Interferon Gamma Release Assays (IGRAs) in the Diagnosis of Tuberculosis

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Chantilly, VA  San Juan Capistrano, CA

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- Laboratory professionals may earn 1.0 contact hour for participation in today’s program
- Learning objectives: upon completion of this program, participants will be able to
  - Discuss tuberculosis statistics and trends in the US and worldwide
  - Identify the differences between active and latent tuberculosis and how each is diagnosed
  - Compare advantages/disadvantages of, and explain the latest CDC guidelines for, using IGRAs in the diagnosis of tuberculosis
  - Describe best practices in conducting and interpreting IGRAs
Tuberculosis (TB): Tip of the Iceberg

Active Cases

Latent TB Infections

Total Population
Tuberculosis Worldwide

- 2 billion latently infected people worldwide
- 9 million new cases each year
- 2 million die each year (vs 200,000 from HIV)

AAC 2009. 53, 849
Tuberculosis in the US

- 10-15 million people infected with latent TB (4%)*
- 11,540 new cases of active TB in 2009 (11.4%) ↓
- Targeted screening and treatment
  - 18-20 million skin tests/year
  - 50% performed in hospitals

*AJRCCM, 2008, 177, 348
Reported TB Cases*
United States, 1982–2008

[Graph showing the trend of reported TB cases from 1982 to 2008.]

*Updated as of May 20, 2009.
Number and Rate* of TB Cases Among US-Born and Foreign-Born Persons by Year Reported: US, 1993-2009

MMWR, 2010, 59(10);289-294.

* Per 100,000 population
Rate* of TB cases by State/Area: US, 2009

MMWR, 2010, 59(10);289-294
* Per 100,000 population
Complexity Caused by Immigration

- TB rate 11 times greater among foreign-born
  - Foreign-born: 18.6 cases/100,000
  - US-born: 1.7 cases/100,000
- 58.9% of all TB cases occurred in foreign-born individuals
- Higher number of foreign-born individuals are BCG-vaccinated

MMWR, 2010, 59(10);289-294
Transmission of TB

- Active TB: Infectious
  - Family, friends, workmates, etc. exposed
  - Infected, but no symptoms ("Latent TB infection [LTBI]")
  - If not identified & treated, ~10% develop TB during their lifetime

- Not infected
Presentation of mycobacterial antigens

Antigen presenting cell

Memory T cell

Skin test

In vitro blood test

Measurement of induration and erythema

IFN-γ

TNFα

IL-8

Measurement of induration and erythema

Image courtesy of Neil W. Schluger, M.D, Columbia University
# Active vs Latent TB

<table>
<thead>
<tr>
<th>Latent TB Infection</th>
<th>Active TB in Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB present</td>
<td>MTB present</td>
</tr>
<tr>
<td>Tuberculin skin test/IGRA +</td>
<td>Tuberculin skin test/IGRA +</td>
</tr>
<tr>
<td>Normal chest x-ray</td>
<td>Lesion in chest x-ray (usually)</td>
</tr>
<tr>
<td>Negative sputum smear, culture</td>
<td>Positive sputum smear, culture</td>
</tr>
<tr>
<td>No symptoms</td>
<td>Cough, fever, weight loss</td>
</tr>
<tr>
<td>Not infectious</td>
<td>Often infectious before treatment</td>
</tr>
<tr>
<td>Not defined as TB case</td>
<td>Defined as TB case</td>
</tr>
</tbody>
</table>
# TB Surveillance

<table>
<thead>
<tr>
<th>High Risk of Transmission</th>
<th>High Risk of Progression/Reactivation (Immunosuppressed)</th>
<th>High Risk of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Healthcare workers</td>
<td>- HIV</td>
<td>- TB suspects</td>
</tr>
<tr>
<td>- Foreign-born</td>
<td>- Rheumatoid arthritis</td>
<td></td>
</tr>
<tr>
<td>- Prisoners</td>
<td>- End-stage renal disease</td>
<td></td>
</tr>
<tr>
<td>- Chronic care residents</td>
<td>- Elderly</td>
<td></td>
</tr>
<tr>
<td>- Military personnel</td>
<td>- Children</td>
<td></td>
</tr>
<tr>
<td>- TB contacts</td>
<td>- Cancer chemotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Organ transplant</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Diabetes</td>
<td></td>
</tr>
</tbody>
</table>
Tuberculin Skin Test
(In Routine Use Since 1910)

- Purified protein derivative (PPD) is injected intradermally (polyvalent mixture of >200 TB proteins)
- Measure size of reaction after 48-72 h
  - Induration (firm area)
  - Not erythema (redness)
Tuberculin Skin Test

Limitations

- Reader variability (requires trained staff)
- Moderate sensitivity (esp. HIV, other immunocompromised patients)
- Variations of results (different anatomical site)
- Boosting
- Need for 2-4 visits
- Poor specificity
  - BCG vaccination (up to 80%)
  - Non-TB environmental mycobacteria (0.1-2%)
  - Latency vs active infection

Picture courtesy of Neil W. Schluger, M.D, Columbia University
What is the Cost of Evaluating and Treating People with False-Positive TSTs?

