

TUBERCULOSIS (TB) SCREENING AND TESTING

Background: TB is a communicable disease caused by *Mycobacterium tuberculosis*, or the tubercle bacillus. It is spread primarily by tiny airborne particles (droplet nuclei) expelled by a person who has infectious TB. If another person inhales air containing these droplet nuclei, transmission may occur. Although the majority of TB cases are pulmonary, TB can occur in almost any anatomical site. TB can cause disability and/or death if not detected and treated appropriately.

Targeted High-Risk Groups for TB Screening:

Close contacts of persons with active TB	Children exposed to adults in high-risk categories
Foreign-born persons from areas where TB is common	Persons who inject illicit drugs
Residents and workers in high-risk congregate settings	High-risk racial or ethnic minority populations defined locally as having an increased prevalence of TB
Health care workers who serve high-risk clients	
Medically under-served, low-income populations	
Persons with certain medical conditions, such as HIV infection, diabetes, cancer, etc.	

Signs and Symptoms of TB:

Pulmonary symptoms

Productive, prolonged cough (≥ 3 weeks)
Chest pain
Hemoptysis

Systemic symptoms

Fever	Loss of appetite
Chills	Weight loss
Night sweats	Becomes easily fatigued

Other symptoms may occur depending on the part of the body affected.

Standard TB Skin Testing Method: Mantoux (intradermal). Multiple puncture tests such as “Tine” are not recommended. Health care workers trained to perform the Mantoux intradermal test should administer TB skin tests.

PPD testing has no effect on the response to MMR vaccination. If tuberculin skin testing is needed at the same time as administration of measles-containing vaccine, PPD and vaccine can be administered at the same visit. If measles-containing vaccine has been administered recently, PPD screening should be delayed at least 4 weeks after vaccination.

Reading TB Skin Test Results:

A trained health care worker should read the reaction to the Mantoux test 48 to 72 hours after the injection. Patients should never be allowed to read their own tuberculin skin test results. If a patient fails to show up for the scheduled reading, a positive reaction may still be measurable up to 1 week after testing. However, if a patient who fails to return within 72 hours has a negative test, tuberculin testing should be repeated.

Classifying the Tuberculin Reaction

Interpretation of a positive tuberculin skin test (TST) has been somewhat controversial in Michigan. Many providers are currently using the 10mm cut off as a determinate of a positive TST in individuals without risk factors. The Michigan Department of Community Health TB Program along with the Michigan Advisory Committee for the Elimination of TB (MIACET) have recently issued recommendations based on the Centers for Disease Control and Prevention (CDC) recommendations which are as follows:

≥ 5 mm is classified as positive in:

- HIV-positive persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest x-ray consistent with old healed TB
- Patients with organ transplants and other immunosuppressed patients

≥ 10 mm is classified as positive in:

- Recent arrivals from high-prevalence countries
- Injection drug users
- Residents and employees of high risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children < 4 years of age, or children and adolescents exposed to adults in high-risk categories

≥ 15 mm is classified as positive in persons with no known risk factors for TB

Skin Test Sensitivity:

Alliance for Immunization in Michigan
2007 AIM Kit – Childhood Immunization Section

January 7, 2008

It may take 2-10 weeks to develop a positive reaction after infection

Active TB Disease versus Latent TB Infection:

Persons who are infected with tuberculosis, but who do not have TB disease cannot spread the infection to other people. TB infection in a person who does not have TB disease is not considered a case of TB and is often referred to as having latent TB infection (LTBI). In some people, the TB bacilli overcome the defenses of the immune system and begin to multiply, resulting in the progression from TB infection to TB disease. This process may occur soon after or many years after infection. In the United States, unless they are treated, approximately 5% of persons who have been infected with tuberculosis will develop TB disease in the first year or two after infection and another 5% will develop disease sometime later in life.

