

Understanding IGRA Results

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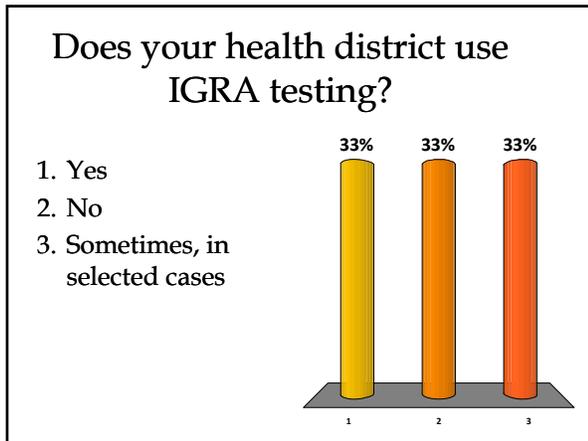
Objectives

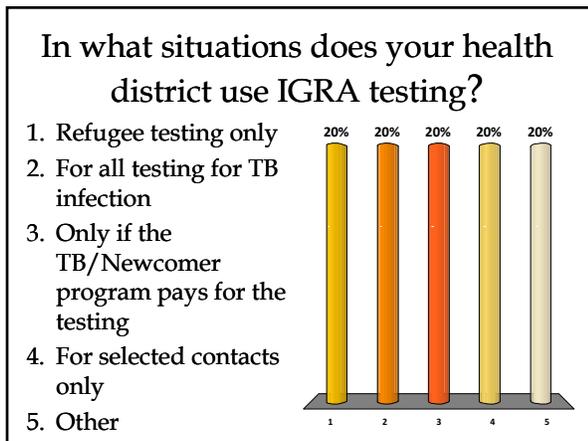
The Participant will:

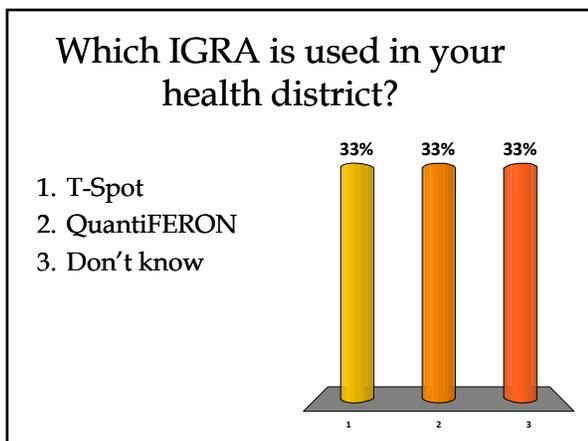
- Understand that IGRA testing results depend on a functioning immune system
- Be able to state the role of IGRA testing in evaluation for TB disease
- Be able to evaluate numerical results of IGRAs to better understand the meaning of test results

What is an IGRA?

- IGRA
 - Interferon gamma release assay
 - Blood test for TB infection
 - Can be used interchangeably with TST
- Two IGRAs approved by FDA in the U.S.
 - QuantiFERON-TB Gold-in-Tube by Qiagen
 - T-Spot.TB by Oxford Immunotec







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. kansasii*
 - *M. marinum*
 - *M. sulgai*
 - *M. fortuitum*
- Does *not* cross react with BCG vaccine

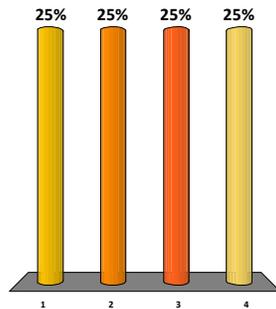
An IGRA is Only a Tool

- 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

TST

- Cheaper
- Two visits
- BCG cross reaction
- Record keeping harder
- More subjective
 - Administration
 - Reading/interpretation

IGRA

- More expensive
- One visit
- No reaction to BCG
- Record keeping easier
- QA moved to lab

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 2. Interpretation criteria for the QuantiFERON-TB Gold In-Tube Test (QFT-GIT)

