LTBI Case Discussion

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Masa Narita, MD
TB Control Officer, Public Health – Seattle & King County
Professor, Division of Pulmonary, Critical Care & Sleep Medicine
University of Washington

LTBI Case Discussion

- IGRA: quantitative values
- Positive predictive value
- BCG

IGRA: quantitative values

QUANTIFERON-TB PLUS

Order: 177990296

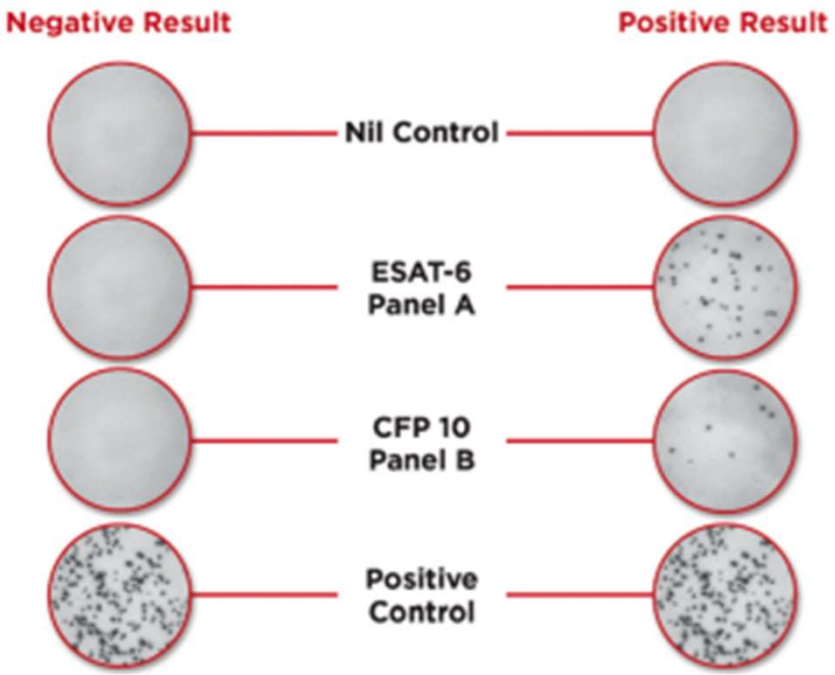
Status: **Final result** Visible to patient: **No (Not Released)** Next appt: **None** Dx: **Screening examination for pulmonary t...**

Component Ref Range & Units	1mo ago
QUANTIFERON	**POSITIVE (MYCOBACTERIUM TUBERCULOSIS INFECTION LIKELY) !**
NIL IU/mL	0.40
TB1 IU/mL	2.71
TB2 IU/mL	2.67
MITOGEN IU/mL	> 10
TB1 MINUS NIL IU/mL	2.31
TB2 MINUS NIL IU/mL	2.27
MITOGEN MINUS NIL IU/mL	> 10
Resulting Agency	KCPH LAB

QFT: review the quantitative values

- First, Nil should be ≤ 8.0 (if not, indeterminate)
- Then, "Mitogen – Nil" should be ≥ 0.5
  (if not indeterminate)
- Then, if either (TB1– nil) or (TB2 – nil) is ≥ 0.35, and at least ≥ 25% of the nil value → positive
- If both (TB1– nil) and (TB2 – nil) are < 0.35
  → negative

T-SPOT.*TB*



1. Nil Control Should be < 10
   → If not, invalid
2. Either Panel A – Nil, or Panel B – Nil:
   - 8 or greater: "Positive"
   - 5, 6, 7: "Borderline"
   - 4 or less: "Negative"
3. Positive Control should be ≥ 20.
   - If <20, AND both Panel A-Nil and Panel B-Nil are negative → Invalid

Positive Predictive Value

Positive Predictive Value

- The proportion of true positive among the positive results.
- In other words, what is the likelihood of a positive result truly telling you that your patient has LTBI?

