



# *Self-Study Modules on Tuberculosis*

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# 3

## **Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease**



# 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 give and interpret a Mantoux tuberculin skin test (TST) and an interferon-gamma release assay (IGRA)
3. Discuss considerations for using either the TST or IGRA for diagnosing infection with *M. tuberculosis*
4. Describe the components of a medical evaluation for diagnosing TB disease

# Module 3: Overview

- **Targeted Testing**
- **Diagnosis of latent tuberculosis infection (LTBI)**
  - **TST**
  - **IGRAs**
  - **TB Testing Programs, the Booster Phenomenon, and Two-Step Testing**
- **Diagnosis of TB Disease**
- **Reporting TB Cases**
- **Case Studies**

# Targeted Testing

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# Targeted Testing (1)

- Targeted testing is a TB control strategy used to identify and treat persons:
  - At high risk for infection with *M. tuberculosis*
  - At high risk for developing TB disease once infected with *M. tuberculosis*

# 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 spread of TB**

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



# **Targeted Testing (5)**

## **High-Risk Groups for TB Infection**

- **Close contacts of people known or suspected to have TB**
- **People who have come to U.S. within 5 years from areas where TB is common**
- **Low-income groups**
- **People who inject drugs**

# **Targeted Testing (6)**

## **High-Risk Groups for TB Infection**

- **People who live or work in high-risk settings**
- **HCWs who serve high-risk clients**
- **Racial or ethnic minority populations**
- **Infants, children, and adolescents exposed to adults in high-risk groups**

# Targeted Testing (7)

## High-Risk Groups for TB Disease

- **People living with HIV**
- **People recently infected with *M. tuberculosis* (within past 2 years)**
- **People with certain medical conditions known to increase risk for TB**
- **People who inject drugs**
- **Infants and children younger than 4 years old**

# Diagnosis of Latent TB Infection (LTBI)

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# 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 test (QFT-G)
    - QuantiFERON®-TB Gold In-Tube (QFT-GIT)
    - T-SPOT

# **Diagnosis of Latent TB Infection (LTBI)**

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## **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 - 72 hours by HCW
- Reaction is an area of induration (swelling) around injection site
  - Induration is measured in millimeters
  - Erythema (redness) is not measured



Only the induration is measured

# Multiple-Puncture Test

- **In the past, multiple-puncture tests (tine tests) were a popular skin testing method for TB**
- **No longer recommended**
  - **Amount of tuberculin that enters skin cannot be measured**
- **Mantoux TST is preferred TB skin test method because amount of tuberculin can always be measured**

# Mantoux Tuberculin Skin Test

## Study Question 3.1

**What is the TST used for? *(pg. 11)***

**The TST is used to determine whether a person has TB infection.**

# Mantoux Tuberculin Skin Test

## Study Question 3.2

**How is the Mantoux TST given? *(pg. 11)***

**The TST is given by a needle and syringe to inject 0.1 ml of 5 tuberculin units of liquid tuberculin between the layers of the skin, usually on the forearm.**

# Mantoux Tuberculin Skin Test

## Study Question 3.3

**With the TST, when is the patient's arm examined?** *(pg. 12)*

**The patient's arm is examined by a health care worker, 48 – 72 hours after tuberculin is injected.**

# Mantoux Tuberculin Skin Test

## Study Question 3.4

**How is the induration measured?** *(pg. 12)*

**The diameter of indurated area is measured across the forearm; erythema (redness) around the indurated area is not measured.**

# Mantoux Tuberculin Skin Test

## Study Question 3.5

**Why is the Mantoux TST preferable to multiple puncture tests? *(pg. 12)***

**Mantoux TST is preferable because it is more accurate and the amount of tuberculin can always be measured.**

# **Diagnosis of Latent TB Infection (LTBI)**

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## **Mantoux Tuberculin Skin Test Interpreting the Reaction**



# Mantoux Tuberculin Skin Test (4)

## Interpreting the Reaction

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



**Module 3 – Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease**

# Mantoux Tuberculin Skin Test (5)

## Interpreting the Reaction

- Induration of  $\geq 5$  mm is considered positive for:
  - People living with HIV
  - Recent close contacts of people with infectious TB
  - People with chest x-ray findings suggestive of previous TB disease
  - People with organ transplants
  - Other immunosuppressed patients

# Mantoux Tuberculin Skin Test (6)

## Interpreting the Reaction

- Induration of  $\geq 10$  mm is considered a positive reaction for:
  - People who have recently come to U.S. from areas where TB is common
  - People who inject drugs
  - People who live or work in high-risk congregate settings
  - Mycobacteriology laboratory workers

# Mantoux Tuberculin Skin Test (7)

## Interpreting the Reaction

- Induration of  $\geq 10$  mm is considered a positive reaction for:
  - People with certain medical conditions that increase risk for TB
  - Children younger than 4 years old
  - Infants, children, or adolescents exposed to adults in high-risk categories

# Mantoux Tuberculin Skin Test (8)

## Interpreting the Reaction

- Induration of  $\geq 15$  mm is considered a positive reaction for people who have no known risk factors for TB

# Mantoux Tuberculin Skin Test

## Study Question 3.6

**What 2 factors determine the interpretation of a skin test reaction as positive or negative? What additional factor is considered for people who may be exposed to TB on the job? (pg. 16)**

- **Size of induration and risk factors for TB**
- **An additional factor is the risk of exposure to TB in the person's job**

# Mantoux Tuberculin Skin Test

## Study Question 3.7

For which groups of people is  $\geq 5$  mm of induration considered a positive reaction?

