Self-Study Modules on Tuberculosis

Module 3

Targeted Testing and the Diagnosis of Latent Tuberculosis Infection

Module 3: Objectives

At completion of this module, learners will be able to:

1. Identify high-risk groups for targeted testing

2. Describe how to place, read, and interpret a Mantoux tuberculin skin test (TST)

3. Describe how to interpret an interferon-gamma release assay (IGRA)

4. Discuss considerations for using either the TST or IGRA for diagnosing latent tuberculosis infection (LTBI)

Targeted Testing

Targeted Testing (1)

- **Targeted testing is a TB control strategy used to identify and treat persons:**

  - **At high risk for latent TB infection (LTBI)**

  - **At high risk for developing TB disease once infected with *M. tb***

Targeted Testing (2)

- **Identifying persons with LTBI is an important goal of TB elimination because LTBI treatment can:**

  - **Prevent the development of TB disease**

  - **Stop the further spread of TB to others**

Targeted Testing (3)
A Decision to Test is a Decision to Treat

- **TB testing activities should be done only when there is a plan for follow-up care**

- **Health care workers (HCWs) should identify and test persons who are at high risk**

  - **People who are not at high risk generally should not be tested**

Targeted Testing (4)
High-Risk Groups

- **High-risk groups can be divided into two categories:**

  - **People who are at high risk for exposure to or infection with *M. tb***

  - **People who are at high risk for developing TB disease once infected with *M. tb***

Diagnosis of Latent TB Infection (LTBI)

Diagnosis of LTBI

- **Available testing methods for *M. tuberculosis* infection:**

  – **Mantoux tuberculin skin test (TST)**

  – **Blood tests known as interferon-gamma release assays (IGRAs):**

    - **QuantiFERON®-TB Gold Plus (QFT-Plus)**

    - **T-SPOT®.*TB* test (T-Spot)**

Diagnosis of Latent TB Infection (LTBI)

Mantoux Tuberculin Skin Test
Administering the Test

Mantoux Tuberculin Skin Test (1)

- **TST is administered by injection**

- **Tuberculin is made from proteins derived from inactive tubercle bacilli**

- **Most people who have TB infection will have a reaction at injection site**

Syringe being filled with 0.1 ml of liquid tuberculin

Mantoux Tuberculin Skin Test (2)

0.1 ml of 5 tuberculin units of liquid tuberculin are injected between the layers of skin on forearm

HCW administering Mantoux TST

Mantoux Tuberculin Skin Test (3)

- **Forearm should be examined within 48 to 72 hours by HCW**

- **Reaction is an area of <u>induration</u> (swelling) around injection site**

  - **Induration is measured in millimeters**

  - **Erythema (redness) is not measured**

Only the induration is measured

Diagnosis of Latent TB Infection (LTBI)

Mantoux Tuberculin Skin Test Interpreting the Reaction

Interpreting the TST Reaction (1)

Interpretation of TST reaction depends on size of induration and person's risk factors for TB

Interpreting the TST Reaction (2)

≥ 5 mm induration	≥ 10 mm induration	≥ 15 mm induration
• People living with HIV • Recent contacts of persons with infectious TB • People with CXR findings suggestive of previous TB disease • People with organ transplants • Other immunosuppressed persons	• People who have recently come to US from areas where TB is common • People who use drugs • Mycobacteriology/laboratory workers • People who live or work in high-risk congregate settings • People with certain medical conditions that increase risk for TB (e.g., silicosis, diabetes, severe kidney disease, certain types of cancer, and certain intestinal conditions) • Children <5 years of age • Infants, children, or adolescents exposed to adults in high-risk categories	• People who have no known risk factors for TB

Diagnosis of Latent TB Infection (LTBI)

Mantoux Tuberculin Skin Test Factors that Affect the Reaction

BCG Vaccination and TST

- **People who have been vaccinated with BCG may have a false-positive TST reaction**

  - **However, there is no reliable way to distinguish a positive TST reaction caused by BCG vaccination from a reaction caused by true TB infection**

- **Individuals should always be further evaluated if they have a positive TST reaction**

False TST Reactions

- **False positive**
  - **BCG vaccination**
  - **Non-tuberculous mycobacteria infection**
  - **Improper administration or interpretation**

- **False negative**
  - **Very young (<6months)**
  - **Inability to mount an immune response (e.g., HIV or TB itself)**
  - **Recent infection (<10 weeks since exposure)**
  - **Very remote infection**
  - **Recent live virus vaccination**
  - **Improper administration or interpretation**

Poll 1

TST results are expected to remain positive during and after treatment?

