Testing & Treatment for TB Infection: Blood Tests, Skin Tests, Who to Screen & Who to Treat?

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Disclosures

• Grant Funding
  – USAID AMPATH, CFAR

• Boards
  – Immediate Past President, The Union (Paris, France)
  – Vital Strategies (NYC, NY)

• Committees
  – Advisory Panel -TB Modeling and Analysis Consortium
  – Global Fund- Committee on Tuberculosis
  – Proposal Review Committee, TB Reach, UNOPS, Geneva

• Consulting
  – Consultant, Global TB Institute, New Jersey, USA
  – Consultant, JSI: Project – Linking Primary Care Sites to TB Control in Massachusetts (Completed May 2015)

• No financial relationship with a commercial entity producing health-care related products and/or services as well as no tobacco related associations.
Outline

• 2 Cases- Not college students but useful to understand concepts
• TB Epidemiology
• Targeted Testing Recommendations
  – TB Infection Testing Options
  – IGRA (Interferon Gamma Release Assays) Operation Characteristics
  – National TB Controllers (Draft) Guidelines for Interpretation
• TB Treatment Options
• Circle back to the Cases
Case 1

• 44 yo F born in the US (RI)
• JRA since age 8- now on Humira for 3 years
  – All past TST have been negative
• Works as RT in a local hospital
• Routine visit to Rheum
  • 6 weeks earlier she remembered caring for someone “coughing a lot” (out of the ordinary)
    – Patient was not diagnosed with TB during hospital stay- not part of a contact investigation
  • Sent for a Quantiferon Gold test
    – Reported as “positive”
Case 2

• 74 yo F
• September jaw pain – treated with short course of steroids
• October started having fevers and night sweats
• Total body scanning – Abd/pelvis normal; Chest thickening of the walls of aorta/brachiocephalic and carotids c/w arteritis
• Developed SOB – echo reveals a small effusion
• Quantiferon gold ordered- reported “negative”
Global TB Burden

• 1/3 of the world’s population is infected
• 8-9 million cases of TB disease registered/year
• 2 million deaths/year
  – In 2014 TB became the leading cause of death from an infectious disease
  – Leading cause of death in those living with HIV/AIDS
  – Leading cause of death in women of child-bearing years
  – 1/6 Tb cases will die
  – 1/3 of Tb cases globally not diagnosed or not reported
• Worldwide a new infection occurs once/second
Reported TB Cases
United States, 1982–2014*

*Updated as of June 5, 2015.
Tuberculosis

• Important on a global scale
• Important locally?
  – If we really want to get to TB elimination, it has to stay on the radar screen
  – TB disease when it does happen, causes a lot of work and costs a lot of money
    • Contact investigations: One index case at a local hospital led to 739 contacts, 49% of whom were reported as evaluated for TB
    • Patients have been hospitalized for months when appropriate housing not available
  – While we are in a low incidence setting, we do a lot of worrying
    • Isolation rooms: TMH range from 2-7 per month for the last 8 months
    • And a lot of screening...
      – 400 Quantiferon gold tests done each month in the Lifespan system
Reported TB Cases
United States, 1982–2014*

*Updated as of June 5, 2015.
Bayes Theorem

- Sensitivity and specificity of the available tests are inherent in the tests
- However, the positive and negative predictive values are inherent in the population on whom the tests are used
- Therefore, all tests are more accurate when used on those with a high index of suspicion
  - epidemiology risk = targeted testing
Why Screen for LTBI?

• Critical to the strategy to eliminate TB

• Patient benefit
  – Simpler regimen than active TB
  – Avoids long term complications of TB disease (lung destruction as the most common)

• Societal benefit
  – Treats patient prior to their becoming contagious
  – Transmission is therefore avoided
Who do we target to screen?

**Persons at increased risk for infection**

- Close contacts of infectious cases
- Foreign born from TB endemic areas
- Residents and employees of high risk congregate settings
- HCWers exposed to active TB patients
- Locally epidemiological populations with increased TB risk
- Some elderly growing up in an era of high prevalence

**Persons at increased risk for progression who may not have increased exposure risk**

- HIV/AIDS
- Persons being considered for immunosuppressive /modulating therapy
  - TNF alpha antagonists
  - Systemic Steroids >15mg per day
  - Immune suppression following organ transplantation
- Pre-transplantation
- Silicosis
- End Stage Disease
- Diabetes (Not a clear US recommendation)
Who do we target to screen for college matriculation?