- Unnecessary return visits to the clinic
- Unnecessary chest radiographs
- Unnecessary blood tests
- Unnecessary INH hepatitis
- Unnecessary liver transplants
  - 2 liver transplants per year\textsuperscript{1,2} in the U.S. from INH-induced acute hepatitis

\textsuperscript{1}Russo et al. Liver Transplantation 2004; 10: 1018-1025
\textsuperscript{2}MMWR 2010; 59: 224-229

Neil W. Schluger, M.D, Columbia University
Diagnosis of Latent TB Infections in the US: A New ERA

- Interferon gamma release assays (IGRA)
  - QuantiFERON®
  - T-SPOT®.TB
Centers for Disease Control and Prevention (CDC)  
2010 Guidelines for Use of IGRA in Detection of LTBI

- Using IGRA for targeted testing:
  - As with the TST, IGRA screens generally should not be used for testing persons who have a low risk for both infection and disease attributable to *M. tuberculosis* (except for those likely to be at increased risk in the future) because screening such persons diverts resources from activities of higher priority and increases the number of false-positive results.
  - If persons at low risk for both infection and progression are to be tested, selection of the test with the greatest specificity will minimize false-positive results, reduce unnecessary evaluation and treatment, and minimize the potential for adverse events from unnecessary treatment.
Centers for Disease Control and Prevention (CDC)
2010 Guidelines for Use of IGRA in Detection of LTBI

- An IGRA is preferred for testing persons from groups that historically have poor rates of return for TST reading
- An IGRA is preferred for testing persons who have received BCG
- TST is preferred for testing children aged <5 years
- An IGRA may be used in place of TST (without preference) to test recent contacts of persons with infectious TB
- An IGRA or TST may be used for periodic screening that addresses occupational exposure to TB (eg, surveillance programs for healthcare workers) with special considerations regarding conversions and reversions
Advantages of IGRAs

- Provides high specificity:
  - Antigens (RD-1 & RD11 genes) used not found in the BCG vaccine
  - BCG vaccinated patients do not test positive
- Only 1 clinic visit required
- No “booster effect”
TB Peptide Antigens

ESAT-6, TB7.7, and CFP-10

- Encoded by RD-1 & RD11 genes
- Absent from BCG (TB-specific)
- Absent from most non-TB Mycobacteria
- Induce IFN-\(\gamma\) responses
- TB7.7 (QuantiFERON® only)
# No Cross-Reactivity to BCG and Most NTMs Among IGRAs

<table>
<thead>
<tr>
<th>Tuberculosis Complex</th>
<th>ESAT-6</th>
<th>CFP-10</th>
<th>TB7.7*</th>
<th>Environmental strains</th>
<th>ESAT-6</th>
<th>CFP-10</th>
<th>TB7.7*</th>
</tr>
</thead>
<tbody>
<tr>
<td>M tuberculosis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>M abcessus</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>M africanum</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>M avium</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>M bovis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>M branderri</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M celatum</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M cheloneae</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>M fortuitum</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>M gordonii</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>-</td>
<td>-</td>
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<tr>
<td>gothenburg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M kansasii</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<td>moreau</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M malmoense</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>tice</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M marinum</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>tokyo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M oenavense</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>danish</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M scrofulaceum</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>glaxo</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M smegmatis</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>montreal</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M szulgai</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<td>pasteur</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>M terrae</td>
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<td></td>
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<td></td>
<td></td>
<td>M vaccae</td>
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<td></td>
<td></td>
<td></td>
<td>M xenopi</td>
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</tr>
</tbody>
</table>

*QuantiFERON only*
QuantiFERON In Tube (QFT-IT)

In the field:
- TB-specific antigen, Nil & mitogen tubes
- Collect blood directly into tubes

Field/Lab: Incubate and centrifuge

In the lab:
- ELISA for detection of IFN-gamma
QFT-IT

- Sampling shipping/logistics
  - *Collect blood, then ship to lab:* Sample must be received with 16 hours of blood collection or…
  - *Collect blood, incubate, then ship to lab:* Incubated blood samples are stable for up to 3 days at RT/refrigerated temperatures (2-27°C) or…
  - *Collect blood, incubate, centrifuge, then ship to lab:* Sample is stable for up to 28 days at refrigerated temperatures (2-8°C)
QuantiFERON-TB Gold In-Tube

Stage 1 – Blood incubation and harvesting

1. Collect 1 mL of blood (x3). Incubate 36-38°C (16-24 h).

2. Centrifuge tubes at 2,000-3,000 x g for 5 minutes.

IFN-γ stable refrigerated for at least 4 weeks.