Reporting Requirements:

Any suspected or confirmed case of TB disease should be reported by their physician within 24 hours of diagnosis to the local health department. Laboratories are also required to report. Individuals with positive TB skin tests who are not infectious (latent TB infection) are not required to be reported.

Laboratory Services Available from Michigan Department of Community Health (these tests are available at no cost):

- sputum smears and/or culture
- drug susceptibilities are performed on all TB specimens
- direct amplification testing

Reminders:

- Persons with a history of a positive reaction to TB skin testing should not be re-tested. Persons with positive TB skin test results should have a chest x-ray as part of the initial evaluation of their tuberculosis skin test, if negative, repeat chest x-rays are not needed unless symptoms develop that could be attributed to TB. Persons with a history of positive TB skin testing who develop signs and symptoms suggestive of TB should undergo a medical evaluation including a chest x-ray.
- Pregnant women should be targeted for tuberculin skin testing only if they have a specific risk factor for latent TB infection or for progression of LTBI to disease.
- Tuberculin skin testing is not contraindicated for BCG vaccinated persons.

Resources Available from your Local Health Department:

- TB medication for county residents
- Medical assessment and treatment
- Consultation/advice
- TB skin test training may be available

Recommendations for TB Screening of Health Care Workers

- New employees with a history of negative skin tests:
 - Complete two-step testing
- New employee with a history of a positive TB skin test:
 - Complete a TB health questionnaire
 - Obtain a chest x-ray if a current (within 6 months) one is not available
- The employer shall offer tuberculin skin tests (TST) or blood assay *M. tuberculosis* (BAMT) annually to employees/health-care workers in settings where risk assessment has determined that employees/health-care workers will or will possibly be exposed to persons with TB disease or to clinical specimens that might contain *M. tuberculosis*.
- Established employee working in a facility with potential ongoing transmission, offer test every eight to ten weeks until the cause of transmission has been corrected and no additional evidence of ongoing transmission is apparent.
- Established employee with a history of positive test, complete annual health questionnaire (no annual chest x-ray)
- Employee with known exposure to TB, test immediately and again in eight to ten weeks.

Additional Resources:

- MDCH TB Control Program (517) 335-8165 or www.michigan.gov/tb
- www.michigantb.org
- www.cdc.gov/nchstp/tb/

Tuberculin Skin Testing

What is It?

The **Mantoux tuberculin skin test (TST)** is the standard method of determining whether a person is infected with *Mycobacterium tuberculosis*. Reliable administration and reading of the TST requires standardization of procedures, training, supervision, and practice.

How is the TST Administered?

The TST is performed by injecting 0.1 ml of tuberculin purified protein derivative (PPD) into the inner surface of the forearm. The injection should be made with a tuberculin syringe, with the needle bevel facing upward. The TST is an intradermal injection. When placed correctly, the injection should produce a pale elevation of the skin (a wheal) 6 to 10 mm in diameter.

How is the TST Read?

The skin test reaction should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will need to be rescheduled for another skin test.

The reaction should be measured in millimeters of the induration (palpable, raised, hardened area or swelling). The reader should not measure erythema (redness). The diameter of the indurated area should be measured across the forearm (perpendicular to the long axis).

How Are TST Reactions Interpreted?

Skin test interpretation depends on two factors:

- Measurement in millimeters of the induration
- Person's risk of being infected with TB and of progression to disease if infected

Classification of the Tuberculin Skin Test Reaction

An induration of **5 or more millimeters** is considered positive in

- HIV-infected persons
- A recent contact of a person with TB disease
- Persons with fibrotic changes on chest radiograph consistent with prior TB
- Patients with organ transplants
- Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-alpha antagonists)

An induration of **10 or more millimeters** is considered positive in

- Recent immigrants (< 5 years) from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children < 4 years of age
- Infants, children, and adolescents exposed to adults in high-risk categories

An induration of **15 or more millimeters** is considered positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.

What Are False-Positive Reactions?