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Persons at increased risk for progression who may not have increased exposure risk

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- Pre-transplantation
- Silicosis
- End Stage Disease
- Diabetes (Not a clear US recommendation)
Foreign born from TB endemic areas

• Easier to think of the exclusion criteria than to list every high burden country
• Exclusions: Canada, Australia and New Zealand, Counties of Western Europe
What tests are available?

<table>
<thead>
<tr>
<th>Tuberculin Skin Tests</th>
<th>Blood Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUBERSOL® (Tuberculin Purified Protein Derivative) - Mantoux – Sanofi Pasteur, Canada</td>
<td>QuantiFERON-TB Gold In-Tube (QFT-GIT) – Cellestis Limited, Carnegie, Australia – now Qiagen, Hilden Germany</td>
</tr>
<tr>
<td>Aplisol (Tuberculin Purified Protein Derivative) – JHP Pharmaceuticals LLC</td>
<td>T-SPOT.TB – Oxford Immunotec, Abingdon, United Kingdom</td>
</tr>
</tbody>
</table>
# Tuberculin Skin Tests

<table>
<thead>
<tr>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Test materials are relatively inexpensive</td>
<td>• Cannot be used to diagnose or rule out active TB</td>
</tr>
<tr>
<td>• Does not require a laboratory</td>
<td>• Requires 2 visits (to apply test and read results)</td>
</tr>
<tr>
<td>• Does not require transportation of viable samples</td>
<td>• Patient compliance can be a problem</td>
</tr>
<tr>
<td>• Well studied and public health familiarity</td>
<td>• Placement, reading and interpretation of the result is subject to human error</td>
</tr>
<tr>
<td>• Recommended for children under 5</td>
<td>• Three cut points may cause confusion</td>
</tr>
<tr>
<td></td>
<td>• False-positive tests may occur (in BCG-vaccinated persons and non-tuberculous mycobacteria (NTM) infection)</td>
</tr>
<tr>
<td></td>
<td>• Establishing baseline for serial testing may require a two-step TST (4 visits)</td>
</tr>
<tr>
<td></td>
<td>• Test variability, particularly in low-risk populations</td>
</tr>
</tbody>
</table>
# IGRA
Interferon Gamma Release Assays

<table>
<thead>
<tr>
<th><strong>Pro</strong></th>
<th><strong>Con</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Require a single encounter**</td>
<td>• Cannot be used to diagnose or rule out active TB</td>
</tr>
<tr>
<td>• No cross reaction with BCG-vaccine and <em>most</em> NTMs</td>
<td>• Relatively expensive</td>
</tr>
<tr>
<td>• May have better acceptance of the results in some populations</td>
<td>• Requires phlebotomy</td>
</tr>
<tr>
<td>• Standardized laboratory test with controls</td>
<td>• Requires a laboratory that performs the test</td>
</tr>
<tr>
<td>• “Objective” results</td>
<td>• Requires specific specimen collection, handling, transport and laboratory processing</td>
</tr>
<tr>
<td></td>
<td>– Leading to false positive or false negative results</td>
</tr>
<tr>
<td></td>
<td>• Test variability, particularly in low-risk populations</td>
</tr>
</tbody>
</table>
Tuberculin Skin Testing

• Test characteristics
  – TST is “planted”
  – Size Measurement of the induration is recorded at 48-72 hours

• Test interpretation
  Epidemiologic risk assessment
  Three cutoffs – 5, 10, 15 mm
## Species Specificity of ESAT-6 and CFP-10