A. True

B. False

C. Unsure

Any patient with symptoms of TB disease should be evaluated for TB disease, regardless of his or her skin test reaction.

Diagnosis of Latent TB Infection (LTBI)

Interferon-Gamma Release Assays (IGRAs)

Types of IGRAs

- **QuantiFERON®-TB Gold Plus)**
  - **Rolled out in 2018**

- **T-Spot®.*TB* test (T-SPOT)**
  - **Type of ELISpot assay**
  - **Approved in 2008**

- **CDC guidelines for IGRAs published in 2010**

QFT-GIT testing materials

T-Spot®.*TB* testing materials

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IGRAs (1)

- **Blood tests that help diagnose *M. tb* infection**

- **Measures a person's immune reactivity to *M. tb***

IGRAs (3)
How it Works

- **Blood samples are mixed with antigens (protein substances that can produce an immune response) and incubated**

- **If the person is infected with *M. tb,* blood cells will recognize antigens and release interferon gamma (IFN-γ) in response**
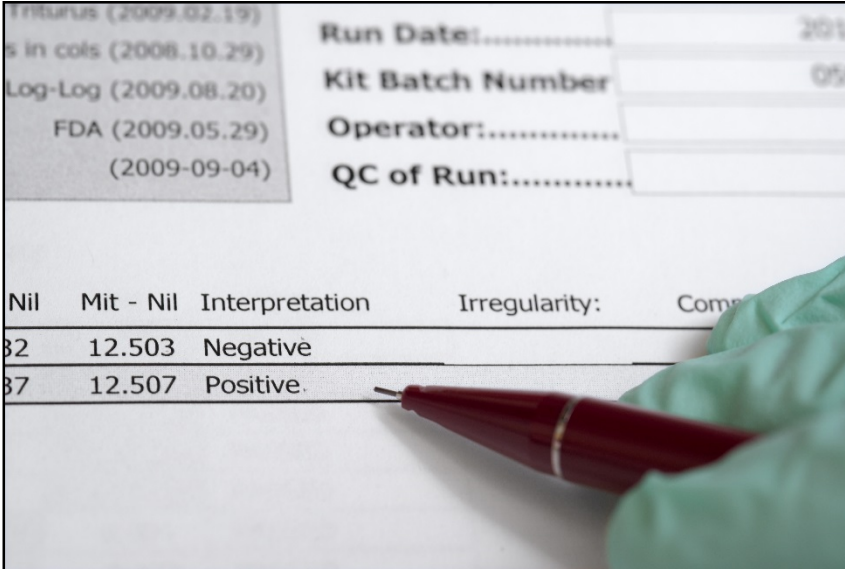
IGRAs (4)
Interpreting Results

- **QFT-Plus Results**
  - **Based on amount of IFN-γ released in response to *M. tb* antigens and control substances**

- **T-Spot Results**
  - **Based on number of IFN-γ producing cells (spots) produced**

IGRAs (5)
Interpreting Results

- **IGRA antigens were selected because they are not found in BCG**

- **Antigens used are *Mycobacterium***
  - *Kansasii*
  - *Gordonae*
  - *Marinum*
  - *Szulgai*

- **May cause a false positive**

QFT-GIT Results

IGRAs (6)
Report of Results

IGRA Result	Interpretation
Positive	*M. tb* infection likely
Negative	*M. tb* infection unlikely, but cannot be excluded especially if 1. Patient has signs and symptoms of TB 2. Patient has a high risk for developing TB disease once infected with *M. tb*
Indeterminate	The test did not provide useful information about the likelihood of *M. tb* infection. Repeating an IGRA or performing a TST may be useful.
Borderline (T-Spot only)	The test did not provide useful information about the likelihood of *M. tb* infection. Repeating an IGRA or performing a TST may be useful.