Name 4. (pg. 16)

- People living with HIV
- Recent contacts of people with infectious TB
- People who have had TB disease before
- Patients with organ transplants and other immunosuppressed individuals

# Mantoux Tuberculin Skin Test

## Study Question 3.8

**For which groups of people is  $\geq 10$  mm of induration considered a positive reaction? (pg. 17)**

- Recent arrivals to the U.S. from areas where TB is common
- People who inject drugs
- Mycobacteriology lab workers
- People who live or work in high-risk congregate settings
- People with certain medical conditions
- Children younger than 4 years old
- Infants, children, and adolescents exposed to adults in high-risk categories



# Mantoux Tuberculin Skin Test

## Study Question 3.9

**For which group of people is  $\geq 15$  mm of induration considered a positive reaction?**  
*(pg. 17)*

**People with no risk factors for TB.**

# **Diagnosis of Latent TB Infection (LTBI)**

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**Mantoux Tuberculin Skin Test  
Factors that Affect the Reaction**

# **Mantoux Tuberculin Skin Test (9)**

## **False-Positive Reaction**

- **Factors that can cause people to have a positive reaction even if they do not have TB infection:**
  - **Infection with nontuberculous mycobacteria**
  - **BCG vaccination**
  - **Administration of incorrect antigen**
  - **Incorrect measuring or interpretation of TST reaction**

# Mantoux Tuberculin Skin Test (10)

## BCG Vaccine

- **People who have been vaccinated with BCG may have a false-positive TST reaction**
  - **However, there is no reliable way to distinguish between reaction caused by TB infection or by BCG vaccine**
- **Individuals should always be further evaluated if they have a positive TST reaction**

# Mantoux Tuberculin Skin Test (11)

## False-Negative Reaction

- **Factors that can cause false-negative reactions:**
  - Anergy
  - Recent TB infection (within past 8 – 10 weeks)
    - It can take 2 – 8 weeks after TB infection for body's immune system to react to tuberculin
  - Younger than 6 months of age
  - Recent live-virus (e.g., measles or smallpox) vaccination
  - Incorrect method of giving the TST
  - Incorrect measuring or interpretation of TST reaction

# Mantoux Tuberculin Skin Test (12)

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



# Mantoux Tuberculin Skin Test (13)

## Anergy

- **Inability to react to skin tests due to weakened immune system**
- **Anergy testing is no longer routinely recommended**

# Mantoux Tuberculin Skin Test

## Study Question 3.10

**Name 4 factors that can cause false-positive reactions to the TST. (pg. 19)**

- **Infection with nontuberculous mycobacteria (NTM)**
- **BCG vaccination**
- **Administration of incorrect antigen**
- **Incorrect measuring or interpretation of TST reaction**



# Mantoux Tuberculin Skin Test

## Study Question 3.11

**Is there a reliable way to distinguish a positive TST reaction caused by vaccination with BCG from a reaction caused by true TB infection? (pg. 19)**

**No. Individuals who have had BCG vaccine should be further evaluated for LTBI or TB disease the same way as if they were not vaccinated with BCG.**

# Mantoux Tuberculin Skin Test

## Study Question 3.12

**Name 6 factors that can cause false-negative reactions to the TST. (pg. 24)**

- **Anergy**
- **Recent TB infection (within past 8-10 weeks)**
- **Very young age**
- **Recent live-virus (e.g., measles or smallpox) vaccination**
- **Incorrect method of giving the TST**
- **Incorrect measuring or interpretation of TST reaction**

# Mantoux Tuberculin Skin Test

## Study Question 3.13

**What is anergy?** *(pg. 24)*

**The inability to react to skin tests  
because of a weakened immune system.**

# Mantoux Tuberculin Skin Test

## Study Question 3.14

**After TB has been transmitted to someone, how long does it take before TB infection can be detected by the TST? *(pg. 24)***

**2 - 8 weeks**

# Mantoux Tuberculin Skin Test

## Study Question 3.15

**What should be done if a patient has a negative TST result, but has symptoms of TB disease? *(pg. 25)***

**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)**

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## **Interferon-Gamma Release Assays (IGRAs)**

# Types of IGRAs

- **QuantiFERON®-TB Gold (QFT-G)**
  - CDC guidelines published in 2005
- **QuantiFERON®-TB Gold In-Tube (QFT-GIT)**
  - Approved 10/2007
- **T-Spot®.TB test (T-SPOT)**
  - Type of ELISpot assay
  - Approved 7/2008
- **CDC guidelines for IGRAs are under development**



T-Spot®.TB test Materials  
Image Credit: U.S. Food and Drug  
Administration (FDA), 2009

# QFT-G and QFT-GIT (1)

- **Measures person's immune reactivity to *M. tuberculosis***
- **Used to help diagnose *M. tuberculosis* infection in persons suspected of having either LTBI or TB disease**



# **QFT-G and QFT-GIT (2)**

## **Conducting the Test**

- **Follow manufacturer's instructions**
  - **Confirm arrangements for delivery and testing of blood within 12 hours of collection**
  - **Draw sample of blood into tube with heparin**
  - **Schedule appointment for patient to receive test results**
    - **If needed, medical evaluation and treatment for LTBI or TB disease**