<table>
<thead>
<tr>
<th>Tuberculosis complex</th>
<th>Antigens</th>
<th>Environmental strains</th>
<th>Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ESAT</td>
<td>CFP</td>
<td></td>
</tr>
<tr>
<td><strong>M tuberculosis</strong></td>
<td>+</td>
<td>+</td>
<td>M abcessus</td>
</tr>
<tr>
<td><strong>M africanum</strong></td>
<td>+</td>
<td>+</td>
<td>M avium</td>
</tr>
<tr>
<td><strong>M bovis</strong></td>
<td>+</td>
<td>+</td>
<td>M branderi</td>
</tr>
<tr>
<td>BCG substrain</td>
<td></td>
<td></td>
<td>M celatum</td>
</tr>
<tr>
<td>gothenburg</td>
<td>-</td>
<td>-</td>
<td>M cheloneae</td>
</tr>
<tr>
<td>moreau</td>
<td>-</td>
<td>-</td>
<td>M fortuitum</td>
</tr>
<tr>
<td>tice</td>
<td>-</td>
<td>-</td>
<td>M gordonii</td>
</tr>
<tr>
<td>tokyo</td>
<td>-</td>
<td>-</td>
<td>M intracellulare</td>
</tr>
<tr>
<td>danish</td>
<td>-</td>
<td>-</td>
<td><strong>M kansasii</strong></td>
</tr>
<tr>
<td>glaxo</td>
<td>-</td>
<td>-</td>
<td>M malmoense</td>
</tr>
<tr>
<td>montreal</td>
<td>-</td>
<td>-</td>
<td><strong>M marinum</strong></td>
</tr>
<tr>
<td>pasteur</td>
<td>-</td>
<td>-</td>
<td>M oenavense</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M scrofulaceum</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M smegmatis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>M szulgai</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M terrae</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M vaccae</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M xenopi</td>
</tr>
</tbody>
</table>
Two types of IGRA

- **T-spot**
  - Elispot
  - Measures Interferon Gamma per stimulated T cell

- **Quantiferon Gold**
  - Elisa
  - Measures total Interferon Gamma produced by stimulated T cells
Stage One – Blood Incubation and Harvesting

1. Collect 1mL of blood (X3). Incubate at 37ºC for 16-24 hrs.

2. Centrifuge tubes for 5 minutes.

IFN-γ stable refrigerated for at least 4 weeks.

Stage Two – Human IFN-γ ELISA

3. Add plasma and conjugate to ELISA plate. Incubate for 120 minutes at Room Temperature.

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

5. Software calculates results and prints report.
Test variability

**Pre-analytical**
- Manufacturing issues
- Improper storage of tubes
- Time of day of draw
- Inadequate cleansing of the skin
- Improper blood volume
- Variability in mixing of Ag/mitogen (shaking issue)
- Specimen temp and transport time to processing (even within the manufacturer’s specification)

**Analytical**
- Imprecise pipetting
- Variable incubation times and temps (even within the manufacturer’s specification)
- Within Assay variability
Effect of Shaking on TB Response

Panel A: Nil (IU/ml) vs. Shaking (Gentle vs. Vigorous). P < 0.001.

Panel B: TB Ag (IU/ml) vs. Shaking (Gentle vs. Vigorous). P = 0.004.

Panel C: TBAg-Nil (IU/ml) vs. Shaking (TBAg_Gen - Nil_Gen vs. TBAg_Vig - Nil_Vig). P = 0.35.

Panel D: TBAg-Nil (IU/ml) vs. Shaking (TBAg_Gen - Nil_Gen vs. TBAg_Vig - Nil_Vig). P = 0.004.

Gaur et al JCM 2013
For those in the audience planning a large employee screening program, here is something to think about........

• Stanford Experience
• > 10,000 TST per year so went to IGRA immediately
• Ongoing Quality Assessment Program required

Niaz Banaei
Stanford QFT-GIT Surveillance Graph Showing Daily Positive Rate

Elevated rate noted

TBAg lot discontinued

Niaz Banaei
J Clin Micro 2012 (50)9:3105
How are the IGRA results reported?

• Three tubes
  – TB Nil (Control to verify that the immune system is not overproducing Interferon gamma)
    • Must be < 8 IU/ml
  – TB Mitogen (Control to verify that the immune system can work and produce interferon Gamma)
  – Tb Antigen (The test to see if the patient produces interferon gamma against TB antigens)
    • TB Antigen – TB Nil must be > 0.35 IU/ml
How are the Quantiferon results reported?