Interpretation	NI*	TB Response ¹	Nitrogen Response ²
Positive ³	≤8.0	≥0.35 IU/ml and ≥25% of NI	Any
Negative**	≤8.0	<0.35 IU/ml or <25% of NI	≥0.5
Indeterminate ¹	≤8.0	<0.35 IU/ml or <25% of NI	<0.5
	>8.0	Any	Any

TB Response=TB Antigen - Nil

QFN Positive Result - Case 1

TEST	RESULT	UNIT	REFERENCE INTERVAL	LAB
QUANTIFERON TB Gold (In Tube)				
QUANTIFERON incubation				01
Specimen incubated at LabCorp, Burlington, NC				
QUANTIFERON TB Gold	Positive Abnormal		Negative	01
QFT Positive Criteria				01
To be considered positive a specimen should have a TB Ag minus Nil value greater than or equal to 0.35 IU/ml and in addition the TB Ag value must be greater than or equal to 25% of the Nil value. There may be insufficient information in these values to differentiate between some positive and some indeterminate test values.				
QUANTIFERON TB Ag Value	>10.00	IU/mL		01
QUANTIFERON Nil Value	1.60	IU/mL		01
QUANTIFERON Nitrogen Value	>10.00	IU/mL		01
QFT TB Ag minus Nil Value	>10.00	IU/mL		01
Interpretation:				01

QFN Positive Result - Case 2

TEST	RESULT	UNIT	REFERENCE INTERVAL	LAB
QUANTIFERON TB Gold (In Tube)				
QUANTIFERON incubation				01
Specimen incubated at LabCorp, Burlington, NC				
QUANTIFERON TB Gold	Positive Abnormal		Negative	01
QUANTIFERON criteria				01
To be considered positive a specimen should have a TB Ag minus Nil value greater than or equal to 0.35 IU/ml and in addition the TB Ag minus Nil value must be greater than or equal to 25% of the Nil value. There may be insufficient information in these values to differentiate between some positive and some indeterminate test values.				
QUANTIFERON TB Ag Value	1.91	IU/mL		01
QUANTIFERON Nil Value	0.34	IU/mL		01
QUANTIFERON Nitrogen Value	>10.00	IU/mL		01
QFT TB Ag minus Nil Value	1.57	IU/mL		01

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

NAME	VALUE	REF RANGE
QuantiferON Inhibition - Substrate, mycobacterin, isoniazid, rifampin, 3H in complex of raw agar.		
QuantiferON TB Gold	Indeterminate	▲ Negative
- Always positive unless you are negative. - This test indicates degree of immune responsiveness. Early onset and accurate result time may occur in low positive control and indeterminate results.		
QuantiferON Gold - To be considered positive a specimen should have a TB Ag index >1.1 - Valid result if time of test is 0-90 mins. Use to justify the TB Ag index. There may be insufficient information to show values in order to justify a result more sensitive and more informative test. - Values:		
QuantiferON TB Ag Value	0.10	IU/mL
QuantiferON Mit Value	0.10	IU/mL
QuantiferON Mitogen Value	0.54	IU/mL
QFT TB Ag Mitogen Nil Value	0.00	IU/mL
Interpretation:		

Interpretation of T-Spot.TB

TABLE 3. Interpretation criteria for the T-SPOT.TB Test (T-Spot)

Interpretation	Nil*	TB Response ¹	Mitogen ¹
Positive ²	≥10 spots	≥8 spots	Any
Borderline ^{3,4}	≤10 spots	5, 6, or 7 spots	Any
Negative ⁵	≤10 spots	≤4 spots	
Indeterminate ^{1, 6}	≥10 spots	Any	Any
	≤10 spots	<3 spots	>20 spots

T-Spot Invalid? - Case 4

T-SPOT. TB Test Results DB

T-SPOT TB Invalid

The T-SPOT TB test was invalid due to a high spot count in the Negative Control. We suggest that you submit a new sample. If you have any questions, please call 1-877-338-2322. Thank you.

NH (Neg) Control Spot Count	>11
Panel A Spot Count	7
Panel D Spot Count	14
Positive Control Spot Count	>20

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??