Stage 2 – Human IFN-γ ELISA

3. Add plasma and conjugate to ELISA plate. Incubate for 120 min. at room temperature.

4. Wash and add substrate. Read absorbance after 30 min.

5. Software calculates results and prints report.

The ELISA stage is easily automated on existing machines.
QuantiFERON Results at Quest Diagnostics

- Reports contain a qualitative result and if desired, 3 quantitative results

- Possible qualitative results are:
  - Detected (positive)
  - Not Detected (negative)
  - Indeterminate

- Three quantitative results:
  - Nil (0-0.5)
  - Mitogen- Nil (≥0.5)
  - TB Antigen – Nil (≥0.35 IU/ml = Positive)
QuantiFERON Indeterminate Results
(Low Mitogen Tube Response)

Technical Factors

- Incorrect handling of blood samples (probable lack of shaking) – PHA not adequately solubilized
- Not incubating samples
- >16 h from blood draw to incubation in lab (36-38°C); sometimes as little as 6 hr can be detrimental to test
- Storage of filled blood collection tubes outside recommended range (22°C ± 5°C)
QuantiFERON Indeterminate Results
(High Nil Tube Response)

Host Factors

- Presence of heterophile antibodies (human anti-mouse)
- Intrinsic gamma interferon secretion
- Recent vaccination(s)
- Lymphocytes responding indiscriminately (poison ivy, rheumatoid arthritis, etc.) – recommendation is to redraw one month later
Centers for Disease Control and Prevention (CDC) 2010 Guidelines for Use of IGRA in Detection of LTBI

- Both the standard qualitative test interpretation and the quantitative assay measurements should be reported, together with the criteria for test interpretation, which will permit more refined assessment of results and promote understanding of the tests.
**TEST PATIENT** 99999999/0 34 YEARS MALE

| COLLECTED: | 02/ 08/ 2010 00:00 | HOSPITAL X |
| RECEIVED: | 02/ 08/ 2010 | URGENT CARE CENTER |
| REPORTED: | 02/ 10/ 2010 | 2000 MAIN ST |
| 2010/ 0/ 14800/ 0/ 32026366 | CHANTILLY VA 20152 |

**PT PHONE #:**

<table>
<thead>
<tr>
<th>TESTS</th>
<th>RESULTS</th>
<th>FLAG</th>
<th>REF. RANGE</th>
<th>UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantiferon (R)-TB Gold ITM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantiferon</td>
<td>DETECTED *</td>
<td>(Not Detected)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td>0.43</td>
<td>IU/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitogen-Nil</td>
<td>&gt;10.00</td>
<td>IU/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB Ag-Nil</td>
<td>&gt;10.00</td>
<td>IU/MI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Nil value adjusts for patient sample background, heterophile antibody effects, or non-specific IFN. The Mitogen serves as a patient positive control. The result "Not Detected" or "Detected" is calculated from these values using an FDA-approved algorithm run on Quantiferon software.
T-SPOT.TB Method

BD Sodium Citrate Vacutainer® CPT™

BD Vacutainer® Lithium Heparin PST™

Greiner Bio-One Lithium Heparin Vacuette®
T-SPOT.TB Method

1. Collect the blood sample. At the lab, PBMCs are separated from whole blood, washed, counted and inoculated into 4 separate microtiter wells.

2. PBMCs [●] and specific TB antigens [ siti] are added to wells pre-coated with antibodies to IFN-γ [γ] and incubated 16 to 20 hours (37o C, CO2).
T-SPOT.TB Method

3. IFN-γ [●] is released from activated T cells and captured. Wash wells, add secondary conjugated antibody [●]. Incubate for one hour.