# QFT-G and QFT-GIT (3)

## How it Works

- **Blood samples are mixed with antigens and incubated for 16 - 24 hours**
- **If infected with *M. tuberculosis*, blood cells will recognize antigens and release interferon gamma (IFN- $\gamma$ ) in response**
- **Results are based on the amount of IFN- $\gamma$  released in response to antigens and control substances**

# QFT-G and QFT-GIT (4)

## Interpreting Results

- Test results are based on IFN- $\gamma$  concentrations
- Laboratories can use software provided by manufacturer to calculate results
- Results are sent to requesting clinician



Processing QFT-G Sample

# QFT-G and QFT-GIT (5)

## Report of Results

<b>Result</b>	<b>Report/Interpretation</b>
<b>Positive</b>	<b><i>M. tuberculosis</i> infection likely</b>
<b>Negative</b>	<p><b><i>M. tuberculosis</i> infection unlikely, but cannot be excluded especially if:</b></p> <ol style="list-style-type: none"> <li><b>1. Patient has TB signs and symptoms</b></li> <li><b>2. Patient has a high risk for developing TB disease once infected with <i>M. tuberculosis</i></b></li> </ol>
<b>Indeterminate</b>	<p><b>Test did not provide useful information about the likelihood of <i>M. tuberculosis</i> infection. Options are to repeat test, administer a TST, or do no additional testing</b></p>

# T-SPOT

- **Type of ELISpot assay**
- **Interferon gamma is presented as spots from T cells sensitized to *M. tuberculosis***
- **Results are interpreted by subtracting the spot count of the control from the spot count of the sample**

# IGRA Advantages

- **Requires single patient visit to conduct test**
- **Results can be available in 24 hours**
- **Does not cause booster phenomenon**
- **Less likely to have incorrect reading of results as compared to TST**
- **BCG vaccination does not affect results**

# IGRA Disadvantages and Limitations

- **Blood samples must be processed within 12 hours for some IGRAs**
- **Errors in running and interpreting test can decrease accuracy**
- **Limited data on its use in certain populations**
- **Limited data on its use to determine who is at risk for developing TB disease**

# **QFT-G and QFT-GIT**

## **Study Question 3.20**

**What are the steps for conducting a QFT-G and QFT-GIT? (pg. 39)**

**Follow manufacturer's instructions**

- **Confirm arrangements for delivery and testing of blood in qualified laboratory within 12 hours of collection**
- **Draw sample of whole blood from patient into tube with heparin**
- **Schedule appointment for patient to receive test results and, if then needed, medical evaluation and possible treatment**



# QFT-G and QFT-GIT

## Study Question 3.21

**How are QFT-G and QFT-GIT results interpreted?** *(pg. 39)*

- **Interpretation is based on the IFN- $\gamma$  concentrations in the test samples**
- **Laboratories can use software to calculate results**
- **Report of results are submitted to requesting clinician**

# QFT-G and QFT-GIT

## Study Question 3.22

**How should a negative QFT-G or QFT-GIT result be interpreted? (pg. 39)**

- **Patient is unlikely to have *M. tuberculosis* infection**
- **Patient may not require further evaluation unless they have signs and symptoms of TB disease**

# IGRAs

## Study Question 3.23

**What are 5 advantages for using an IGRA as compared to the TST? (pg. 39)**

- **Requires a single patient visit**
- **Results can be available in 24 hours**
- **Does not cause the booster phenomenon**
- **Less likely to have incorrect reading of results**
- **BCG vaccine does not affect IGRA results**

# **Diagnosis of Latent TB Infection (LTBI)**

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**TB Testing Programs, the Booster  
Phenomenon, and Two-Step Testing**

# TB Testing Programs (1)

- **Many health care facilities have TB testing programs**
  - **Employees and residents are periodically given TSTs or IGRAs**
- **Testing programs:**
  - **Identify people who have LTBI or TB disease and give them treatment**
  - **Determine whether TB is being transmitted in facility**

# **TB Testing Programs (2)**

## **Baseline Test**

- **Employees and/or residents are given TSTs or IGRAs when they first enter facility**
  - **If person is negative, they may be retested at regular intervals thereafter**

# TB Testing Programs (3)

## Conversion

- **Persons whose TST or IGRA result converts from negative to positive have probably been infected with *M. tuberculosis***
  - **TST or IGRA conversions may indicate that TB is being transmitted in facility**