<table>
<thead>
<tr>
<th>Quantitative</th>
<th>Qualitative</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nil</td>
<td>• Positive</td>
</tr>
<tr>
<td>• TB Antigen</td>
<td>• Negative</td>
</tr>
<tr>
<td>• Mitogen</td>
<td>• Indeterminate</td>
</tr>
<tr>
<td>• TB Antigen minus Nil</td>
<td></td>
</tr>
<tr>
<td>– &gt;0.35 IU/ml defines positivity</td>
<td></td>
</tr>
<tr>
<td>• Mitogen minus Nil</td>
<td></td>
</tr>
</tbody>
</table>

Per CDC guidelines, lab should report the qualitative test interpretation, the quantitative assay measurements and the criteria for test interpretation. MMWR 2010/ Vol. 59/no RR 5
What are the causes of an indeterminate test?

Qualitative

• Positive
• Indeterminate

Patient Factors:
Compromised immune state
Age < 2 years
Certain immunosuppressive drugs
(TNF alpha blockers and immunomodulators)
Immunosuppressant conditions
HIV, Cancer, post transplant
Recent live viral vaccination

Specimen /laboratory factors:
Transportation or storage outside of recommended range
Improper incubation,
**Insufficient mixing of the blood collection tubes**
Compromised Mitogens
What to do with an indeterminate test?

• This is where you need to look at the numbers
  – A high Nil (>8.0), irrespective of the TB Antigen results, suggests an error with the Negative control- You can repeat the Quantiferon
  – A low mitogen control (<0.5) in the absence of a TB antigen response suggests a problem with the patient’s immune system- here is where you have to return to the patient’s epidemiologic risk history.
Does Boosting occur with IGRA?

• Boosting- remember this has to do with cell memory......

• Drawing an IGRA does not cause the results of a subsequent TST or IGRA

• Placement of a TST > 72 hours prior to the IGRA can affect the IGRA for up to 6 months (usually low positive but.........)
Can treatment for TB infection (or disease) impact (meaning revert) the test?

- NO
- NO
- NO
- NO

- Do not draw an IGRA (or perform a TST) to see if treatment was sufficient in the past
- If a patient has been treated in the past (and need to be in a screening program such as a HCW), they do NOT NEED either a TST or a IGRA but rather a symptoms screen checklist.
Are there times when the IGRA should be repeated?

• Repeating the IGRA may be useful when the initial IGRA is
  – Indeterminate
  – Low positive (0.35-1.0 IU/ml)
    • In low risk individuals, repeat testing reverts to negative 70% of the time
  – An unexpected positive or negative result
    • In low risk individuals, repeating the QTF will increase specificity of the testing (2 negatives, 99% accuracy)
When should a patient have both an IGRA and a TST?

• Use of both tests may increase sensitivity for Tb infection and therefore might be considered in patients at high risk of TB infection and progression or for poor outcome (HIV infected, children < 2 years of age)

• In situations where use of both may enhance compliance with LTBI treatment
  – Typical scenario is someone (usually BCG vaccinated and/or a HCW) with a +TST who asks for an IGRA before considering treatment

• Retesting with a TST post an indeterminate IGRA test is NOT recommended
What should I do if my patient has discordant results from different types of tests for TB infection?

• Very careful consideration should be done prior to using a second test or second testing method.

• A second test should **NOT** be done to search for the answer that you wanted. **This is NOT an indication for a different test.**

