The Big Three:

No, not these.........Or these.
The Big Three: Commonly asked questions when interpreting IGRA results:

- How should I interpret a negative IGRA result?
- How should I interpret a positive IGRA result?
- Really...it’s indeterminate?

How should I interpret a negative IGRA result?:

- A negative IGRA result does not rule out the diagnosis of LTBI or active TB infection.
- Pooled sensitivity data (culture-confirmed TB):
  - T-Spot.TB = 90%
  - QFT-IT = 83%
  - TST = 89%
  
  Mazurek et al., MMWR 2010; 59:1-25

- IGRAs may lack sensitivity for detection of LTBI after a recent exposure.
  - Repeat testing in 8-10 weeks is recommended
How should I interpret a positive IGRA result?:

- IGRAs cannot distinguish LTBI from active TB
- Pooled specificity data:
  - T-Spot.TB = 88%
  - QFT-IT = 99%
  - TST = 85%

Mazurek et al., MMWR 2010; 59:1-25

What about quantitative data from IGRA results?
- “…quantitative results from IGRAs have not been shown to have prognostic value and, therefore, should not be used for that purpose…” Herrera V, CID 2011

How should I interpret a positive IGRA result?:

What about quantitative data from IGRA results?
- “…quantitative results are useful for predicting the likelihood for reversion or conversion when the IFN-γ signal is close to the assay cutoff.” Herrera V, CID 2011

Example: 0.30 IU/mL → 0.4 IU/mL
0.30 IU/mL → 1.0 IU/mL

T-Spot.TB has an equivocal zone: 5-7 ‘spots’

Proposed QFT “grey zone” for patients with fluctuating TB antigen values near cutoff:
- 0.35 IU/mL – 0.69 IU/mL (Pai M, Am J Respir Crit Care Med 2006)
How should I interpret an indeterminate IGRA result?:

- Indeterminate results can result from 1) immune suppression, 2) patients with extremes of age (e.g., children <5), 3) technical factors (e.g., improper collection, storage or incubation)
- Goal: Indeterminate rate \( \leq 5\% \)
- Typical protocol for indeterminate results:
  - Repeat by same method using *newly collected* sample
  - If patient is ICH, recommend T-Spot.TB
  - If Indeterminate repeats, use second method

Reaction and Key “Take-Home” Points from This Session
Difficulty centers on borderline / “Wobbler” results:

- “Grey-zone” for T-Spot.TB (5-7 spots) established
- Grey-zone needed for QFT-IT, but what range?
  - 0.35 – 0.69 IU/mL (Pai et al; Marder et al)
  - 0.25 – 0.45 IU/mL (Graviss et al)
  - 0.2 – 0.7 IU/mL (Metcalfe et al)
- How should Indeterminate results be handled?
  - Repeat testing using same sample? Repeat once? In duplicate?
  - Repeat testing using newly collected sample?

For patients with “difficult to interpret” results, a multi-pronged approach may be needed:

- Multiple tools are now available and can be used to help “clarify” the interpretation...or in some cases, muddy the waters.
- For example:
  - Initial testing by QFT-IT = 0.5 IU/mL (positive)
  - Repeat testing by QFT-IT = 0.3 IU/mL (negative)
  - Recommend T-Spot.TB = 0 spots (negative)
Contact Information

Matthew J. Binnicker, Ph.D.
Director, Infectious Diseases Serology
Division of Clinical Microbiology
Mayo Clinic
200 First St SW
Rochester, MN 55905
binnicker.matthew@mayo.edu
Office: +1-507-538-1640