# 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**



**Person is infected with *M. tuberculosis***

**Person is skin tested**

**Person has negative reaction due to decreased ability to react to tuberculin**

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

**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)**

**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**

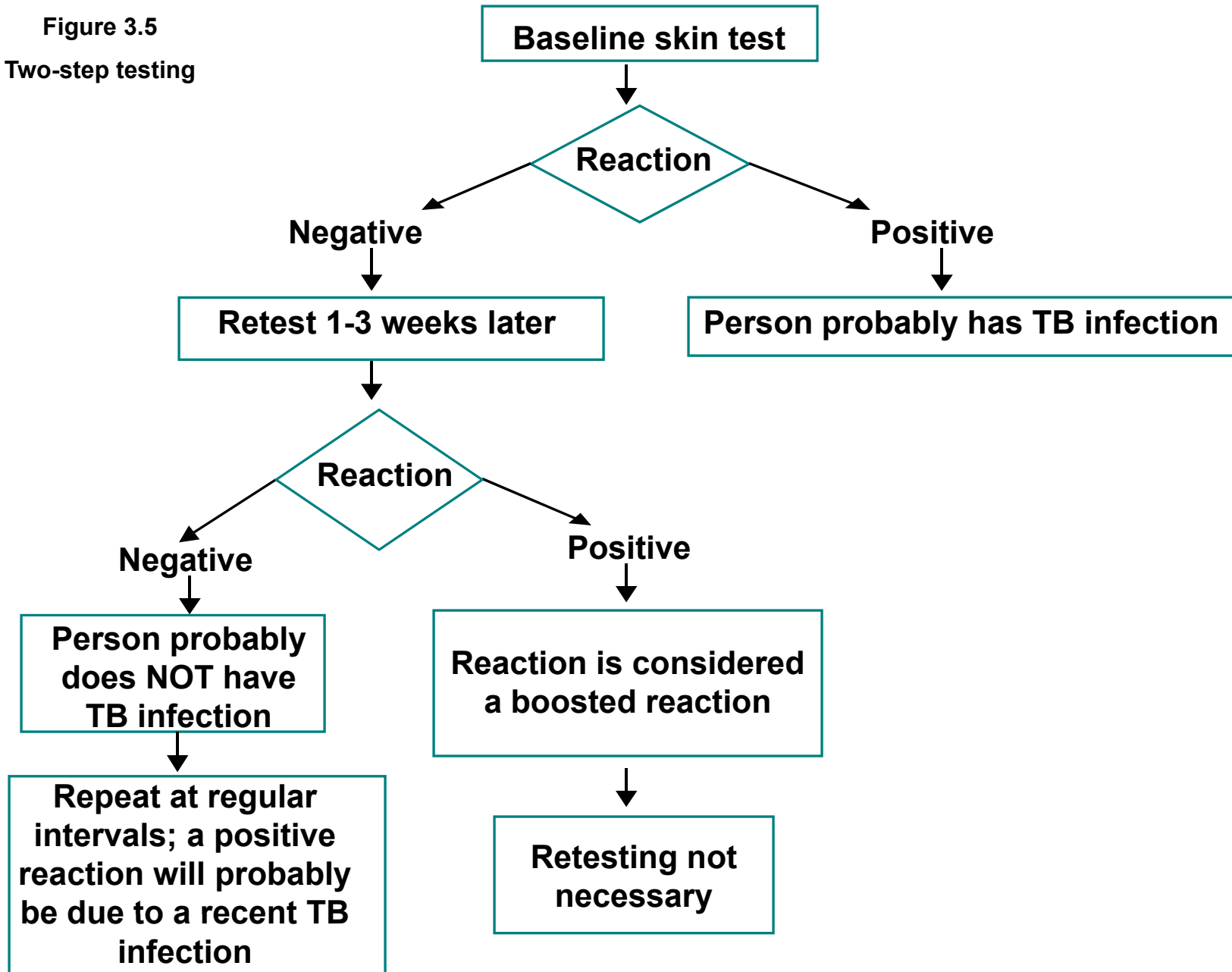
**Figure 3.4**  
**The booster phenomenon**

**As years pass, person’s ability to react to tuberculin lessens**

# 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 1-3 weeks later**
  - **Second test positive: probably boosted reaction**
  - **Second test negative: considered uninfected**

Figure 3.5  
Two-step testing



# Booster Phenomenon

## Study Question 3.16

**What is the booster phenomenon? (pg. 31)**

- Phenomenon in which people who are skin tested many years after becoming infected with *M. tuberculosis* have a negative reaction to an initial skin test, followed by a positive reaction to a skin test given up to a year later
- Occurs because the ability to react to tuberculin lessens over time in some people

# Two-Step Testing

## Study Question 3.17

**What is the purpose of two-step testing?**

*(pg. 31)*

**To distinguish between boosted reactions and reactions caused by recent infection.**

# Two-Step Testing

## Study Question 3.18

**In what type of situation is two-step testing used? (pg. 31)**

**It is used in many programs for skin testing employees when they start their job.**

# Two-Step Testing

## Study Question 3.19

**How is two-step testing done? (pg. 31)**

**If a person has a negative reaction to an initial skin test, he or she is given a second test 1-3 weeks later.**

- If reaction to second test is positive, it is considered a boosted reaction**
- If reaction to second test is negative, person is considered to be uninfected**

# Diagnosis of TB Disease

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# Medical Evaluation

- **Anyone with TB symptoms or positive TST or IGRA result should be medically evaluated for TB disease**
- **Components of medical evaluation:**
  - 1. Medical history**
  - 2. Physical examination**
  - 3. Test for TB infection**
  - 4. Chest x-ray**
  - 5. Bacteriological examination**

# **Diagnosis of TB Disease**

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## **Medical Evaluation**

- 1. Medical History**
- 2. Physical Examination**
- 3. Test for TB Infection**

# 1. Medical History (1)

- **Clinicians should ask patients if they have:**
  - **Symptoms of TB disease**
  - **Been exposed to a person with infectious TB or have risk factors for exposure to TB**
  - **Any risk factors for developing TB disease**
  - **Had LTBI or TB disease before**

# 1. Medical History (2)

## General Symptoms of TB Disease

- **Fever**
- **Chills**
- **Night sweats**
- **Weight loss**
- **Appetite loss**
- **Fatigue**
- **Malaise**

# 1. Medical History (3)

## Symptoms of Pulmonary TB Disease

- **Cough lasting 3 or more weeks**
- **Chest pain**
- **Coughing up sputum or blood**