4. Wells are washed. A substrate is added which produces spots [●] where interferon gamma was secreted by T cells. Spots are counted.
Interpretation of T-SPOT.TB Results

Negative Result

Nil Control

ESAT-6 Panel A

CFP 10 Panel B

Positive Result

Positive Control
Interpretation of T-SPOT.TB Results

- Positive: Panel A–NIL and/or Panel B–NIL ≥8 spots
- Borderline (equivocal) when higher of Panel A–NIL or Panel B–NIL spot count is 5, 6, or 7; retesting by collecting another sample is recommended
- Negative if Panel A–NIL and/or Panel B–NIL ≤4 spots; includes values <0

Video on T-Spot
http://www.youtube.com/watch?v=QBB2rcDGjbg&NR=1
TST vs. QFT-IT vs. T-SPOT

Diagnosing Active TB compared to the Gold Standard:
Positive Smear and/or Positive Culture
Case Report

62 YO male hospital phlebotomist who underwent a routine employee QuantiFERON screening test. The QuantiFERON test was positive and patient was worked up by employee health nurse for TB. Chest x-ray showed infiltrate in right lung. Bronchoscopy was performed and samples collected for AFB studies. AFB smear was negative; however, culture was (+) for TB. Phlebotomist was removed from hospital duties and monitored by local county health department. Anti-TB medication was started and phlebotomist recovered uneventfully and returned to work. Subsequent county health department investigation revealed no TB transmission to other people/patients.
## Sensitivity of TST/IGRA Tests (Active TB Cases)

<table>
<thead>
<tr>
<th>Assay</th>
<th>Pooled Estimates</th>
<th>No. Studies</th>
<th>Mix Developed, Developing</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>70% (67-72%)</td>
<td>25</td>
<td>23, 2</td>
</tr>
<tr>
<td>QFT-IT</td>
<td>81% (78-83%)</td>
<td>19</td>
<td>13, 6</td>
</tr>
<tr>
<td>QFT-IT</td>
<td>84% (81-87%)</td>
<td>13</td>
<td>13, 0</td>
</tr>
<tr>
<td>QFT-IT</td>
<td>74% (69-79%)</td>
<td>6</td>
<td>0, 6</td>
</tr>
<tr>
<td>T-SPOT</td>
<td>87% (85-90%)</td>
<td>17</td>
<td>15, 2</td>
</tr>
</tbody>
</table>

Diel, Loddenkemper, Nienhaus, Chest 2010;137;952-968
## Sensitivity of TST/IGRA Tests (Active TB Cases)

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>QFT-IT</th>
<th>T-SPOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Children</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>2</td>
<td>Adults &amp; Children</td>
<td>79%</td>
<td>86%</td>
</tr>
<tr>
<td>3</td>
<td>Children</td>
<td>80%</td>
<td>56%</td>
</tr>
<tr>
<td>4</td>
<td>Adults</td>
<td>93%</td>
<td>62%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>84.3%</td>
<td>77.8%</td>
</tr>
</tbody>
</table>

*Note: Sensitivity values are based on patient counts of 91 and 84 patients for QFT-IT and T-SPOT, respectively.*

Diel, Loddenkemper, Nienhaus, Chest 2010;137;952-968
Specificity of TST/IGRA Tests
(Population in Low Incidence Area With No Known Exposure to TB)

<table>
<thead>
<tr>
<th>Assay</th>
<th>Pooled Estimates</th>
<th>No. of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>Not stated</td>
<td></td>
</tr>
<tr>
<td>QFT</td>
<td>99% (98-100%)</td>
<td>5</td>
</tr>
<tr>
<td>T-SPOT</td>
<td>86% (81-90%)</td>
<td>3</td>
</tr>
</tbody>
</table>

Note: T-SPOT Cut-off of ≥6 spots used
FDA cleared Pkg insert is ≥8
QFT-IT & T-SPOT Indeterminate Results

Host Factors

- Compromised immune status of test individual (ie, HIV CD4 counts <200 cells/mm³): QFT-IT
- Insufficient lymphocytes
- Inability of patient’s lymphocytes to generate gamma interferon
- Extremes of age (<5 and >80 years old)
- Lack of response to PHA by some individuals (<0.1%): QFT-IT
# Indeterminates: QFT-IT vs. T-SPOT

<table>
<thead>
<tr>
<th>Patients</th>
<th>QFT-IT</th>
<th>T-SPOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled</td>
<td>2.14</td>
<td>3.8</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>4.42</td>
<td>6.12</td>
</tr>
</tbody>
</table>

Diel, Loddenkemper, Nienhaus, Chest 2010;137;952-968
Gold Standard Test For Latent TB Infection?

