

TEACHER KEY

Unit 3: Diagnosis

Activity 1: Types of Diagnostic Tools

Description:

Students will read the online exhibition section “Diagnosis” and complete an activity sheet that asks them to correctly name diagnostic techniques based on provided descriptions, and to assess provided test results for the presence of TB.

Time:

Exhibition review: 20 minutes

Activity Sheet: 30 minutes + 15 minutes review

Objectives:

- To understand that there are a range of diagnostic tests that are used to identify TB infection.
- To demonstrate comprehension about how each diagnostic test works.
- To apply knowledge about the diagnostic tests.

Curriculum Links:

Reading	1. Reading for Meaning	1.4 demonstrate understanding of a variety of texts by summarizing important ideas and citing supporting details
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Materials:

Online exhibition [Fighting for Breath: Stopping the TB epidemic](http://museumofhealthcare.ca/explore/exhibits/breath/) :

<http://museumofhealthcare.ca/explore/exhibits/breath/>

Handout

Procedure:

1. Ask students to read-through the exhibition page Diagnosis.
2. Provide students with the worksheet and ask them to complete it. It is recommended that students have access to the exhibition while completing the work-sheet.
3. Review the work-sheet with the students and clarify any common misconceptions.

Background Info:

Introductory Text:

There are a number of **diagnostic** tests used to find out whether a person has been infected with tuberculosis at some point, meaning they may have a **latent** case of the disease or may have cured themselves, or whether they currently have the active disease. The nature of tuberculosis, its ability to lay dormant within the body for years, means that determining that a person has been infected with tuberculosis is not enough to know whether they are presently capable of transmitting the disease. Multiple types of tests are often required to accurately **diagnose** cases of tuberculosis.

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Past exposure to tuberculosis, and the current possibility of either **latent** or active TB, is indicated by skin and blood tests that measure the body's immune response to TB **antigens**. These tests indicate only that an individual has once had the TB bacteria in their system, not whether the disease is still present. They are useful insofar as a negative result is a fairly accurate indicator that the individual does not have TB. A positive result requires further diagnosis to conclusively identify whether it is a case of active or **latent** TB.

Active tuberculosis is suggested by presentation of the signs and symptoms of TB, as well as by tests that seek to find tuberculosis bacteria in sputum. Though such tests have taken weeks to conduct in the past, making them an imperfect **diagnostic** tool, new technologies have made the process of identifying *Mycobacterium tuberculosis* move much more quickly.

Testing for Latent Infection

- **Mantoux Skin Test (tuberculin) (*4 slides)**

A skin test is most commonly used to test for tuberculosis. A small amount, 0.1mL, of **purified protein derivative (PPD) tuberculin** is injected **intradermally**, under the skin of the forearm.

Within 48-72 hours of the injection, the site will be examined for reactions, such as swelling, hardness, and blistering by a health care professional. They will measure the **induration** (raised area) and compare the measurement to standards, and patient history, to ascertain whether the reaction is a positive indication of infection.

For example, the American Center for Disease Control and Prevention notes that an **induration** of 5 millimeters is considered positive for persons with HIV, who have had organ transplant, or who have been in recent contact with an infected individual, while an **induration** of 10 millimeters is required for a positive result for recent immigrants, injection drug users, children under 4 years of age, and some lab personnel. For people with no known risk factors for TB an **induration** of 15 millimeters would be considered a positive result; however, such individuals would rarely be given a skin test.

If the body has been exposed to the tuberculosis bacteria it will likely react to this injection; however, the test only indicates that the individual has been exposed to tuberculosis, not whether they have the active disease or a **latent** infection. If the body does not react to the injection it is likely that TB infection is not present. Even if the test result is negative, more tests may be required if signs of tuberculosis are present (e.g. coughing, chest pain, fever). Similarly, some people may have false-positive results, in particular individuals who have been vaccinated by the BCG vaccine.

- **Blood Test / Interferon Gamma Release Assay (*2 slides)**

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TB blood tests, also called **interferon-gamma** release assays, measure the immune response to TB bacteria to assess whether infection or **latent** disease are likely. In this way these tests are similar to the skin tests.

A sample of whole blood is taken and sent to a laboratory, where it is exposed to **antigens** derived from *Mycobacterium tuberculosis*. White blood cells that recognize these **antigens** because of prior exposure to the bacteria will release **interferon-gamma** as part of their immune response (see Etiology – How it Works). The blood test measures the amount of **interferon-gamma** produced to assess whether the individual had been exposed to tuberculosis in the past.