Some persons may react to the TST even though they are not infected with *M. tuberculosis*. The causes of these false-positive reactions may include, but are not limited to, the following:

- Infection with nontuberculosis mycobacteria
- Previous BCG vaccination
- Incorrect method of TST administration
- Incorrect interpretation of reaction
- Incorrect bottle of antigen used

What Are False-Negative Reactions?

Some persons may not react to the TST even though they are infected with *M. tuberculosis*. The reasons for these false-negative reactions may include, but are not limited to, the following:

- Cutaneous anergy (*anergy* is the inability to react to skin tests because of a weakened immune system)
- Recent TB infection (within 8-10 weeks of exposure)
- Very old TB infection (many years)
- Very young age (less than 6 months old)
- Recent live-virus vaccination (e.g., measles and smallpox)
- Overwhelming TB disease
- Some viral illnesses (e.g., measles and chicken pox)
- Incorrect method of TST administration
- Incorrect interpretation of reaction

Who Can Receive a TST?

Most persons can receive a TST. TST is contraindicated only for persons who have had a severe reaction (e.g., necrosis, blistering, anaphylactic shock, or ulcerations) to a previous TST. It is not contraindicated for any other persons, including infants, children, pregnant women, persons who are HIV-infected, or persons who have been vaccinated with BCG.

How Often Can TSTs Be Repeated?

In general, there is no risk associated with repeated tuberculin skin test placements. If a person does not return within 48-72 hours for a tuberculin skin test reading, a second test can be placed as soon as possible. There is no contraindication to repeating the TST, unless a previous TST was associated with a severe reaction.

What is a Boosted Reaction?

In some persons who are infected with *M. tuberculosis*, the ability to react to tuberculin may wane over time. When given a TST years after infection, these persons may have a false-negative reaction. However, the TST may stimulate the immune system, causing a positive, or boosted reaction to subsequent tests. Giving a second TST after an initial negative TST reaction is called two-step testing.

Why is Two-Step Testing Conducted?

Two-step testing is useful for the initial skin testing of adults who are going to be retested periodically, such as health care workers or nursing home residents. This two-step approach can reduce the likelihood that a boosted reaction to a subsequent TST will be misinterpreted as a recent infection.

Can TSTs Be Given To Persons Receiving Vaccinations?

Vaccination with live viruses may interfere with TST reactions. For persons scheduled to receive a TST, testing should be done as follows:

- Either on the same day as vaccination with live-virus vaccines or 4-6 weeks after the administration of the live-virus vaccine
- At least one month after smallpox vaccination

Additional Information

American Thoracic Society and CDC. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000; 161. www.thoracic.org/adobe/statements/tbadult1-20.pdf

CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005; 54 (No. RR-17). www.cdc.gov/mmwr/pdf/rr/rr5417.pdf

CDC. Mantoux Tuberculin Skin Test: Training Materials Kit (2003).

CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000; 49 (No. RR-6). www.cdc.gov/MMWR/PDF/rr/rr4906.pdf

THE MANTOUX TUBERCULIN SKIN TEST

A GUIDE FOR PROVIDERS



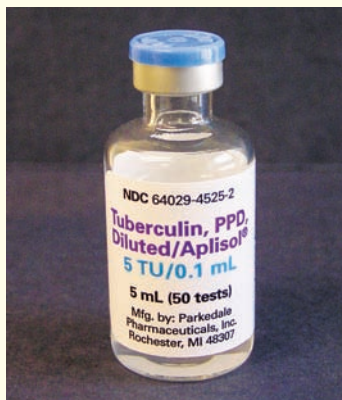
Talk to your patient about:

- Taking care of the injection site
- Returning in 48-72 hours to have test read
- Who to contact with questions or problems

ADMINISTER THE TEST

Prepare the Materials

1. **Wash** hands and put on gloves.
2. **Explain** to patient why test is being done and how it will be performed.
3. **Check** expiration/opening date on PPD vial.
4. **Place** patient's arm on flat surface, exposing palm side surface of forearm.
5. **Locate** injection site (2-4 inches below elbow; no scars, bumps, veins).
6. **Clean** injection site with alcohol swab.
7. **Wipe** top of vial with new alcohol swab.
8. **Place** vial on flat surface and insert syringe into vial.
9. **Invert** vial, keeping needle tip below fluid level.
10. **Pull** back plunger, drawing in slightly more than 0.1 ml PPD solution.
11. **Remove** syringe from vial and tap lightly to dispel air bubbles.
12. **Hold** syringe point up and expel air/excess fluid, leaving exactly 0.1 ml PPD solution in syringe.



