGRAs have high specificity, even among populations that have received bacille Calmette–Guérin (BCG) vaccination. Sensitivity was suboptimal for TST and IGRAs.

Purpose: To incorporate new evidence into an updated meta-analysis on the sensitivity and specificity of IGRAs.

Data Sources: PubMed was searched through 31 March 2008, and citations of all original articles, guidelines, and reviews for studies published in English were reviewed.

Study Selection: Studies that evaluated QuantiFERON-TB Gold, QuantiFERON-TB Gold In-Tube (both from Cellestis, Victoria, Australia), and T-SPOT.TB (Oxford Immunotec, Oxford, United Kingdom) or its precommercial ELISpot version, when data on the commercial version were lacking. For assessing sensitivity, the study sample had to have microbiologically confirmed active tuberculosis. For assessing specificity, the sample had to comprise healthy, low-risk individuals without known exposure to tuberculosis. Studies with fewer than 10 participants and those that included only immunocompromised participants were excluded.

Data Extraction: One reviewer abstracted data on participant characteristics, test characteristics, and test performance from 38 studies; these data were double-checked by a second reviewer. The original investigators were contacted for additional information when necessary.

Data Synthesis: A fixed-effects meta-analysis with correction for overdispersion was done to pool data within prespecified subgroups. The pooled sensitivity was 78% (95% CI, 73% to 82%) for QuantiFERON-TB Gold, 70% (CI, 63% to 78%) for QuantiFERON-TB Gold In-Tube, and 90% (CI, 86% to 93%) for T-SPOT.TB. The pooled specificity for both QuantiFERON tests was 99% among non–BCG-vaccinated participants (CI, 98% to 100%) and 96% (CI, 94% to 98%) among BCG-vaccinated participants. The pooled specificity of T-SPOT.TB (including its precommercial ELISpot version) was 93% (CI, 86% to 100%). Tuberculin skin test results were heterogeneous, but specificity in non–BCG-vaccinated participants was consistently high (97% [CI, 95% to 99%]).

Limitation: Most studies were small and had limitations, including no gold standard for diagnosing latent tuberculosis and variable TST methods and cutoff values. Data on the specificity of the commercial T-SPOT.TB assay were limited.

Conclusion: The IGRAs, especially QuantiFERON-TB Gold and QuantiFERON-TB Gold In-Tube, have excellent specificity that is unaffected by BCG vaccination. Tuberculin skin test specificity is high in non–BCG-vaccinated populations but low and variable in BCG-vaccinated populations. Sensitivity of IGRAs and TST is not consistent across tests and populations, but T-SPOT.TB appears to be more sensitive than both QuantiFERON tests and TST.

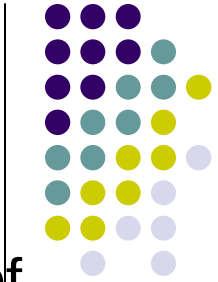
Ann Intern Med. 2008;149. www.annals.org

For author affiliations, see end of text.

Summary of Evidence

- TST specificity is high in BCG non-vaccinated; but low and variable in BCG vaccinated
- IGRAs (especially QFT) have very high specificity
  - IGRA specificity is higher than TST
  - IGRAs are not affected by BCG vaccination
    - Maybe very helpful in settings that give BCG after infancy or give multiple vaccinations
- Sensitivity of IGRAs and TST is not consistent across tests and populations
  - QFT is as sensitive as TST
  - QFT sensitivity is significantly higher in low incidence than high incidence countries
  - T-SPOT.TB appears to be more sensitive than both QuantiFERON tests and TST
    - Maybe helpful in evaluation of immunocompromised
- In low-incidence settings, IGRAs correlate well with markers of exposure

Summary of Evidence



- Diagnosis of active TB rests on microbiological detection of *M. tuberculosis*.
- Immune-based tests, such as IGRAs and TST, do not directly detect *M. tuberculosis*; they merely indicate a cellular immune response to recent or remote sensitization with *M. tuberculosis*.
- Because IGRAs cannot distinguish between LTBI and active TB, a positive IGRA result may not necessarily indicate active TB.
- Furthermore, a negative IGRA result would not conclusively rule out active disease in an individual suspected to have TB; this also applies to the TST.

Limitations of current evidence

- Almost all the available studies on IGRAs have limitations, namely lack of a gold standard for LTBI, cross-sectional design, use of sensitivity and specificity as surrogates for patient-important outcomes, and lack of adequate data on important outcomes such as accuracy of diagnostic algorithms (rather than single tests), incremental or added value of IGRAs, impact of IGRAs on clinical decision-making and therapeutic choices, and the prognostic ability of IGRAs.
- Thus, available evidence on IGRAs cannot be considered high quality, and further research is likely to have an important impact on current recommendations and guidelines.
- Ongoing studies should resolve these issues within the next few years and inform evidence-based guidelines on how to implement IGRAs in clinical practice

Can IGRAs be improved?