Does not exist

The IGRAs are measuring a lasting TB immune response & not specifically latent/active TB
# TST versus IGRA Tests in Contacts (LTBI)

<table>
<thead>
<tr>
<th>TST Results (mm)</th>
<th>QFT % Pos.</th>
<th>T-SPOT % Pos</th>
<th>% Both Pos (No. discordant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-10</td>
<td>19.8</td>
<td>17.4</td>
<td>16.2</td>
</tr>
<tr>
<td>11-15</td>
<td>80.8</td>
<td>80.8</td>
<td>75.3</td>
</tr>
<tr>
<td>&gt;15</td>
<td>97.4</td>
<td>97.4</td>
<td>97.4 (0)</td>
</tr>
<tr>
<td>6-10</td>
<td>9.8</td>
<td>9.5</td>
<td>6.3</td>
</tr>
<tr>
<td>11-15</td>
<td>38.8</td>
<td>34.7</td>
<td>32.7</td>
</tr>
<tr>
<td>&gt;15</td>
<td>78.9</td>
<td>76.3</td>
<td>76.3 (1)</td>
</tr>
</tbody>
</table>

Overall agreement between both IGRA tests = 93.9 %

Diel et al. Chest 2009; 135;1010-1018
# Specificity of TST/IGRA (LTBI)

<table>
<thead>
<tr>
<th>Assay</th>
<th>All Studies</th>
<th>BCG-Vaccinated</th>
<th>Not Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>66% (46-86%)</td>
<td>56% (34-78%)</td>
<td>98% (96-100%)</td>
</tr>
<tr>
<td>QFT</td>
<td>97% (95-99%)</td>
<td>96% (93-99%)</td>
<td>100% (94-100%)</td>
</tr>
<tr>
<td>T-SPOT</td>
<td>92% (88-95%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Employee Services
Cost Analysis of TST vs QFT

- 76 employees (new and hospital employees)
  - TST +/QFT +: 14
  - TST +/QFT -: 17
  - TST -/QFT +: 0
  - TST-/QFT -: 45

- Cost/test
  - TST: $22
  - QFT: $45
  - Chest x-ray: $180
Cost Analysis of TST vs QFT

- Assume TST + gold standard:
  TST cost (76 x $22) $1,672
  Chest x-ray cost (31 x $180) $5,580
  Total cost $7,252

- Assume QFT + gold standard:
  QFT cost (76 x $45) $3,420
  Chest x-ray cost (17 x $180) $3,060
  Total cost $6,480

- Savings: $10.16 (per tested employee)
## DISCORDANT QFT RESULTS
### HIV PATIENT
(What is the correct result?)

### Results (IU/mL)

<table>
<thead>
<tr>
<th>Date</th>
<th>Nil</th>
<th>Mitogen Nil</th>
<th>TB Ag-Nil</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/25/09</td>
<td>0.35</td>
<td>&gt;10</td>
<td>0.09</td>
<td>Negative</td>
</tr>
<tr>
<td>4/28/10</td>
<td>0.25</td>
<td>&gt;10</td>
<td>0.510</td>
<td>Positive</td>
</tr>
<tr>
<td>5/17/10</td>
<td>0.480</td>
<td>&gt;10</td>
<td>0.310</td>
<td>Negative</td>
</tr>
</tbody>
</table>

(+ = TB Ag-Nil ≥ 0.35 IU/mL)
QFT Results in Serial Testing of HCWs

$P < 0.001$

- Persistently positive
- Reversion
- Conversion
- Persistently negative

Baseline IFN-γ (IU/ml)

Baseline and follow-up QFT-GIT results
# Comparison of IGRAs

<table>
<thead>
<tr>
<th>Property</th>
<th>QFT</th>
<th>T-SPOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA cleared</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Draw to process time</td>
<td>&lt;16 h</td>
<td>&lt;8 h*</td>
</tr>
<tr>
<td>Vendor-supplied transport tubes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Technically complex</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Potential advantage in patients with low PBMC</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*32 hours, if use T-Cell Xtend Reagent (not FDA-cleared)
Advantages of IGRAs

- Requires single patient visit
- Results available within 24 h
- Not subject to reader interpretation
- Not affected by prior BCG vaccination
- May reduce number of X-rays
- May reduce INH usage and resulting liver toxicity
- More sensitive and specific than TST

MMWR, 59,RR-5, June 25, 2010
Disadvantages of IGRAs

- Blood samples must be processed within 16 h (QFT) or within 8/32 h (TB-Spot) after draw
- QFT needs vendor-supplied transport tubes
- T-Spot technically complex
- Don’t differentiate between active/latent TB
- Limited data in
  - Children
  - Immunocompromised (AIDS, etc.)—not recommended for routine use in HIV pediatric patients (MMWR, 2009, 58, (RR11: 1-166))
Questions?

- Press *1 on your telephone keypad to speak with the presenters live

  OR

- Use the chat feature to send your question to the host
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