# 1. Medical History (4)

## Symptoms of Extrapulmonary TB Disease

- **Symptoms of extrapulmonary TB disease depend on part of body that is affected**
- **For example:**
  - **TB disease in spine may cause back pain**
  - **TB disease in kidneys may cause blood in urine**

## 2. Physical Examination

**A physical examination cannot confirm or rule out TB disease, but can provide valuable information**



**Module 3 – Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease**

# 3. Test for TB Infection (1)

- Types of tests available for diagnosing TB infection in U.S.:

- TST

- IGRAs

- QFT-G
- QFT-GIT
- T-SPOT



QFT-G lab kit



## 3. Test for TB Infection (2)

- **Patients with symptoms of TB disease should always be evaluated for TB disease, regardless of their TST or IGRA test result**
  - **Clinicians should not wait for TST or IGRA results before starting other diagnostic tests**
  - **TST or IGRA should be given at the same time as other steps in the diagnosis of TB disease**

# Diagnosis of TB Disease

## Study Question 3.24

**What are the 5 components for conducting a medical evaluation for diagnosing TB disease?**  
(pg. 44)

- **Medical history**
- **Physical examination**
- **Test for TB infection**
- **Chest x-ray**
- **Bacteriologic examinations**

# Diagnosis of TB Disease

## Study Question 3.25

**What parts of a patient's medical history should lead a clinician to suspect TB? (pg. 45)**

- **Symptoms of TB disease**
- **Exposure to a person who has infectious TB or has other risk factors for exposure to TB**
- **Risk factors for developing TB disease**
- **TB infection or TB disease in the past**

# Diagnosis of TB Disease

## Study Question 3.26

**What are the symptoms of pulmonary TB disease? What are the symptoms of extrapulmonary TB disease? (pg. 45)**

- **General symptoms of TB disease: Weight loss, fatigue, malaise, fever, and night sweats**
- **Pulmonary: Coughing, pain in chest, coughing up sputum or blood**
- **Extrapulmonary: Depends on the part of the body that is affected by the disease. For example, TB of the spine may cause pain in the back; TB of the kidney may cause blood in the urine**

# Diagnosis of TB Disease

## Study Question 3.27

**For patients with symptoms of TB disease, should clinicians wait for TST or IGRA results before starting other diagnostic tests? (pg. 45)**

**No, clinicians should not wait for TST or IGRA results before starting other diagnostic tests.**

# **Diagnosis of TB Disease**

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## **Medical Evaluation**

### **4. Chest X-Ray**

## 4. Chest X-Ray (1)

- When a person has TB disease in lungs, the chest x-ray usually appears abnormal. It may show:
  - Infiltrates (collections of fluid and cells in lung tissue)
  - Cavities (hollow spaces within lung)



Abnormal chest x-ray with cavity

## 4. Chest X-Ray (2)

- **Chest x-rays can:**
  - **Help rule out possibility of pulmonary TB disease in persons who have a positive TST or IGRA result**
  - **Check for lung abnormalities**



## 4. Chest X-Ray (3)

- Chest x-rays cannot confirm TB disease
  - Other diseases can cause lung abnormalities
  - Only bacteriologic culture can prove patient has TB disease
  - Chest x-ray may appear unusual or even appear normal for persons living with HIV

# **Chest X-Ray**

## **Study Question 3.28**

**Name 2 purposes of the chest x-ray. (pg. 47)**

- **Help rule out possibility of pulmonary TB disease in a person who has positive TST or QFT-G result and no symptoms of TB**
- **Check for lung abnormalities in people who have symptoms of TB disease**

# Chest X-Ray

## Study Question 3.29

**Can the results of a chest x-ray confirm that a person has TB disease? Why or why not?**  
*(pg. 47)*

**No. A variety of illnesses may produce abnormalities on chest x-ray. Only bacteriologic culture can prove whether or not a patient has TB disease.**

# **Diagnosis of TB Disease**

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## **Medical Evaluation**

### **5. Bacteriologic Examination**

# 5. Bacteriologic Examination (1)

- **TB bacteriologic examination is done in a laboratory that specifically deals with *M. tuberculosis* and other mycobacteria**
  - **Clinical specimens (e.g., sputum and urine) are examined and cultured in laboratory**

# 5. Bacteriologic Examination (2)

- **Bacteriologic examination has 5 parts**
  - **Specimen collection**
  - **Examination of acid-fast bacilli (AFB) smears**
  - **Direct identification of specimen (nucleic acid amplification)**
  - **Specimen culturing and identification**
  - **Drug susceptibility testing**

# 5. Bacteriologic Examination (3)

## Specimen Collection

- For pulmonary TB, specimens can be collected by:
  - Sputum sample
  - Induced sputum sample
  - Bronchoscopy
  - Gastric washing



TB patient coughing up sputum in a sputum collection booth

# 5. Bacteriologic Examination (4)

## Sputum Sample Specimen Collection

- **Easiest and least expensive method is to have patient cough into sterile container**
- **HCWs should coach and instruct patient**
- **Should have at least 3 sputum specimens examined**
  - **Collected in 8-24 hour intervals**
  - **At least one early morning specimen**



# **5. Bacteriologic Examination (5)**

## **Induced Sputum Collection**

- **Induced sputum collection should be used if patient cannot cough up sputum on their own**
- **Patient inhales saline mist, causing deep coughing**
- **Specimen often clear and watery, should be labeled “induced specimen”**