IGRA Recommendations (1)

- **IGRAs are the preferred method of testing in**

  - **Groups of people who might be less likely to return for TST reading and interpretation**

  - **Persons who have received the BCG vaccine**

- **TST is preferred for children younger than 2 years of age (AAP guidance change)**

IGRA Recommendations (2)

- **Routine testing using both TST and IGRAs is NOT recommended**

- **Certain situations where results from both tests may be useful:**

  - **When the initial test is <u>negative</u> and:**

    - **Risk for infection, progression to disease, or a poor outcome is high**

    - **There is clinical suspicion for TB disease and confirmation of *M. tb* infection is desired**

IGRA Recommendations (3)

- **Certain situations where results from both tests may be useful**

  - **When the initial test is <u>positive</u> and:**

    - **Additional evidence of infection is required to encourage the patient's acceptance and adherence to treatment**

    - **Person has a low risk of both infection and progression from infection to TB disease**

IGRA Advantages

- **Requires single patient visit to conduct test**

- **Results can be available in 24 hours**

- **Does not cause booster phenomenon which can happen with repeat TSTs**

- **BCG vaccination does not affect IGRA results**

IGRA Disadvantages and Limitations (1)

- **Blood samples must be processed within 8 to 30 hours after collection**

- **Errors in collecting or transporting blood specimens or in running and interpreting test can decrease accuracy**

- **Limited data on its use in certain populations (e.g., children younger than 2, persons recently infected, immunocompromised persons, and serial testing)**

IGRA Disadvantages and Limitations (2)

- **Limited data on its use to predict who will progress to TB disease**

- **Tests may be expensive**

Poll 2

Mycobacterium Avium can cause a false positive IGRA result?

A. True

B. False

C. Unsure

Diagnosis of Latent TB Infection (LTBI)

Booster Phenomenon, and Two-Step Testing

Booster Phenomenon

- **Phenomenon in which people who are skin tested many years after they became infected with TB have:**

  - **Negative reaction to initial TST**

  - **Positive reaction to subsequent TST given up to one year later**

- **Occurs mainly in older adults**

- **May affect accuracy of baseline skin test**

- **TST can boost subsequent IGRA results**

Figure 3.6
The booster phenomenon with the TST

Person becomes infected with *M. tuberculosis*

↓

Person is skin tested years later

↓

Person has negative reaction due to lessened ability to react to tuberculin

However, this skin test "jogs the memory" of the immune system to recognize and react to tuberculin

As years pass, person's ability to react to tuberculin lessens

↓

Person is skin tested again, up to 1 year later. For this example, we assume that the person was NOT exposed to TB during this time

↓

Occurs mainly in previously infected, older adults whose ability to react to tuberculin has decreased over time
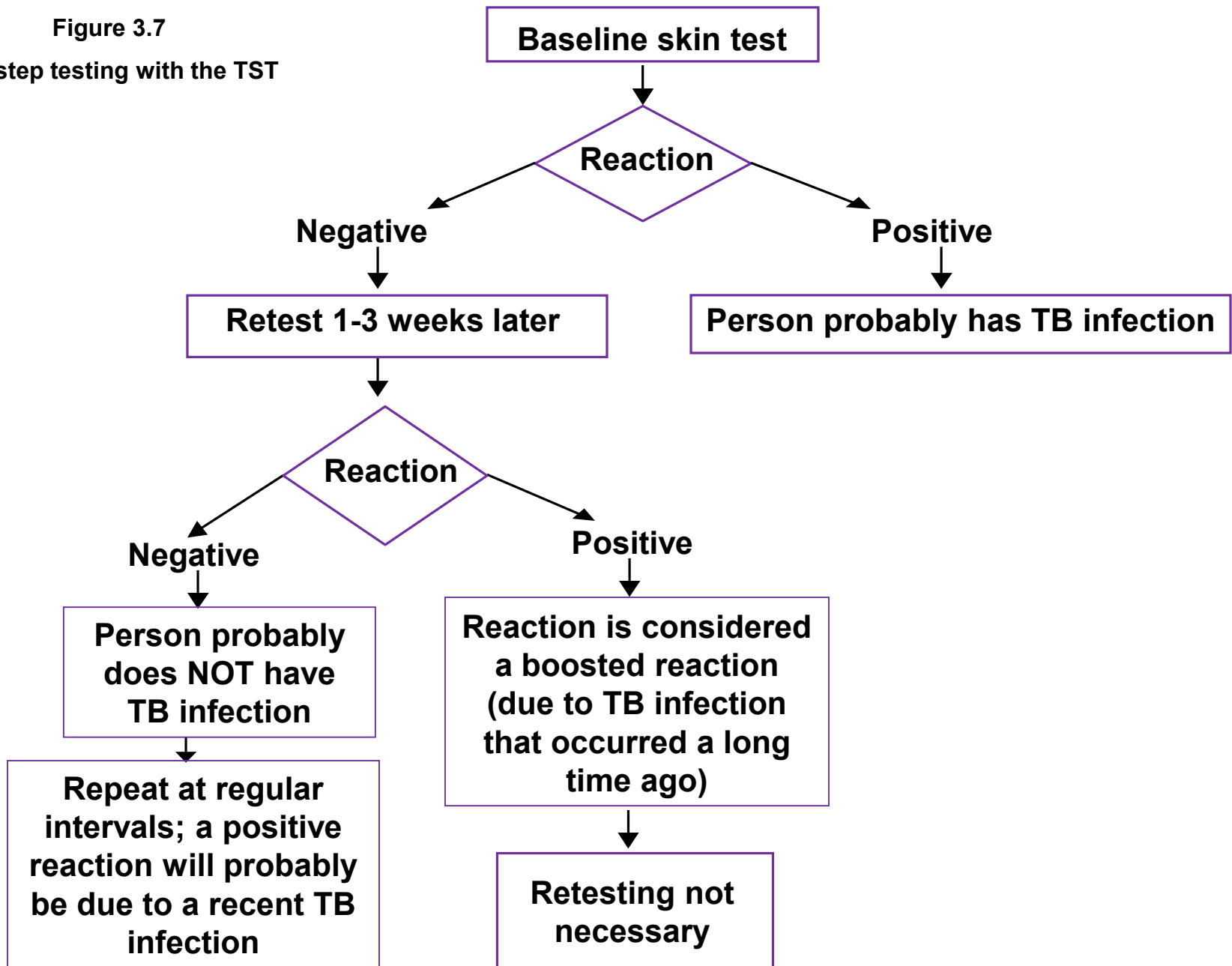
Person has a positive reaction. This is a boosted reaction due to TB infection that occurred a long time ago, not during the time between the two skin tests