Keep the PPD Vial Cool

- Always store in refrigerator
- Place in cooling container when in use

Inject the PPD Solution

1. **Stretch** skin of injection site with the thumb of your non-dominant hand.
2. **Insert** needle intradermally, bevel up, at a 5-15 degree angle.
3. **Inject** the PPD solution slowly (you should feel firm resistance).
4. **Remove** needle (DO NOT RECAP) and discard immediately in sharps container.
5. **Ensure** 6-10 mm diameter wheal (measure using TST ruler).

If wheal < 6 mm, repeat test 2 inches from site, or on opposite arm. If wheal is still < 6 mm, talk to supervisor.



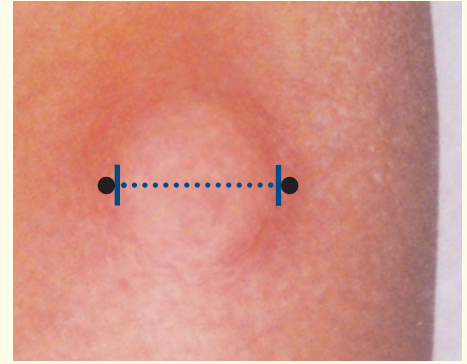
Educate Your Patient

1. **Educate** patient on possible reactions and care of the TST site.
2. **Document** each test on the patient card.
3. **Schedule** patient for an appointment to read the test in 48-72 hours.

READ THE RESULTS

Measure the Induration




1. **Inspect** visually for reaction at injection site.
2. **Palpate** for hard, dense, and raised formation (induration).
3. **Mark** opposite edges of induration with dots, using a black water mark pen.
4. **Measure** induration (not redness) **transversely**, from one marked edge to the other, using a TST ruler.
5. **Interpret** positive/negative results based on size of induration and risk factors (see chart below).
6. **Explain** meaning of positive/negative results and necessary follow-up.
7. **Give** patient literature and copy of TST results.
8. **Document** results in your medical records.



Measure induration with a TST ruler

Interpret the Test Results

The following measurements of induration are classified as positive, based on individual risk factors:

INDURATION DIAMETER	INDIVIDUAL RISK FACTORS
<p>≥5 mm</p> 	<p>Positive test result for:</p> <ul style="list-style-type: none"> ▪ Persons with HIV infection ▪ Recent contacts of persons with active TB disease ▪ Persons with evidence of old, healed TB lesions on chest X-rays ▪ Persons with organ transplants and other immunosuppressed persons, including those receiving prolonged corticosteroid therapy (the equivalent of >15 mg/d of prednisone for one month or more) and TNF-α blockers
<p>≥10 mm</p> 	<p>Positive test result for:</p> <ul style="list-style-type: none"> ▪ Persons who have immigrated within the past 5 years from areas with high TB rates* ▪ Injection drug users ▪ Persons who live or work in institutional settings where exposure to TB may be likely, such as hospitals, prisons, homeless shelters, SROs, and nursing homes ▪ Mycobacteriology laboratory personnel ▪ Persons with clinical conditions associated with increased risk of progression to active TB, including: silicosis; chronic renal failure; diabetes; more than 10% below ideal weight or BMI < 18.5; gastrectomy/jejunioileal bypass; some hematologic disorders (such as leukemia and lymphomas); and certain cancers (such as carcinoma of the head, neck, or lung, leukemias, and lymphomas) ▪ Children < 5 years, and children or adolescents exposed to adults in high-risk categories ▪ Persons with prolonged stay in areas with high TB rates*
<p>≥15 mm</p> 	<p>Positive test result for:</p> <ul style="list-style-type: none"> ▪ Persons at low risk for active TB disease for whom testing is not generally indicated

* Countries with high rates of TB include China, Dominican Republic, Ecuador, Haiti, Honduras, India, Mexico, Pakistan, Peru, Philippines, South Korea, and all of Africa.