# 5. Bacteriologic Examination (6)

## Bronchoscopy

- **Bronchoscopy may be used:**
  - If patient cannot cough up enough sputum
  - If an induced sputum cannot be obtained
- **Procedure: instrument is passed through nose or mouth into lung to obtain pulmonary secretions or lung tissue**



Bronchoscopy being performed on a patient

# **5. Bacteriologic Examination (7)**

## **Gastric Washing**

- **Usually only used if sample cannot be obtained from other procedures**
- **Often used with children**
- **Tube is inserted through nose and into stomach to obtain gastric secretions that may contain sputum**

# **5. Bacteriologic Examination (8)**

## **Extrapulmonary TB**

- **Specimens other than sputum may be obtained**
- **Depends on part of body affected**
- **For example:**
  - **Urine samples for TB disease of kidneys**
  - **Fluid samples from area around spine for TB meningitis**

# 5. Bacteriologic Examination (9)

## Examination of AFB Smears

- Specimens are smeared onto glass slide and stained
- AFB are mycobacteria that remain stained after being washed in acid solution



AFB smear

# **5. Bacteriologic Examination (10)**

## **Examination of AFB Smears**

- **Number of AFB on smear are counted**
- **According to number of AFB seen, smears are classified as 4+, 3+, 2+, or 1+**
  - **For example, 4+ smear has 10 times as many AFB than 3+ smear**
- **If very few AFB are seen, the smear is classified by the actual number of AFB seen**

# 5. Bacteriologic Examination (11)

## Examination of AFB Smears

<b>Classification of Smear</b>	<b>Smear Result</b>	<b>Infectiousness of Patient</b>
4+	Strongly positive	Probably very infectious
3+	Strongly positive	Probably very infectious
2+	Moderately positive	Probably infectious
1+	Moderately positive	Probably infectious
Actual number of AFB seen (no plus sign)	Weakly positive	Probably infectious
No AFB seen	Negative	May not be infectious

# Bacteriologic Examination

## Study Questions 3.30

**What are the 4 ways to collect sputum specimens? Indicate which procedure is the least expensive and easiest to perform. (pg. 55)**

- Patient simply coughs up sputum and the sputum is collected in a sterile container. This is the least expensive and easiest procedure.
- Induced sputum
- Bronchoscopy
- Gastric washing



# Bacteriologic Examination

## Study Question 3.31

**What do laboratory personnel look for in a smear? (pg. 55)**

**Acid-fast bacilli (AFB)**

# Bacteriologic Examination

## Study Question 3.32

**What does a positive smear indicate about a patient's infectiousness? (pg. 55)**

**Patients who have any tubercle bacilli seen in their sputum have a positive smear. Patients who have positive smears are considered infectious because they can cough tubercle bacilli into the air.**

# **Diagnosis of TB Disease**

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## **Medical Evaluation**

### **5. Bacteriologic Examination**

# 5. Bacteriologic Examination (12)

## Nucleic Acid Amplification Tests (NAA)

- **NAA tests directly identify *M. tuberculosis* from sputum specimens by:**
  - **Amplifying (copying) DNA and RNA segments**
- **Can help guide clinician's decision for patient therapy and isolation**
- **Does not replace need for AFB smear, culture, or clinical judgment**

# **5. Bacteriologic Examination (13)**

## **Nucleic Acid Amplification Tests (NAA)**

- **If NAA test and AFB smears are positive:**
  - **Patients are presumed to have TB and should begin treatment**
- **If NAA test is negative and AFB smears are positive:**
  - **Patients may have nontuberculous mycobacteria infection (NTM)**

# 5. Bacteriologic Examination (14)

## Culturing and Identifying Specimen

- **Culturing:**
  - **Determines if specimen contains *M. tuberculosis***
  - **Confirms diagnosis of TB disease**
- **All specimens should be cultured**



Colonies of *M. tuberculosis* growing on media

# **5. Bacteriologic Examination (15)**

## **Culturing and Identifying Specimen**

- **Step 1: Detect growth of mycobacteria**
  - **Solid media: 3 - 6 weeks**
  - **Liquid media: 4 - 14 days**
- **Step 2: Identify organism that has grown**
  - **Nucleic acid probes: 2 - 4 hours**
  - **Biochemical tests: 6 - 12 weeks**

# 5. Bacteriologic Examination (16)

## Culturing and Identifying Specimen

- **Positive culture: *M. tuberculosis* identified in patient's culture**
  - **Called *M. tuberculosis* isolate**
  - **Confirms diagnosis of TB disease**



# 5. Bacteriologic Examination (17)

## Culturing and Identifying Specimen

- **Negative culture: *M. tuberculosis* NOT identified in patient's culture**
  - **Does not rule out TB disease**
  - **Some patients with negative cultures are diagnosed with TB based on signs and symptoms**

# **5. Bacteriologic Examination (18)**

## **Culturing and Identifying Specimen**

- **Bacteriological examinations are important for assessing infectiousness and response to treatment**
- **Specimens should be obtained monthly until 2 consecutive cultures are negative**
- **Culture conversion is the most important objective measure of response to treatment**

# 5. Bacteriologic Examination (19)

## Drug Susceptibility Testing

- **Conducted when patient is first found to have positive culture for TB**
- **Determines which drugs kill tubercle bacilli**
- **Tubercle bacilli killed by a particular drug are susceptible to that drug**
- **Tubercle bacilli that grow in presence of a particular drug are resistant to that drug**

# 5. Bacteriologic Examination (20)

## Drug Susceptibility Testing

- Tests should be repeated if:
  - Patient has positive culture after 3 months of treatment; or
  - Patient does not get better



