Diagnosis of tuberculosis

Global TB Case Detection
A major concern

- 2.6 million new smear + cases notified in 2007
- 64% of the estimated 4.1 million cases
- 5.3 million new cases overall notified in 2007
- 57% of the estimated 9.3 million cases

WHO Report 2009 – Global Tuberculosis Control
Why is diagnosis the Achilles’ heel of TB control?

Diagnostic tools that Koch used…

Microscopy  Culture  Tuberculin test
are still in use today!

- **Active TB**
  - Sputum microscopy [1882]
  - Mycobacterial culture [1882]
  - Chest X-rays [1896]

- **Latent TB (LTBI)**
  - Tuberculin skin test [1890]
Diagnosis of latent tuberculosis infection (LTBI)

Importance of LTBI

- It is estimated that nearly one-third of the world’s population is infected with *M. tuberculosis*.
- In most individuals, *M. tuberculosis* infection is contained initially by host defences, and infection remains latent.
- However, latent TB infection (LTBI) has the potential to develop into active disease at any time.
- Identification and treatment of latent tuberculosis infection can reduce the risk of development of disease by as much as 60 - 90 percent, and so has potential to protect the health of the individuals as well as the public by reducing the number of potential sources of infection.
Indications for LTBI testing

- The goal of testing for LTBI is to identify individuals who are at increased risk for the development of tuberculosis and therefore would benefit from treatment of latent TB infection.
- Only those who would benefit from treatment should be tested.
- So a decision to test presupposes a decision to treat if the test is positive.
- In general, testing for LTBI is warranted to identify individuals who are at risk of new infection, and to identify individuals at increased risk of reactivation due to associated conditions.
- However, LTBI testing is a challenge
  - There is no definite method to confirm or rule out LTBI.

LTBI: a diagnostic challenge [case #1]

My 19 year old son is being worked up for his 2nd kidney transplant and is currently on hemodialysis. He has been through numerous drug reactions (some of them extremely rare) and he is not too keen on the skin test. The TB skin test is a part of the protocol of the Ottawa Hospital as there were two people last year who died of TB post renal transplant.

From the studies I have found on the internet it appears that the TB skin test is not a very accurate method of detection of LTBI in hemodialysis patients.

Is there anyone in Canada who is using this test and would it be possible to bring it to Ottawa? We are told that the Ottawa hospitals have a great concern about TB as they service the Inuit population. That said, I would assume that employing a TB blood test would be of great benefit to our renal patient population.
LTBI: a diagnostic challenge [case #2]

I am a healthcare worker, and have just had a positive TB skin test.

It’s only been one year since my last skin test which was negative.

My primary care doctor read my chest x-ray as negative and did not recommend INH, but the Health Dept. here recommends taking INH for 6-9 months.

Doctors and nurses whom I work with say that false positives happen all the time and to not worry about it. I have read about the side effects of this drug, and want to be sure that I actually am a carrier before taking it.

I have been reading about the QFT-G and am wondering if it will help resolve my dilemma about taking INH?

Who should be tested?

Who should be tested for latent TB infection?

<table>
<thead>
<tr>
<th>Those with increased risk of new TB infection (all patients should be tested regardless of age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Close contacts of patients with active pulmonary/respiratory TB</td>
</tr>
<tr>
<td>Casual contacts of patients with highly contagious active TB</td>
</tr>
<tr>
<td>Health care workers and other occupations in which there is risk of exposure to patients with untreated contagious active TB (prison facilities, homeless shelters)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Those with increased risk of reactivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk (all patients should be tested regardless of age)</td>
</tr>
<tr>
<td>HIV infection (any stage of disease)</td>
</tr>
<tr>
<td>Transplant, chemotherapy, or other major immunosuppressing condition</td>
</tr>
<tr>
<td>Lymphoma, leukemia, head &amp; neck cancer</td>
</tr>
<tr>
<td>Abnormal chest x-ray with evidence of prior disease (not including granulomas)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Renal failure (requiring dialysis)</td>
</tr>
<tr>
<td>Treatment with TNF-alpha inhibitors</td>
</tr>
</tbody>
</table>