- Inclusion of new antigens
- Measure additional cytokines/chemokines
- Include other biomarkers

Improved Diagnostic Evaluation of Suspected Tuberculosis

Davinder P.S. Dosanjh, DPhil; Timothy S.C. Hinks, MD; John A. Innes, MD; Jonathan J. Deeks, PhD; Geoffrey Pasvol, DPhil; Sarah Hackforth, RGN; Hansa Varia, RGN; Kerry A. Millington, DPhil; Rubamalar Gunatheesan, MD; Valerie Guyot-Revol, PhD; and Ajit Lalvani, DM

Background: The role of new T-cell–based blood tests for tuberculosis in the diagnosis of active tuberculosis is unclear.

Objective: To compare the performance of 2 interferon-γ assays and tuberculin skin testing in adults with suspected tuberculosis.

Design: Prospective study conducted in routine practice.

Setting: 2 urban hospitals in the United Kingdom.

Patients: 389 adults, predominantly of South Asian and black ethnicity, with moderate to high clinical suspicion of active tuberculosis.

Intervention: Tuberculin skin testing, the enzyme-linked immunospot assay (ELISpot) incorporating early secretory antigenic target-6 and culture filtrate protein-10 (standard ELISpot), and ELISpot incorporating a novel antigen, Rv3879c (ELISpot^{PLUS}) were performed during diagnostic assessment by independent persons who were blinded to results of the other test.

confirmed and highly probable tuberculosis was 89% (95% CI, 84% to 93%) with ELISpot^{PLUS}, 85% (CI, 79% to 90%) with standard ELISpot, 79% (CI, 72% to 85%) with 15-mm threshold tuberculin skin testing, and 83% (CI, 77% to 89%) with stratified thresholds of 15 and 10 mm in vaccinated and unvaccinated patients, respectively. The ELISpot^{PLUS} assay was more sensitive than tuberculin skin testing with 15-mm cutoff points ($P = 0.01$) but not with stratified cutoff points ($P = 0.10$). The ELISpot^{PLUS} assay had 4% higher diagnostic sensitivity than standard ELISpot ($P = 0.02$). Combined sensitivity of ELISpot^{PLUS} and tuberculin skin testing was 99% (CI, 95% to 100%), conferring a negative likelihood ratio of 0.02 (CI, 0 to 0.06) when both test results were negative.

Limitations: Local standards for tuberculin skin testing differed from others used internationally. The study sample included few immunosuppressed patients.

Conclusion: The ELISpot^{PLUS} assay is more sensitive than standard

OPEN ACCESS Freely available online — PLoS one

Heparin-Binding-Hemagglutinin-Induced IFN-γ Release as a Diagnostic Tool for Latent Tuberculosis

Jean-Michel Hougardy[1], Kinda Schepers[1], Sammy Place[1], Annie Drowart[2,3], Véronique Lechevin[4,5], Virginie Verscheure[1], Anne-Sophie Debrie[6,7], T. Mark Doherty[8], Jean-Paul Van Vooren[4], Camille Locht[6,7], Françoise Mascart[1,9]*

CVI Accepts, published online ahead of print on 27 August 2008
Clin. Vaccine Immunol. doi:10.1128/CVI.00185-08

1 IL-7 Enhances Human Antigen-specific Memory T-cell Responses: Importance for

2 Improved Diagnosis of Tuberculosis Infection

Accuracy of an immune diagnostic assay based on RD1 selected epitopes for active tuberculosis in a clinical setting: a pilot study

D. Goletti[1,2], S. Carrara[2], D. Vincenti[2], C. Saltini[3], E. Busi Rizzi[4], V. Schininà[4], G. Ippolito[5], M. Amicosante[3] and E. Girardi[5]

CLINICAL AND VACCINE IMMUNOLOGY, Dec. 2007, p. 1578–1586 Vol. 14, No. 12
1556-6811/07/$08.00+0 doi:10.1128/CVI.00289-07

Longitudinal Tracking of Cytokines after Acute Exposure to Tuberculosis: Association of Distinct Cytokine Patterns with Protection and Disease Development[▽]

Rabia Hussain,[1]* Najeeha Talat,[1] Firdaus Shahid,[1] and Ghaffar Dawood[2]