Drug susceptibility testing on solid media

# 5. Bacteriologic Examination (21)

## Types of Drug-Resistant TB

<b>Mono-resistant</b>	<b>Resistant to any one TB treatment drug</b>
<b>Poly-resistant</b>	<b>Resistant to at least any two TB drugs (but not both isoniazid and rifampin)</b>
<b>Multidrug-resistant (MDR TB)</b>	<b>Resistant to at least isoniazid and rifampin, the two best first-line TB treatment drugs</b>
<b>Extensively drug-resistant (XDR TB)</b>	<b>Resistant to isoniazid and rifampin, PLUS resistant to any fluoroquinolone AND at least 1 of the 3 injectable second-line drugs (e.g., amikacin, kanamycin, or capreomycin)</b>

# Culture Specimen

## Study Question 3.33

**Why is it necessary to culture a specimen?**

*(pg. 65)*

**It is necessary to culture a specimen to determine whether the specimen contains *M. tuberculosis* and to confirm diagnosis of TB disease.**

# Culture Specimen

## Study Question 3.34

**What does a positive culture for *M. tuberculosis* mean? How is this important for the TB diagnosis? (pg. 65)**

**It means that *M. tuberculosis* has been identified in a patient's culture. A positive culture for *M. tuberculosis* confirms the diagnosis of TB disease.**

# **Drug Susceptibility Study Question 3.35**

**Why are drug susceptibility tests done? (pg. 65)**

**To determine which drugs will kill the tubercle bacilli that are causing disease in a particular patient. Test results can help clinicians choose the appropriate drugs for each patient.**



# Drug Susceptibility Study Question 3.36

**How often should drug susceptibility tests be done?** (pg. 65)

- Should be done when the patient is first found to have a positive culture for *M. tuberculosis*
- Tests should be repeated if a patient has a positive culture for *M. tuberculosis* after 3 months of treatment or if a patient is not getting better

# Reporting TB Cases

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# Reporting TB Cases

- TB programs report TB cases to CDC using a standard case report form called the *Report of Verified of Case of Tuberculosis (RVCT)*

– All cases that meet criteria are called verified TB cases

REPORT OF VERIFIED CASE OF TUBERCULOSIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FORM APPROVED OMB NO. 0920-0001 Exp. Date 06/30/2014

1. Date Reported  
Month Day Year

2. Date Submitted  
Month Day Year

3. Case Numbers  
Year Reported (YYYY) State Code Locally Assigned Identification Number  
State Case Number City/County Case Number  
Linking State Case Number Linking State Case Number

4. Reporting Address for Case Counting  
City Within City Limits (select one) Yes No  
County ZIP CODE

5. Count Status (select one)  
Countable TB Case  
Count as a TB case  
Noncountable TB Case  
Verified Case: Counted by another U.S. area (e.g., county, state)  
Verified Case: TB treatment initiated in another country. Specify  
Verified Case: Recurrent TB within 12 months after completion of therapy

6. Date Counted  
Month Day Year

7. Previous Diagnosis of TB Disease (select one)  
Yes No  
If YES, enter year of previous TB disease diagnosis:

8. Date of Birth  
Month Day Year

9. Sex at Birth (select one)  
Male Female

10. Ethnicity (select one)  
Hispanic or Latino  
Not Hispanic or Latino

11. Race (select one or more)  
American Indian or Alaska Native  
Asian: Specify  
Black or African American  
Native Hawaiian or Other Pacific Islander: Specify  
White

12. Country of Birth  
"U.S.-born" (or born abroad to a parent who was a U.S. citizen)  
Yes No  
Country of birth: Specify

13. Month-Year Arrived in U.S.  
Month Year

14. Pediatric TB Patients (<15 years old)  
Country of Birth for Primary Guardian(s): Specify  
Guardian 1  
Guardian 2  
Patient lived outside U.S. for >2 months? Yes No Unknown  
If YES, list countries, specify:

15. Status at TB Diagnosis (select one)  
Alive Dead  
If DEAD, enter date of death: Month Day Year  
If DEAD, was TB a cause of death? (select one)  
Yes No Unknown

16. Site of TB Disease (select all that apply)  
Pulmonary Bone and/or Joint  
Pleural Genitourinary  
Lymphatic: Cervical Meningeal  
Lymphatic: Intrathoracic Peritoneal  
Lymphatic: Axillary Other: Enter anatomic code(s) (see list)  
Lymphatic: Other Site not stated  
Lymphatic: Unknown  
Laryngeal

Public reporting burden of this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC, Project Clearance Officer, 1600 Clifton Road, NE D-74, Atlanta, GA 30333, ATTN: PPA (0920-0001). Do not send the completed form to this address.

Information contained on this form which would permit identification of any individual has been collected with a guarantee that it will be held in strict confidence, will be used only for surveillance purposes, and will not be disclosed or released without the consent of the individual in accordance with section 309(c) of the Public Health Service Act (42 U.S.C. 242c).