Test results suggest the likelihood of infection only; diagnosis should also consider other test results and patient history. Blood tests provide more accurate results for individuals who have been vaccinated with BCG than do skin tests.

Testing for Active Disease

- **Symptoms** (*1 slide)

As is typically the case, one of the first **diagnostic** tools used by physicians to test for tuberculosis is patient history and an assessment of the signs and symptoms exhibited by the patient. The physician will review patient charts and speak with the patient about past activities, such as travel, lab work, or exposure to another infected person. They will also seek to find out whether the patient has been experiencing any of the typical signs of the disease, such as coughing, fever, night sweats, or paleness, or symptoms of the disease, such as weakness and chest pain. If these signs or symptoms are present, further testing for infection will be undertaken.

- **Chest X-ray** (*3 slides)

Chest x-rays have been used since the early twentieth century to diagnose cases of pulmonary tuberculosis.

Chest x-rays can show evidence of active tuberculosis, or scarring and **calcifications** that suggest that the bacteria have been contained by the body.

Further tests are needed to ascertain whether the disease is currently active or **latent**.

- **Smear microscopy (sputum examination)** (*2 slides)

Examination of **sputum** under a microscope can show the presence of bacteria. This method of testing for tuberculosis has been used since the 1880s. *Mycobacterium tuberculosis* are acid-fast bacteria, meaning that they will stain positive with special dyes. A sample of **sputum** secreted from the lungs can be applied to a slide and tested for the presence of acid-fast bacilli. Not all acid-fast bacilli are tuberculosis though, so a culture of the bacteria is necessary to confirm the diagnosis.

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The slide will be examined under a microscope for the presence of bacteria. Here, the tuberculosis bacteria are red. Their presence indicates active infection.

- **Cultures** (*2 slides)

In addition to viewing **sputum** samples under the microscope, such samples are usually also **cultured**, meaning allowed to grow in special incubators and mediums. This method of diagnosing tuberculosis has been used since Koch's discovery in the early 1880s.

The growth of bacteria colonies allows lab technicians and physicians to identify the type of bacteria that is present and make a positive identification of *Mycobacterium tuberculosis*. These colonies are also able to be tested for drug resistance, which helps facilitate the development of treatment plans for the patient.

The bacteria replicate very slowly, though, only once every twenty four hours, and take up to one month to form a colony. Because of this, new **diagnostic** tools that can identify the presence of the bacteria more quickly have been sought.

- **Molecular analysis – GeneXpert MTB/RIF** (*1 slide)

More recent advances in tuberculosis **diagnostics** have focused on the detection of nucleic acids, RNA and DNA, specific to *M. tuberculosis* within **sputum** samples. Such samples can be amplified using **polymerase chain reaction (PCR)** to facilitate their identification, and studied to detect also gene mutations that indicate drug resistance. The advantage of this type of testing is that it takes only 24-48 hours to obtain results, as compared to cultures, which can take several weeks.

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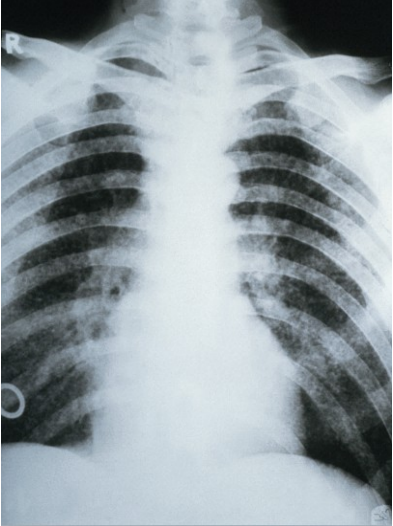

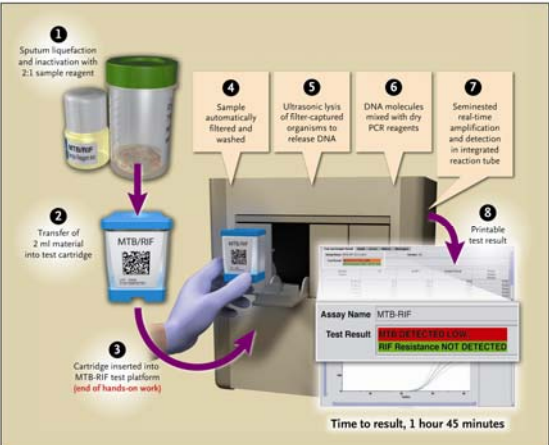
TB Unit 3: Diagnosis

ANSWER KEY: Identifying Latent and Active TB Infections

1. For each of the following images indicate
 - a) the test it represents
 - b) whether the test is for latent or active TB, and
 - c) briefly describe how the test works.