Moderate risk (patients under age 65 should be tested)

- Systemic glucocorticoids (≥15 mg/day for ≥1 month)

Highly increased risk (patients under age 50 should be tested)

- Underweight (10th percentile of ideal body weight)
- For most individuals this is equivalent to body mass index (BMI) < 20.
- Opiate smoker (1 packet/day)
- Chest x-ray with solitary granulomas

* Only those with medical reasons for treatment should be tested, or a decision to test presupposes a decision to treat if the test is positive.
* A negative test should not preclude treatment for patients with a strong clinical suspicion.
* Moderate risk testing should be performed without interval screening.
* This algorithm is based on the 2006 American Thoracic Society/Centers for Disease Control and Prevention (ATS/CDC) statement.

Pai & Menzies. UpToDate 2009
How do we test for LTBI?

- **Tuberculin skin test**
  - Mantoux method, using purified protein derivative (PPD) at the recommend dose of 5 tuberculin units (0.1 mL); in other regions, PPD RT-23 is used at the standard dose of 2 TU
- **Interferon-gamma release assays (IGRAs)**
  - QuantiFERON-TB Gold In Tube
  - T-SPOT.TB

- Both tests are imperfect!

**Tuberculin skin test**

- **TST**
  - Measures cell-mediated immune response (CMI)
    - Uses PPD: a crude antigenic mixture
- **Limitations of TST:**
  - false positives and false negatives are possible
  - technical issues 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
Administering the TST

- Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally on volar surface of lower arm using a 27-gauge needle
- Produce a wheal 6 to 10 mm in diameter

Source: US CDC

Reading the TST

- Measure reaction in 48 to 72 hours
- Measure induration, not erythema
- Record reaction in millimeters, not “negative” or “positive”
- Ensure trained health care professional measures and interprets the TST
- Self reading is not accurate

Source: US CDC
Factors That May Cause False-Positive TST Reactions

- Nontuberculous mycobacteria
  - Reactions caused by nontuberculous mycobacteria are usually ≤ 10 mm of induration

- BCG vaccination
  - Reactivity in BCG vaccine recipients generally wanes over time; positive TST result is likely due to TB infection if risk factors are present

Source: US CDC
Factors That May Cause False-Negative TST Reactions

Potential causes of false negative tuberculin tests

Technical (potentially correctable)

- Tuberculin material:
  - Improper storage (exposure to light or heat)
  - Contamination, improper dilution, or chemical deterioration
- Administration:
  - Injection of too little tuberculin, or too deeply (should be subcutaneous)
  - Administration more than 20 minutes after drawing up into the syringe
- Reading:
  - Inexperienced or biased reader
  - Error in recording

Biologic (not correctable)

- Infections:
  - Active TB (especially if advanced)
  - Other bacterial infection (typhoid fever, brucellosis, typhus, leprosy, pertussis)
  - HIV infection (especially if CD4 count <200)
  - Other viral infection (measles, mumps, varicella)
  - Fungal infection (South American blastomycosis)
  - Live virus vaccination: (measles, mumps, polio)
  - Immunosuppressive drugs: (corticosteroids, TNF inhibitors, and others)
- Metabolic disease: chronic renal failure, severe malnutrition, stress (surgery, burns)
- Diseases of lymphoid organs: (lymphoma, chronic lymphocytic leukemia, sarcoidosis)
- Age: infants <6 months, elderly

TST requires a 3-dimensional interpretation

www.tstin3d.com
When BCG is given after infancy or repeated many times, it can affect TST results

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

M. Farhat,*1 C. Greenaway,*4 M. Pal,*5 D. Mendes*6

*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 Parasitological 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

**In India, BCG has limited effect on TST**

![BCG World Atlas](WWW.BCGATLAS.ORG)
In Uganda, BCG has limited effect on TST

In Japan, BCG has a major effect on TST
In Ukraine, BCG has a major effect on TST