Prevalence of LTBI ("pre-test probability")

By TST (*Horsburgh NEJM 2011*)

- Close contacts: 37%
- Foreign-born: 19%
- IV drug users: 14 – 27%
- Prisoners: 17%
- US born, no other risk: 1.8%

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- Homeless in Seattle: 15% using both TST and QFT
- US born in WA: 0.8% using mathematical modeling

More on LTBI

Estimating the cumulative risk of developing active TB, up to the age of 80 (or the "lifetime risk")

- Annual risk of development of active TB
  = 0.1% per year (x relative risk)
- If recent exposure (close contact), add 5%
  - Throwing you a curve ball: if non-US born and immigrated at an older age → likely to be previously infected, and thus add less than 5%
- For example, age 50, (+) TB exposure risk in the past, but no recent exposure or progression risk

→ 30 more years until age 80

→ lifetime risk of progression from LTBI to active TB: 3%

Disclaimer: rough estimate

Multiple test results

- For example, someone had multiple negative TSTs in the past, and positive IGRA this year for the first time without TB exposure

  → TSTin3D may not be able to incorporate all the info.

- Handling discordant results:
  - Common scenario: first IGRA positive → second IGRA negative
    - ♦ Low pre-test probability and no risk for progression from LTBI to active TB disease → "prioritize specificity" (i.e., no LTBI)
    - ♦ High pre-test probability and/or high risk of progression to TB → "prioritize sensitivity" (i.e., consider LTBI treatment)
    - ♦ Rarely requires a third LTBI test.

Interpreting the quantitative values of QFT

- QFT-Plus: positive
  - Nil 0.80
  - TB1 1.20
  - TB2 0.78
  - Mitogen 8.0
  - TB1 – nil = 0.40 (and >25% of the nil value)

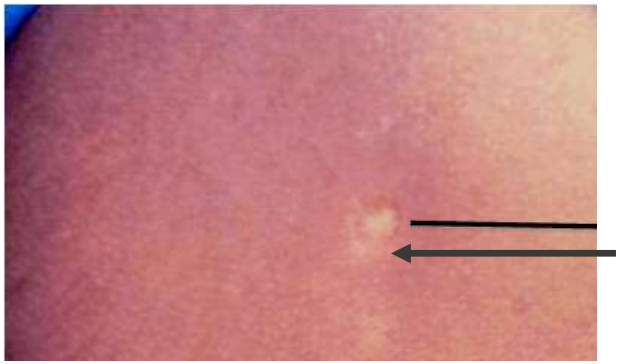
- Depends on the pre-test probability and the risk of progression.

BCG

BCG atlas: www.bcgatlas.org

- Provides info on current/past BCG policies for >180 countries
- May assist clinicians in
  (1) interpreting TST
  (2) determining if TST would be a valid tool to use

Bacille Calmette-Guérin (BCG)
Background info:



- Live, attenuated vaccine derived from *M. bovis*
- Data on efficacy is conflicting:
  - Meta-analysis: 51% efficacy (range 0-80%) in preventing any TB disease
  - Greatest efficacy in mycobacteria-naïve newborns:
    - 70-80% protective against meningeal, disseminated TB, mortality
  - Duration of protection unknown, but possibly 10-15 yrs
  - Protective against acquiring latent TB infection (19-28%)

Colditz, et al. JAMA. 1994;271(9):698
Michelsen, et al. Thorax. 2014 Sep;69(9):851
Roy, et al. BMJ. 2014;349:g4643

TST interpretation following BCG vaccination

TST reaction depends on (1) the interval between vaccination and testing, and (2) age at time of vaccination

- If received within 1st year of life: TST likely < 10mm after 10 years of age
- If received between 1-5 years: 10-15% may have a positive TST even 20-25 years later
- If received ≥6 years old, up to 40% will have a positive TST persistently.
- In serial testing, boosting can occur
- IGRA is NOT affected by BCG

BCG World Atlas (www.bcgatlas.org)

- Provides info on current/past BCG policies for >180 countries
- Assists clinicians to determine if TST would be a valid tool to use and help interpret TST