For detailed information on the testing and treatment of latent TB infection in children and adults see: www.nyc.gov/html/doh/downloads/pdf/chi/chi25-4.pdf

ALWAYS WASH HANDS AND CHANGE GLOVES AFTER EACH PATIENT

QuantiFERON[®]-TB Gold Test

What is it?

The QuantiFERON[®]-TB Gold test (QFT-G) is a whole-blood test for use as an aid in diagnosing *Mycobacterium tuberculosis* infection, including latent tuberculosis infection (LTBI) and tuberculosis (TB) disease. This test was approved by the U.S. Food and Drug Administration (FDA) in 2005.

How does it work?

Blood samples are mixed with antigens (substances that can produce an immune response) and controls. For QFT-G, the antigens include mixtures of synthetic peptides representing two *M. tuberculosis* proteins, ESAT-6 and CFP-10. After incubation of the blood with antigens for 16 to 24 hours, the amount of interferon-gamma (IFN-gamma) is measured.

If the patient is infected with *M. tuberculosis*, their white blood cells will release IFN-gamma in response to contact with the TB antigens. The QFT-G results are based on the amount of IFN-gamma that is released in response to the antigens.

Clinical evaluation and additional tests (such as a chest radiograph, sputum smear, and culture) are needed to confirm the diagnosis of LTBI or TB disease.

What are the advantages?

- Requires a single patient visit to draw a blood sample.
- Results can be available within 24 hours.
- Does not boost responses measured by subsequent tests, which can happen with tuberculin skin tests (TST).
- Is not subject to reader bias that can occur with TST.
- Is not affected by prior BCG (bacille Calmette-Guérin) vaccination.

What are the disadvantages and limitations?

- Blood samples must be processed within 12 hours after collection while white blood cells are still viable.
- There are limited data on the use of QFT-G in children younger than 17 years of age, among persons recently exposed to *M. tuberculosis*, and in immunocompromised persons (e.g., impaired immune function caused by HIV infection or acquired immunodeficiency syndrome [AIDS], current treatment with immunosuppressive drugs, selected hematological disorders, specific malignancies, diabetes, silicosis, and chronic renal failure).
- Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of QFT-G.
- Limited data on the use of QFT-G to determine who is at risk for developing TB disease.

When should you use the test?

QFT-G can be used in all circumstances in which the tuberculin skin test (TST) is currently used, including contact investigations, evaluation of recent immigrants who have had BCG vaccination, and TB screening of health care workers and others undergoing serial evaluation for *M. tuberculosis*. However, caution should be used when testing certain populations because of limited data in the use of QFT-G.

Before the QFT-G is conducted, arrangements should be made with a qualified laboratory and courier service, if needed, to ensure prompt and proper processing of blood.

What are the steps in administering the test?

- Confirm arrangements for testing in a qualified laboratory and arrange for delivery of the blood sample in time for the laboratory to initiate testing within 12 hours of blood collection.
- Draw a sample of whole blood from patient into a tube with heparin anti-clotting agent, according to manufacturer's instructions.
- Schedule an appointment for the patient to receive test results and, if then needed, medical evaluation and possible treatment for TB disease or LTBI.

How do you interpret test results?

Interpretation of QFT-G results is based on IFN-gamma concentrations in test samples. Each QFT-G result and its interpretation should be considered in conjunction with other epidemiological, historical, physical, and diagnostic findings.