IGRAs

T-SPOT.TB® [Oxford Immunotec, UK]

QuantiFERON-TB Gold® In Tube [Cellestis Ltd, Australia]
Quick Summary of Evidence

- TST specificity is high in BCG non-vaccinated; but lower and variable in BCG vaccinated
- IGRAs (especially QFT) have very high specificity (>95%)
  - 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
  - Overall, IGRAs are ~80% sensitive in culture+ TB patients
    • Sensitivity is lower in high incidence countries
  - QFT is as sensitive as TST (~80%)
    • QFT sensitivity is higher in low incidence than high incidence countries
  - T-SPOT.TB appears to be more sensitive (~90%) than both QuantiFERON tests and TST
    • But this may partly be because of cut-offs used for T-SPOT vs QFT
- In low-incidence settings, IGRAs correlate well with markers of exposure


Countries that may benefit from IGRAs

Zwerling A et al.
IGRAs in immunocompromised

• Immunocompromised groups are highly variable, and most studies are small:
  – All tests underperform in severely immunocompromised patients
    • Using both TST and IGRA might help increase sensitivity
  – IGRA sens in HIV+ is lower (~60 – 65%) than HIV- (~80 – 90%)
  – About 15% of HIV+ TB patients have indeterminate IGRA results
  – Indeterminate IGRA results increase with level of immunosuppression (i.e. low CD4 counts)
  – Very limited data on predictive value
  – Utility as rule out test for active TB is not well established
    • Unlikely to have a rule out value, given the modest sensitivity

IGRAs for active TB diagnosis

• No role in adults
  – Cannot distinguish between latent and active TB
  – Sensitivity is not high
    • Cannot rule out
  – Specificity will always be low in high TB incidence settings
    • Cannot rule in
  – No evidence that IGRAs offer any added value over conventional microbiological tests

• In children
  – Cannot be used in isolation
    • A negative IGRA does not rule out active TB at any age.
  – Cannot replace microbiological investigations
  – Useful as “evidence of infection” which should be interpreted with other information (e.g. contact, symptoms, radiological findings)
## Predictive value: Incidence rates of TB by IGRA status

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Publication Year</th>
<th>ELISPOT Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ELISPOT (in-house)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Turkey</td>
<td>Baki (2008)</td>
<td>21/1000 person-yr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ELISPOT (T-SPOT.TB)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colombia</td>
<td>del Corral (2009)</td>
<td>7/1000 person-yr</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>Lienhardt (2010)</td>
<td>14/1000 person-yr</td>
</tr>
<tr>
<td></td>
<td>China</td>
<td>Leung (2010)</td>
<td>22/1000 person-yr</td>
</tr>
</tbody>
</table>

### Incidence rate per 1000 person-years
Rangaka M et al.

## Rates of disease progression in IGRA+ in the largest high burden country studies

<table>
<thead>
<tr>
<th>Country</th>
<th>N</th>
<th>Test</th>
<th>Incidence of active TB in IGRA+ groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Gambia</td>
<td>2348</td>
<td>ELISPOT (in-house)</td>
<td>9/1000 person-yr</td>
</tr>
<tr>
<td>Turkey</td>
<td>908</td>
<td>ELISPOT (T-SPOT.TB)</td>
<td>21/1000 person-yr</td>
</tr>
<tr>
<td>S Africa</td>
<td>5248</td>
<td>QFT</td>
<td>6/1000 person-yr</td>
</tr>
<tr>
<td>Colombia</td>
<td>2060</td>
<td>In-house whole-blood CFP-10 assay</td>
<td>11/1000 person-yr</td>
</tr>
<tr>
<td>Senegal</td>
<td>2679</td>
<td>ELISPOT (in-house)</td>
<td>14/1000 person-yr</td>
</tr>
</tbody>
</table>
Results: IGRA vs TST: Which has greater predictive ability?