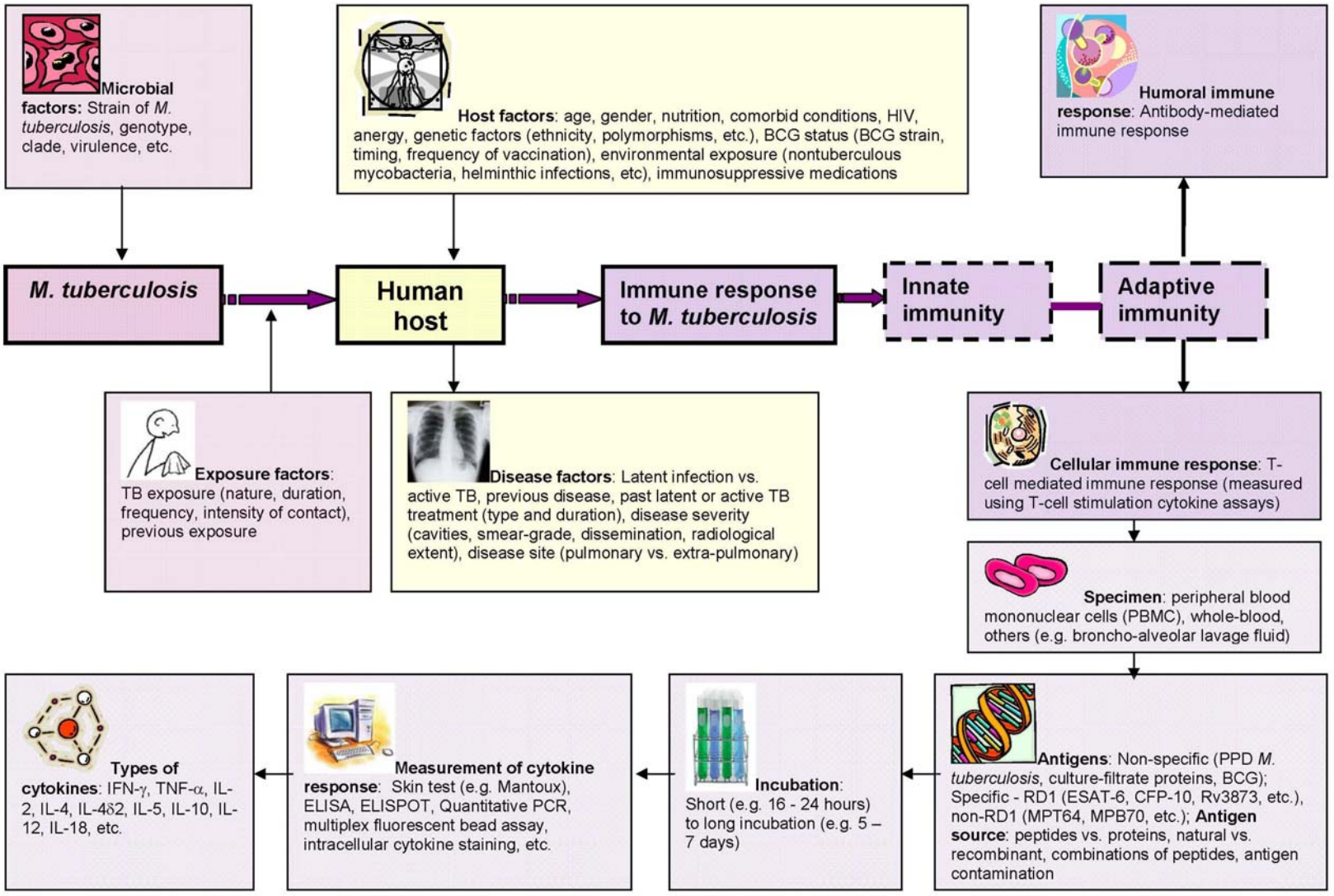
IFN-g/IL-10 ratio

OPEN ACCESS Freely available online — PLoS one

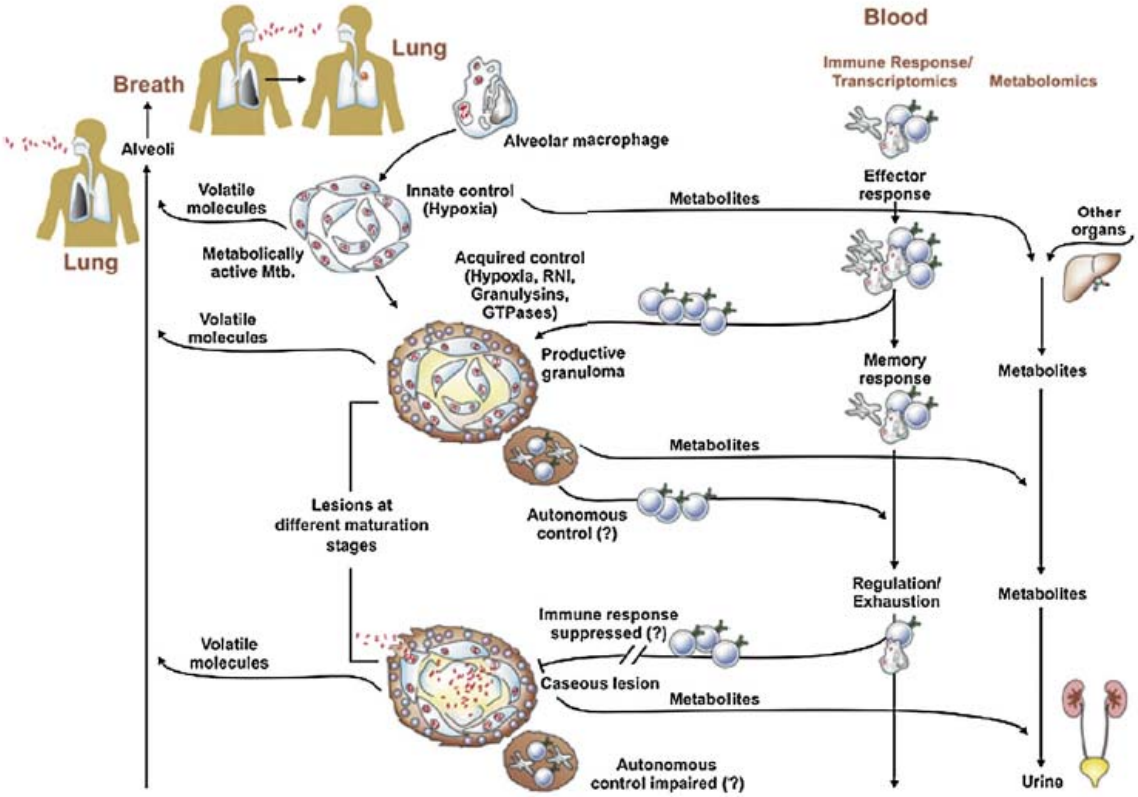
Improving T-Cell Assays for the Diagnosis of Latent TB Infection: Potential of a Diagnostic Test Based on IP-10

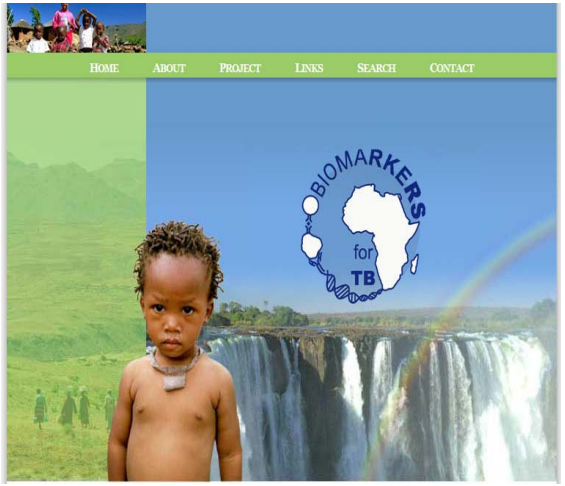
Morten Ruhwald[1,2]*, Janne Petersen[2], Kristian Kofoed[2], Hiroshi Nakaoka[3], Luis Eduardo Cuevas[3], Lovett Lawson[4], Stephen Bertil Squire[3], Jesper Eugen-Olsen[2], Pernille Ravn[2,5]

Immune-based biomarkers of latent TB



The search for biomarkers continues…





Cell Host & Microbe
Review

Tuberculosis in Africa: Learning from Pathogenesis for Biomarker Identification

Stefan H.E. Kaufmann[1,*] and Shreemanta K. Parida[1]
[1]Max Planck Institute for Infection Biology, Department of Immunology, Charitéplatz 1, D-10117 Berlin, Germany
*Correspondence: kaufmann@mpiib-berlin.mpg.de
DOI 10.1016/j.chom.2008.08.002

Stay tuned for more updates…

THE SAVE DATE
May 30–June 1, 2009*
Dubrovnik, Croatia

A satellite symposium of the Congress of the IUATLD-ER

5th Congress of the International Union Against Tuberculosis and Lung Disease (The Union), Europe Region
27th - 30th May 2009 Dubrovnik, Croatia

* This symposium will take place immediately after the Congress of the IUATLD-ER, to be held from May 27-30, 2009

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Disclosure of conflicts

- No financial conflicts
  - No stocks, no advisory boards, no speaker fees, no funds for research

- I consult for Foundation for Innovative New Diagnostics, a non-profit agency
  - FIND partners with several industries to develop new diagnostics for neglected diseases