<p style="text-align: center;">Symptoms of Tuberculosis</p> <p>(Established) pulmonary tuberculosis Productive cough</p> <p>Primary pulmonary tuberculosis Structural abnormalities</p> <p>Tuberculous pleuritis Chest pain</p> <p>Extrapulmonary tuberculosis Common sites: Meninges Lymph nodes Bone and joint sites Genitourinary tract</p> <p>Legend: Grey lines = More specific Colored lines = Overlapping</p>	<p>a) Patient History / Symptoms</p> <p>b) Active</p> <p>c) The doctor discusses with the patient how they have been feeling, recent trips or contact with other sick people, and family history in order to decide whether tuberculosis is a likely fit for the patient's signs and symptoms.</p>
<p style="text-align: center;">CDC PHIL #4428, CDC/Dr. George Kubica</p>	<p>a) Culture</p> <p>b) Active</p> <p>c) A sample of sputum is sent to a lab where the bacteria contained within the sample are allowed to grow. Once the bacteria colony has multiplied in size the type of bacteria is identified.</p>
<p style="text-align: center;">CDC PHIL #6806, CDC/Gabrielle Benenson</p>	<p>a) Skin Test</p> <p>b) Latent</p> <p>c) Tuberculin is injected under the skin. If the patient has been exposed to TB previously, their immune system will react to this tuberculin injection, causing swelling and redness. The severity of the reaction indicates whether the patient has been infected with TB before.</p>

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 <p style="text-align: right; font-size: small;">Wellcome Images</p>	<p>a) X-Rays</p> <p>b) Active</p> <p>c) Images of the lungs will show whether tubercles are present, indicating active infection. They can also show scarring in the lungs from previous tubercles.</p>
 <p style="text-align: center; font-size: small;">© Ocean/Corbis, 42-15559904</p>	<p>a) Blood-test</p> <p>b) Latent</p> <p>c) A blood sample is exposed to antigens from the <i>Mycobacterium tuberculosis</i> bacteria. If the patient has been infected by tuberculosis before their immune system (including white blood cells) will react to these antigens by releasing interferon-gamma. The amount of interferon-gamma is able to be measured, indicating the likelihood of previous infection.</p>
 <p>From <i>The New England Journal of Medicine</i>, C. C. Boehme, P. Nabeta, D. Hillemann et al., “Rapid Molecular Detection of Tuberculosis and Rifampin Resistance,” 363 n.11 Copyright © 2010 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.</p>	<p>a) Molecular Analysis</p> <p>b) Active</p> <p>c) A sputum sample is taken and placed into a machine, which analyses the DNA in the sample to identify any bacteria present.</p>

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2. You're the Doctor! Below you will find a number of test results. Consider these results carefully to decide whether your patient has active TB, latent TB, or no TB infection, and/or whether you would like to conduct another test to verify your diagnosis.

a) Patient A is complaining of night sweats, weakness, and of coughing up blood. She is a 34 year old immigrant from South Africa whose husband was recently diagnosed with active TB.

Active (symptoms)

Conduct further tests to confirm: X-Ray, Cultures or Molecular Analysis

b) Patient B had a positive skin test, so you collected a sputum sample and sent it to the lab. The lab technicians report seeing acid-fast bacilli under the microscope.

Active

Because not all acid-fast bacilli are TB, you should complete a culture or molecular analysis to confirm.

c) Patient C has applied to immigrate to Canada. As required, they have provided an x-ray of their lungs for examination. The x-ray shows some scarring and calcifications in the upper lungs.

Latent

Scarring and calcifications may indicate that TB has been active in the lungs at some point.

To ensure that the TB is latent, it would be a good idea to take a sputum sample for testing.

d) Patient D presented with the classic signs and symptoms of tuberculosis, so you drew a blood sample and sent it to the lab for testing. Results show that a significant amount of interferon-gamma was released upon testing.

Inconclusive--The high-amounts of interferon-gamma released indicate that the patient's immune system recognizes the TB bacteria, but does not indicate whether the TB infection is latent or active.

You must conduct further testing – X-Rays, Cultures, or Molecular Analysis – to confirm whether the disease is active or not.

e) Patient E presented with a persistent fever and cough after travelling in South America for three months. You gave a skin test that had a negative result. The cough and fever went away after a 2 week course of antibiotics and have not returned in the past six months.

No TB indicated.

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f) Patient F was treated for TB with antibiotics two years ago. Recently they have complained of persistent cough and a pain in their chest. You collect a sputum sample and send it to the lab for culture. Results show the presence of *Mycobacterium tuberculosis*.

Active TB