Understanding IGRA Results
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TB and Newcomer Health Program
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Objectives
The Participant will:

• Understand that IGRA testing results depend on a functioning immune system
• Be able to state the role of IGRA testing in evaluation for TB disease
• Be able to evaluate numerical results of IGRA to better understand the meaning of test results

What is an IGRA?

• IGRA
  • Interferon gamma release assay
  • Blood test for TB infection
  • Can be used interchangeably with TST
• Two IGRA approved by FDA in the U.S.
  • QuantiFERON-TB Gold-in-Tube by Qiagen
  • T-Spot.TB by Oxford Immunotec
Does your health district use IGRA testing?

1. Yes 33%
2. No 33%
3. Sometimes, in selected cases 33%

In what situations does your health district use IGRA testing?

1. Refugee testing only 20%
2. For all testing for TB infection 20%
3. Only if the TB/Newcomer program pays for the testing 20%
4. For selected contacts only 20%
5. Other 20%

Which IGRA is used in your health district?

1. T-Spot 33%
2. QuantiFERON 33%
3. Don’t know 33%
What is an IGRA?

A blood test that:
- Measures production of interferon gamma after exposure to TB antigens
- Reflects prior contact with *M. tuberculosis* and a few other Mycobacteria
  - *M. kansasi*
  - *M. marinum*
  - *M. sulgai*
  - *M. fulvacin*
- Does not cross react with BCG vaccine

An IGRA is Only a Tool

- Depends on a functioning immune system
- Measure different aspects of the immune response
- Because different tests use different antigens and interpretation criteria, TEST RESULTS MIGHT NOT BE INTERCHANGEABLE!

An IGRA tests for...

1. TB disease
2. The degree of infectiousness of a TB case
3. TB infection
4. Latent TB infection
TB Suspect Evaluation

- Test for TB infection
- Symptom review
- History, including
  - Past history of test for TB infection
  - Past treatment for TB infection or disease
  - Risks for possible TB exposure
  - Risk for progression to disease
- Chest X-ray or Chest CT

TST vs. IGRA

<table>
<thead>
<tr>
<th>TST</th>
<th>IGRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheaper</td>
<td>More expensive</td>
</tr>
<tr>
<td>Two visits</td>
<td>One visit</td>
</tr>
<tr>
<td>BCG cross reaction</td>
<td>No reaction to BCG</td>
</tr>
<tr>
<td>Record keeping harder</td>
<td>Record keeping easier</td>
</tr>
<tr>
<td>More subjective</td>
<td>QA moved to lab</td>
</tr>
<tr>
<td>Administration</td>
<td></td>
</tr>
<tr>
<td>Reading/interpretation</td>
<td></td>
</tr>
</tbody>
</table>

The Two IGRAs – QuantiFERON Gold-in-Tube

- Three tubes of blood collected
- Mitogen – positive control
- Antigen – response to TB antigen
- Nil – negative control
- Filled exactly to 1 ml and shaken vigorously, 5 sec.
- Incubation within 16 hours
- QA divided between draw site, incubation location and lab
The Two IGRAs – T-Spot.TB

- One or two lithium heparin tubes collected
- Shipped to Oxford Labs via FedEx
- Incubated within 32 hours
- Most of QA is in the lab

QFN vs. T-Spot

QFN
- Incubate in 16 hrs.
- Special tubes required
- Can be incubated on site
- Training for phlebotomy
- QA spread from draw to lab processing

T-Spot
- Incubate in 32 hrs.
- Generic tubes used
- No incubation on site
- No special training for phlebotomy
- QA in the lab

CDC Recommends...

- IGRA used in place of (but not in addition to) a TST in all situations where CDC recommends TST
- IGRA preferred but TST acceptable:
  - BCG vaccine recipients
  - Pops. with low rate of return (SA, homeless)
- TST preferred but IGRA acceptable:
  - Children < 5 yrs.
Interpretation of QFN

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>QFN</th>
<th>TB Response</th>
<th>Nilogen Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>-</td>
<td>-</td>
<td>Any</td>
</tr>
<tr>
<td>0.3-0.55</td>
<td>+</td>
<td>+</td>
<td>&lt;3</td>
</tr>
<tr>
<td>0.56-0.85</td>
<td>++</td>
<td>++</td>
<td>+2</td>
</tr>
<tr>
<td>&gt;0.85</td>
<td>+3</td>
<td>+3</td>
<td>Any</td>
</tr>
</tbody>
</table>

TB Response = TB Antigen - Nil

QFN Positive Result – Case 1

QFN Positive Result – Case 2
QFN Indeterminate - Case 3

- First QFN
  - Nil 0.03, Mitogen 0.06, TB Response <0.0
  - Result indeterminate
- Second QFN 11 days later
  - Nil 0.04, Mitogen 0.07, TB Response 0.02
  - Result indeterminate
- Workplace was demanding a C x-ray

QFN Indeterminate - Case 4

Interpretation of T-Spot.TB

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>MT*</th>
<th>TB Reaction</th>
<th>Mitogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive**</td>
<td>&lt;3 spots</td>
<td>0, 1, or 2 spots</td>
<td>0, 1</td>
</tr>
<tr>
<td>Negative**</td>
<td>&gt;3 spots</td>
<td>0, 1, or 2 spots</td>
<td>0, 1</td>
</tr>
<tr>
<td>Indeterminate**</td>
<td>3 or 4 spots</td>
<td>0, 1, or 2 spots</td>
<td>0, 1</td>
</tr>
<tr>
<td>Intermediate**</td>
<td>&gt;3 spots</td>
<td>0, 1, or 2 spots</td>
<td>0, 1</td>
</tr>
</tbody>
</table>
T-Spot Negative Result – Case 1

T-Spot Negative Result

Case 1

T-Spot Positive Result – Case 2

T-Spot Positive Result

Case 2

T-Spot Positive Result – Case 3

T-Spot Positive Result

Case 3
T-Spot Invalid? – Case 4

- Possible Causes of High Mitogen Results
  - Malnutrition
  - Exposed to significant radiation
  - Methotrexate or interferon Rx
  - Live viral vaccines within 6 weeks
  - Occasionally in pregnancy
  - Some auto-immune conditions

A Challenge

- Recognize that IGRAs are only one tool
- Read the result – negative, positive, etc.
- Look at the numbers!
- Please share any unusual findings!!!
Questions??