• Best advice- try to stay away from the situation in the first place- don’t switch tests when you are confused by ( or just unhappy with) the first test!
  – Don’t enter the shark pool without thinking about it first!
<table>
<thead>
<tr>
<th>IGRA</th>
<th>TST</th>
<th>Risk for Progression (refer to definitions of High and Low on page “5”)</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive or Borderline</td>
<td>Unknown/not done</td>
<td>High</td>
<td>Consider the individual infected with <em>M. tuberculosis</em> and treat accordingly</td>
<td>Low positive: Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. (see section xxx) Borderline: Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample.</td>
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<td></td>
<td></td>
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<td></td>
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<td>-------------------------------------------------------------------------</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Low</td>
<td>Consider testing with an IGRA to increase specificity, especially if the patient is likely BCG-vaccinated or likely infected with an NTM</td>
<td>In individuals who are BCG-vaccinated, testing with an IGRA offers increased specificity over testing with the TST. In US-born individuals, there is no data to suggest increased utility of one test over the other.</td>
</tr>
<tr>
<td>Positive or Borderline</td>
<td></td>
<td>High</td>
<td>Consider the individual infected with <em>M. tuberculosis</em> and treat accordingly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>Low</td>
<td>Consider repeating the IGRA as soon as feasible, especially if low positive (QFT) or borderline (T-Spot). If repeat test negative, treat first IGRA as a false positive. If a first IGRA is NOT low positive or if second IGRA is positive on retesting, consider the individual infected with <em>M. tuberculosis</em> and treat accordingly</td>
<td>Low positive: Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. Borderline: Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample.</td>
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<td>------------</td>
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<td>---------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Positive or Borderline</td>
<td>Positive</td>
<td>High</td>
<td>Individuals who test positive by both tests can be considered as infected with ( M. tuberculosis ) and should be treated accordingly</td>
<td>Low positive: Data suggests low risk individuals with QFT results in the 0.35 to 1.0 IU/ml range show a high rate of reversion to negative upon retesting. Low-risk Individuals with test results in this range should be retested. Borderline: Borderline results are clinically meaningful and should be followed up by retesting through collection of another sample.</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Low</td>
<td>Consider repeating the IGRA as soon as feasible if low positive (QFT) as boosting effects and variability or borderline (T-Spot).</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>High</td>
<td>The greater likelihood is the individual can be considered not to be infected with ( M. tuberculosis ). Patients with signs, symptoms or radiographic evidence of infection may undergo further evaluation despite negative TST/IGRA.</td>
<td>Children &lt; 5 years of age who are part of a contact investigation who are screening test/exam/radiographically negative should receive window prophylaxis until the test can be repeated 8-10 weeks after break in contact.</td>
</tr>
<tr>
<td>IGRA</td>
<td>TST</td>
<td>Risk for Progression</td>
<td>Recommendation</td>
<td>Comments</td>
</tr>
<tr>
<td>-------</td>
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<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>Consider the individual potentially infected with <em>M. tuberculosis</em> and treat accordingly based on clinical assessment weighing the risk/benefit of treatment vs. non-treatment. If BCG-vaccinated, may be false positive TST.</td>
<td>In individuals who are BCG-vaccinated, testing with an IGRA offers increased specificity over testing with the TST.</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>Low</td>
<td>The individual can be considered not to be infected with <em>M. tuberculosis</em></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td>Low</td>
<td>Document that the TST is likely a false-positive and act on the IGRA result. Recommend that the individual be tested with an IGRA for future testing.</td>
<td></td>
</tr>
</tbody>
</table>
How are unexpected results best addressed?

- **Unexpected Positive Results:**
  - Healthy individuals
    - Most will be a false positive
    - Assure no symptoms and then repeat
      - If TST, do TST or IGRA
      - If IGRA, do an IGRA
      - If 2\(^{nd}\) test +, treat as +
      - If 2\(^{nd}\) test -, nothing further done (including a CXR - don’t do it!)
  - Individuals with Risk Factors for progression
    - Moderate Risk – same as above unless local epi suggests differently
    - High Risk – back to weighing risk and benefits
Treatment of Latent TB Infection
Intent to screen should be coupled with intention to treat
### Recommended Regimens for Treatment of LTBI

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration</th>
<th>Notes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INH</strong></td>
<td>9 m qd</td>
<td>A (II)</td>
<td>A (II)</td>
</tr>
<tr>
<td></td>
<td>9 m 2x/wk</td>
<td>B (II)</td>
<td>B (II)</td>
</tr>
<tr>
<td><strong>INH</strong></td>
<td>6 m qd</td>
<td>B (I)</td>
<td>C (I)</td>
</tr>
<tr>
<td></td>
<td>6 m 2x/wk</td>
<td>B (II)</td>
<td>C (I)</td>
</tr>
<tr>
<td><strong>Rif</strong></td>
<td>4 m qd</td>
<td>B (II)</td>
<td>B (III)</td>
</tr>
<tr>
<td><strong>INH+ Rifapentine</strong></td>
<td>12 doses</td>
<td>B (I)*</td>
<td>B (I)*</td>
</tr>
<tr>
<td></td>
<td>1x/wk DOT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treatment Issues