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Two-Step Testing

- **Only conducted when TST is used**

- **Distinguishes between boosted reactions and reactions caused by recent infections**

- **Should be used for initial skin testing of persons who will be retested periodically**

- **If person's initial skin test is negative, they should be given a second test 1 to 3 weeks later**
  - **Second test positive: probably boosted reaction**
  - **Second test negative: considered uninfected**

Figure 3.7
Two-step testing with the TST

Baseline skin test

Reaction

Negative → Retest 1-3 weeks later

Positive → Person probably has TB infection

Reaction

Negative → Person probably does NOT have TB infection → Repeat at regular intervals; a positive reaction will probably be due to a recent TB infection

Positive → Reaction is considered a boosted reaction (due to TB infection that occurred a long time ago) → Retesting not necessary

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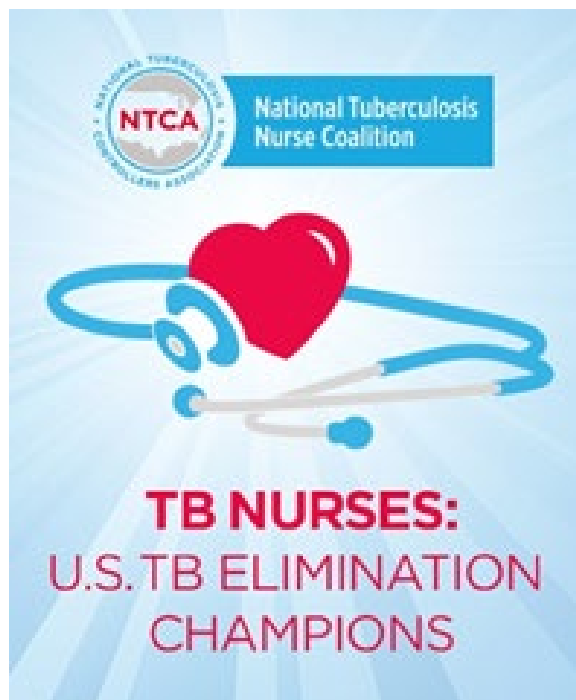
Occupational Exposure

- **For people who may be exposed to TB on the job (e.g., Health Care Personnel, staff of nursing homes or correctional facilities), interpretation of TST depends on:**

  – **The employee's individual risk factors for TB**

  – **The risk of exposure to TB in the person's job**