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>(Publication Year)</th>
<th>IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGRA</td>
<td>Cambodia</td>
<td>Hill (2008)</td>
<td>1.90 (0.80, 4.50)</td>
</tr>
<tr>
<td></td>
<td>Turkey</td>
<td>Bakr (2008)</td>
<td>3.41 (1.08, 10.70)</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>Lienhardt (2010)</td>
<td>2.00 (0.84, 5.41)</td>
</tr>
<tr>
<td></td>
<td>China</td>
<td>Leung (2010)</td>
<td>4.20 (1.03, 19.68)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>IGRA</td>
<td></td>
<td>2.42 (1.44, 4.07)</td>
</tr>
<tr>
<td>TST</td>
<td>Cambodia</td>
<td>Hill (2008)</td>
<td>2.10 (0.89, 5.11)</td>
</tr>
<tr>
<td></td>
<td>Turkey</td>
<td>Bakr (2008)</td>
<td>2.65 (0.72, 14.62)</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>Lienhardt (2010)</td>
<td>1.40 (0.48, 4.74)</td>
</tr>
<tr>
<td></td>
<td>China</td>
<td>Leung (2010)</td>
<td>1.64 (0.53, 5.02)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>TST</td>
<td></td>
<td>1.86 (1.07, 3.22)</td>
</tr>
</tbody>
</table>

Conclusions on predictive value

• Incidence rates of TB, even in IGRA positive individuals, are low, suggesting that a vast majority (>95%) of IGRA+ individuals do not progress to TB disease during follow-up. This is similar to the TST.
• All existing LTBI tests (TST and IGRAs) have only modest predictive value and may not help identify those who are at highest risk of progression to disease.
• Based on the evidence thus far, IGRAs appear to have similar predictive value as the TST.
• In some settings, the % IGRA+ will be less than % TST+, reducing the number needed for IPT
• The search for highly predictive biomarkers must continue
USA: CDC Guidelines, 2010

IGRAs can be used in place of (but not in addition to) TST in all situations in which CDC recommends TST as an aid in diagnosing LTBI (contact investigations, testing during pregnancy, and screening of health care workers and others undergoing serial evaluation for LTBI).

IGRAs are preferred over TST in individuals who have received BCG and individuals from groups that have poor rates of return for TST reading.

TST is preferred over IGRAs for testing children less than 5 years of age.

Canadian IGRA guidelines

• For persons with a positive TST and low pretest probability of recently acquired LTBI, as well as no other risk factors for progression to active disease, IGRAs may be used as a confirmatory test to exclude the possibility of a false positive TST.

• For persons with high risk of progression to active disease if infected, a TST should be used; if this is positive the person should be considered to have LTBI. If negative, an IGRA could be done; if positive the person should be considered to have LTBI.
Canadian IGRA guidelines

• In immunocompromised individuals, the TST should be the initial test used to detect LTBI. If the TST is positive, the person should be considered to have LTBI. However, given the rate of false-negative TST results in immunocompromised populations, IGRA testing is appropriate in the setting of negative TST results. If the IGRA result is positive, the person may be considered to have LTBI.

• In children, IGRA may be used as a supplementary diagnostic tool, together with clinical specimens for definitive microbiologic diagnosis, TST and other investigations. However, IGRA should not be a substitute for, or obviate the need for, appropriate microbiologic specimen collection. A negative IGRA (or TST) does NOT rule out active TB at any age.

Diagnosis of active TB and drug-resistance
Diagnostic options

- Smear microscopy
- Culture
- NAAT
- Drug Susceptibility Testing

Smear Microscopy

- 50-70% sensitive, very specific
- Quick, cheap, relatively easy
- Stains take advantage of mycolic acid in cell walls of Mycobacteria
- “Acid Fast Bacilli”
- Stain → Decolorize → Counterstain
**LIGHT MICROSCOPY**

- Traditional method
- More experienced microscopists
- Tedious

**FLUORESCENT MICROSCOPY**

- Need lower magnification → 45% less time to examine slides
- 10% more sensitive
- Easier staining procedure

---

**WHO policies on Smear Microscopy**

**Definition of a new sputum smear-positive TB case**

The revised definition of a new sputum smear-positive pulmonary TB case is based on the presence of at least one acid-fast bacilli (AFB+) in at least one sputum sample in countries with a well-functioning external quality assurance (EQA) system.