CDC 72-5A, Rev 09/15/2008 CS 121321 set Copy REPORT OF VERIFIED CASE OF TUBERCULOSIS Page 1 of 3

# Criteria for Reporting TB Cases (1)

**Cases that meet one of these four sets of criteria are counted as verified TB cases:**

- 1. Patient has positive culture for *M. tuberculosis***
- 2. Patient has positive NAA test for *M. tuberculosis***
  - NAA test must be accompanied by culture for mycobacteria species**

# Criteria for Reporting TB Cases (2)

- 3. Patient has positive AFB smear, but culture has not or cannot be done**
- 4. In the absence of laboratory confirmation, patient has:**
  - Positive TST reaction**
  - Other signs and symptoms of TB disease**
  - Been treated with 2 or more TB drugs**
  - Been given a complete diagnostic evaluation**

# Criteria for Reporting TB Cases (3)

- **Cases that do not meet any of these sets of criteria may be counted as a verified TB case if health care provider has decided to treat the patient for TB disease**

# Case Studies

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# Module 3: Case Study 3.1

Which of the following patients have a positive TST reaction? Circle the best answer(s). (pg. 17)

- a. Mr. West, 36 yrs. old, HIV infected, 8 mm induration
- b. Ms. Hernandez, 26 yrs. old, native of Mexico, 7 mm induration
- c. Ms. Jones, 56 yrs. old, diabetic, 12 mm induration
- d. Mr. Sung, 79 yrs. old, nursing home resident, 11 mm induration
- e. Mr. Williams, 21 yrs. old, no known risk factors, 13 mm induration
- f. Mr. Marcos, 42 yrs. old, chest x-rays findings suggestive of previous TB, 6 mm induration
- g. Ms. Rayle, 50 yrs. old, husband has pulmonary TB, 9 mm of induration



## **Module 3: Case Study 3.2 (1)**

**A 30 year-old man who recently immigrated from India is given a TST and found to have 14mm of induration. He reports that he was vaccinated with BCG as a child. He also says that his wife was treated for pulmonary TB disease last year. (pg. 20)**

## **Module 3: Case Study 3.2 (2)**

**How should this man's results be interpreted?**

- **Positive reaction to TST**
- **Should be further evaluated for LTBI or TB disease**

**What factors make it more likely that this man's positive reaction is due to TB infection?**

- **From area of the world where TB is common**
- **Wife had pulmonary TB**

## **Module 3: Case Study 3.3 (1)**

**Mr. Bell comes to the TB clinic for a TST. He believes that he has been exposed to TB, and he knows he is at high risk for TB because he is HIV infected. He is given a TST, and his reaction is read 48 hours later as 0 mm of induration. (pg. 25)**

# Module 3: Case Study 3.3 (2)

**What are 3 ways to interpret this result?**

- **May not have TB infection**
- **May be anergic**
- **It may be less than 8–10 weeks since he was exposed to TB**

## **Module 3: Case Study 3.4 (1)**

**Ms. Wilson is a 60 year-old nurse. When she started a job at the local hospital, she was given a TST, her first test in 25 years. Her reaction was read 48 hours later as 0 mm induration. Six months later, she was retested as part of the TB testing program in the unit where she works. Her skin test reaction was read 48 hours later as 11 mm of induration. (pg. 32)**

# Module 3: Case Study 3.4 (2)

**What are 2 ways to interpret this result?**

- **She was exposed to TB sometime in the 6 months between her first and second skin tests**
- **Booster phenomenon**

# Module 3: Case Study 3.5 (1)

**Mr. Lee has a cough and other symptoms of TB disease, and he is evaluated with a chest x-ray. However, he is unable to cough up any sputum on his own for the bacteriologic examination. (pg. 52)**

# **Module 3: Case Study 3.5 (2)**

**What should be done?**

**Other techniques can be used to obtain sputum. First, clinicians can try to obtain an induced sputum sample. If they cannot obtain the sample, a bronchoscopy or gastric washing may be done.**



# Module 3: Case Study 3.6 (1)

**Ms. Thompson gave three sputum specimens, which were sent to the laboratory for smear examination and culture. The smear results were reported as 4+, 3+, and 4+. (pg. 56)**

## **Module 3: Case Study 3.6 (2)**

**What do these results tell you about Ms. Thompson's diagnosis and her infectiousness?**

- **Results show that Ms. Thompson's sputum specimens contain many acid-fast bacilli**
- **Smears are positive, clinicians should suspect that she has TB disease and should consider her infectious**
- **It is possible that the AFB are mycobacteria other than tubercle bacilli**
- **Diagnosis cannot be proven until culture results are available**

# Module 3: Case Study 3.7 (1)

**Mr. Sagoo has symptoms of TB disease and a cavity on his chest x-ray, but all of his sputum smears are negative for acid-fast bacilli. (pg. 57)**

## Module 3: Case Study 3.7 (2)

**Does this rule out the diagnosis of pulmonary TB disease?**

**No**

**Why or why not?**

***M. tuberculosis* may grow in the cultures even though there were no acid-fast bacilli on the smear. Mr. Sagoo's symptoms and his abnormal chest x-ray suggest that he does have pulmonary TB disease.**

# Module 3: Case Study 3.8 (1)

**In the public health clinic, you see a patient, Ms. Sanchez, who complains of weight loss, fever, and a cough of 4 weeks' duration. When questioned, she reports that she has been treated for TB disease in the past and that she occasionally injects heroin. (pg. 66)**

## **Module 3: Case Study 3.8 (2)**

**What parts of Ms. Sanchez's medical history lead you to suspect TB disease?**

- **Symptoms of TB disease (weight loss, fever, persistent cough)**
- **Past treatment for TB disease**
- **History of injecting illegal drugs**

**What diagnostic tests should be done?**

- **Chest x-ray**
- **Sputum smear and culture**
- **Drug susceptibility testing**