• Side Effect Monitoring
  – INH or RIF- Hepatitis rates low, particularly in a young population
  – Rif or Rifapentine- Drug Drug Interactions and red secretions
  – 3HP regimen- nausea, Immunologic Side Effect monitoring prior to next dose

• Adherence Monitoring
  – Number of doses is what matters
  – Clear documentation of treatment at end of therapy
Case 1

- 44 yo F born in the US (RI)
- JRA since age 8- now on Humira for 2-3 years
  - All past TST have been negative
- Works as RT in a local hospital
- Routine visit to Rheum
  - 6 weeks earlier she remembered caring for someone “coughing a lot” (out of the ordinary)
    - Patient was not diagnosed with TB during hospital stay- not part of a contact investigation
  - Sent for a Quantiferon Gold test
    - Reported as “positive”
Case 1

• She went to employee health where another TST was planted (but they decided not to read it….Patient said it was “negative” and looked like it always had)
• She then went to the ER where a CXR was done
• CXR abnormal so was taken out of work
  – Friday afternoon
• Pulmonary consult
Case 1

• Call to DOH - no infectious cases diagnosed during the time period of interest
• Extensive questioning – no epi risk
  – No travel
  – No one ill in family
  – No exposures
• CXR findings – benign Thymic cyst
• Her Quantiferon report only gave the qualitative results
IGRA testing

<table>
<thead>
<tr>
<th>#1</th>
<th>#2</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Nil</td>
<td>TB Nil</td>
</tr>
<tr>
<td>0.03</td>
<td>0.006</td>
</tr>
<tr>
<td>TB Mitogen</td>
<td>TB Mitogen</td>
</tr>
<tr>
<td>18.19</td>
<td>&lt;10</td>
</tr>
<tr>
<td>TB Antigen</td>
<td>TB Antigen</td>
</tr>
<tr>
<td>0.43</td>
<td>0.03</td>
</tr>
</tbody>
</table>

No epidemiologic risk
Negative repeat testing with the same test

Patient deemed not infected at this time
Cleared to restart her humira and to return to work

2 ½ weeks out of work
2 IGRA
CXR, CT, MRI
Pulmonary consult
Case 2

- 74 yo F
- September jaw pain – treated with short course of steroids
- October started having fevers and night sweats
- Total body scanning – Abd/pelvis normal; Chest thickening of the walls of aorta/brachiocephalic and carotids c/w arteritis
- Developed SOB – echo reveals a small effusion
- Quantiferon gold ordered- reported “negative”
Case 2  -  TB history

• Born in Iceland
• At age 10, her aunt and her GF died of TB
• She was thought to have TB and placed at bed rest for months
• She became a nurse and worked in the last TB sanitarium in Iceland until it was closed.
• On coming to the US, she worked in a hospital in NYC
• TST there was very large and she was told not to have TST testing again (Never treated)
Case 2

• Quantiferon Gold: Negative
  – TB Nil 0.120 IU/ml
  – Mitogen 0.544 IU/ml
  – TB Antigen 0.134 IU/ml

• Treated with INH and Rifampin
  – Unable to rule out active disease causing her pericardial effusion
  – Going on steroids for ?PMR
Is a blood test “better”? 

- IGRA has more specificity than TST (takes out the noise from BCG and most NTMS) 
- Both tests have performance limitations 
- Both tests, when applied in a low incidence setting, will have false positives 
- Not a better test, just a different test 
- We still need a better test
Intent to screen should be coupled with intention to THINK

......about the TB history, the pretest probability of TB infection, about the inherent limitations and variability of the test you are using, etc, etc etc
Can you imagine a world without TB? We can.

National TB Controllers Association
http://www.tbcontrollers.org

TB Global Institute
Medical Consultation Line
1-800-4 TB DOCS (1-800-482-3627)

Questions?