**Reduction of number of smears for the diagnosis of pulmonary TB**

WHO recommends the number of specimens to be examined for screening of TB cases can be reduced from three to two, in places where a well-functioning external quality assurance (EQA) system exists, where the workload is very high and human resources are limited.

LED microscopy

---

Commercial LED Microscopes

Table 1. Comparison of commercial light-emitting diode products currently available for TB diagnostics.

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Isolation cap</th>
<th>Attachment</th>
<th>Transmission</th>
<th>Power supply</th>
<th>Weight (kg)</th>
<th>Cost (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primus star LED</td>
<td>Carl Zeiss, Oberkochen, Germany</td>
<td>Yes</td>
<td>NA</td>
<td>Epifluorescent</td>
<td>Yes</td>
<td>9.5</td>
<td>4825*</td>
</tr>
<tr>
<td>Luxam™</td>
<td>L.K. Scientific, Lawrenceville, USA, USA</td>
<td>Yes</td>
<td>Objective lenses replacement (10x, 40, 60, and 100x)</td>
<td>Epifluorescent</td>
<td>Yes</td>
<td>0.443</td>
<td>700-4200*</td>
</tr>
<tr>
<td>Focus™</td>
<td>QPC™ Diagnostics, Pittsburgh, PA, USA</td>
<td>No</td>
<td>Objective lenses replacement (40, 60, and 100x - 46)</td>
<td>Epifluorescent</td>
<td>Yes</td>
<td>1.27</td>
<td>995*</td>
</tr>
<tr>
<td>FluidLED</td>
<td>Flowmon Corporation Srl, Genova, Milanese, Italy</td>
<td>No</td>
<td>Adapter attached to base and filter</td>
<td>Transmission</td>
<td>Yes</td>
<td>5</td>
<td>1077-2105*</td>
</tr>
<tr>
<td>Cycles™</td>
<td>Nikon, Grifiti, Germany</td>
<td>Yes</td>
<td>NA</td>
<td>Epifluorescent</td>
<td>Yes</td>
<td>2.7</td>
<td>2392-3655*</td>
</tr>
</tbody>
</table>


Culture-based diagnostics

- “Gold Standard”
- High Sensitivity, Isolate Available for DST and molecular typing
- Slow Turnaround, Biosafety Issues, Requires Specimen Processing, Relatively Expensive
Policy on Culture-based Diagnostics

The use of liquid medium for culture and DST

WHO recommends, as a step-wise approach:
1. The use of liquid medium for culture and DST in middle- and low-income countries.
2. The rapid species identification to address the needs for culture and drug susceptibility testing (DST).

Taking into consideration that liquid systems will be implemented in a phased manner, integrated into a country specific comprehensive plan for laboratory capacity strengthening and addressing the following key issues:

- Appropriate biosecurity level;
- Detailed customer plan describing guarantees and commitments of the manufacturer;
- Appropriate training of staff;
- Maintenance of infrastructure and equipment in laboratories;
- Quick transportation of samples from the peripheral to the culture laboratory;
- Rapid communication of results.

Conventional NAATs

- High specificity and PPV
- Sensitivity is lower and highly variable
  - Especially in extrapulmonary specimens
  - Especially in smear negative specimens
    (>95% smear + vs. 40-80% smear -)
- Expensive
- Should not be used on follow-up specimens

- In house assays
- Roche Cobas Amplicor
- Gen-Probe AMTD
- BD ProbeTec ET

Ling D et al.
Newer NAAT: Cepheid Xpert MTB/RIF

- Automated nested RT-PCR
- Simple 1-step specimen preparation
- Can be used at the point-of-treatment
- Results in 2 hours
- Detects TB and RIF resistance
- Equipment ~$20k; ~$20/test

1462 symptomatic patients (4386 samples)
- 50.7% culture positivity

Sensitivity:
- 98.2% in smear (+)
- 72.5% in smear (-) [3 specimens increases to 90.2%]

Specificity 99.2%

- 97.6% accurate for Rif-R
- 98.1% accurate for Rif-S

Results in <2hrs
Upcoming WHO Policy

Expert Committee Recommendations

1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (strong recommendation)

2. Xpert MTB/RIF may be used as a follow-on test to microscopy where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (conditional recommendation, recognising major resource implications)

Raviglione M et al.

Detecting Drug Resistance

% of MDR-TB among new TB cases since 1994

Multidrug and extensively drug-resistant TB (MDR-TB): 2010 global report on surveillance and response
Conventional Drug Susceptibility Testing

- **Agar Proportion Method**
  - Plate isolate onto drug-free and drug-containing media
  - Count colonies on each – if >1% of drug-free growth present on drug-containing growth = Resistant

- **BACTEC 460/MGIT**
  - Inoculate drug-containing bottles
  - Inoculate drug-free bottle with 1:100 diluted isolate
  - Growth Index (growth units) compared

Line Probe Assays

- Detection of MTB & RIF-resistance (*rpoB*)
- Requires extraction, amplification
- Colorimetric development using immobilized probes
- Innogenetics, INNO-LiPA Rif TB
- Hain, GenoType MTBDRplus
Policy on Line Probe Assays

WHO policy statement: molecular line probe assays for rapid screening of patients at risk of multidrug-resistant tuberculosis

Rapid diagnosis of drug-resistant TB using line probe assays: from evidence to policy

Rapid rifampin resistance detection using Xpert MTB/RIF

Table 3. Sensitivity and Specificity of the MTB/RIF Test for the Detection of Rifampin and Multidrug Resistance, as Compared with Phenotypic Drug-Susceptibility Testing Alone and in Combination with Sequencing of Disparate Cases, According to Site.*

<table>
<thead>
<tr>
<th>Site and Site Total</th>
<th>Phenotypic Drug-Susceptibility Testing</th>
<th>Phenotypic Drug-Susceptibility Testing and Disparate Resolution by Sequencing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Specificity for Rifampin Resistance</td>
<td>Specificity for Rifampin Resistance</td>
</tr>
<tr>
<td>Lima, Peru — no/total no. (%)</td>
<td>16/16 (100.0)</td>
<td>100/100 (100.0)</td>
</tr>
<tr>
<td>Baku, Azerbaijan — no/total no. (%)</td>
<td>47/49 (95.9)</td>
<td>90/94 (95.7)</td>
</tr>
<tr>
<td>Cape Town, South Africa — no/total no. (%)</td>
<td>15/16 (93.8)</td>
<td>126/126 (100.0)</td>
</tr>
<tr>
<td>Durban, South Africa — no/total no. (%)</td>
<td>3/3 (100.0)</td>
<td>58/58 (100.0)</td>
</tr>
<tr>
<td>Mumbai, India — no/total no. (%)</td>
<td>119/121 (98.3)</td>
<td>61/64 (95.5)</td>
</tr>
<tr>
<td>Total for rifampin resistance</td>
<td>Correct — no/total no. (%)</td>
<td>200/205 (97.6)</td>
</tr>
<tr>
<td>95% CI — %</td>
<td>94.4–99.6</td>
<td>96.5–99.9</td>
</tr>
<tr>
<td>Total for multidrug resistance</td>
<td>Correct — no/total no. (%)</td>
<td>195/200 (97.5)</td>
</tr>
<tr>
<td>95% CI — %</td>
<td>94.3–98.9</td>
<td>96.3–99.7</td>
</tr>
</tbody>
</table>

Boehme C et al. NEJM 2010
In conclusion, much progress has been made in improving TB diagnosis, but…

We still do not have a good point of care test
Global Plan to Stop TB

Evidence-Based Tuberculosis Diagnosis

www.tbevidence.org