A positive result suggests that *M. tuberculosis* infection is likely; a negative result suggests that infection is unlikely; and indeterminate result suggests QFT-G results cannot be interpreted as a result of low mitogen response or high background response.

A diagnosis of LTBI requires that TB disease be excluded by medical evaluation, which should include checking for signs and symptoms suggestive of TB disease, a chest radiograph, and, when indicated, examination of sputum or other clinical samples for the presence of *M. tuberculosis*.

Additional Information

Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis and Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005; 54 (No. RR-15).

<http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf>

Centers for Disease Control and Prevention. Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005. *MMWR* 2005; 54 (No. RR-17).

<http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf>

Get-QFT (Locator site for QuantiFERON®-TB Gold)

<http://www.quantiferon.com>*

* This link is provided solely as a service to our users. It does not constitute an endorsement of the QFT-Gold testing institutions included on the website by CDC or the Federal Government, and none should be inferred. CDC is not responsible for the content found at this link.

The Difference Between Latent TB Infection and Active TB Disease

What Is TB?

Tuberculosis (TB) is a disease caused by a germ called *Mycobacterium tuberculosis* that is spread from person to person through the air. TB usually affects the lungs, but it can also affect other parts of the body, such as the brain, the kidneys, or the spine. When a person with infectious TB coughs or sneezes, droplet nuclei containing *M. tuberculosis* are expelled into the air. If another person inhales air containing these droplet nuclei, he or she may become infected. However, not everyone infected with TB bacteria becomes sick. As a result, two TB-related conditions exist: latent TB infection and active TB disease.

What Is Latent TB Infection?

Persons with latent TB infection do not feel sick and do not have any symptoms, but usually have a positive reaction to the tuberculin skin test or QuantiFERON®-TB Gold test. They are infected with *M. tuberculosis*, but do not have active TB disease. **Persons with latent TB infection are not infectious and cannot spread TB infection to others.**

Overall, about 5 to 10% of infected persons will develop active TB disease at some time in their lives. About half of those people who develop active TB will do so within the first two years of infection. For persons whose immune systems are weak, especially those with HIV infection, the risk of developing active TB disease is considerable higher than for persons with normal immune systems.

Of special concern are persons infected by someone with extensively drug-resistant TB (XDR TB) who later develop active TB disease; these persons will have XDR TB, not regular TB disease.

A person with latent TB infection (LTBI)

Usually has a skin test or blood test result indicating TB infection

Has a normal chest x-ray and a negative sputum test

Has TB bacteria in his/her body that are alive, but inactive

Does not feel sick

Cannot spread TB bacteria to others

Needs treatment for latent TB infection to prevent TB disease; however, if exposed and infected by a person with multidrug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option

What Is Active TB Disease?

In some people, TB bacteria overcome the defenses of the immune system and begin to multiply, resulting in the progression from latent TB infection to active TB disease. Some people develop active TB disease soon after infection, while others develop active TB disease later when their immune system becomes weak.

The general symptoms of active TB disease include

- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue
- Chills

The symptoms of TB of the lungs include

- Coughing for 3 weeks or longer
- Hemoptysis (coughing up blood)
- Chest pain

What Is Active TB Disease? (cont.)

Other symptoms depend on the part of the body that is affected.

Persons with active TB disease are considered infectious and may spread TB bacteria to others. If TB disease is suspected, persons should be referred for a complete medical evaluation. If it is determined that a person has active TB disease, therapy is given to treat it. TB disease is a serious condition and can lead to death if not treated.

A person with active TB disease
Usually has a skin test or blood test result indicating TB infection
May have an abnormal chest x-ray, or positive sputum smear or culture
Has active TB bacteria in his/her body
Usually feels sick and may have symptoms such as coughing, fever, and weight loss
May spread TB bacteria to others
Needs treatment to treat active TB disease

Additional Information

American Thoracic Society (ATS) and CDC. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000; 161.

www.thoracic.org/adobe/statements/tbadult1-20.pdf

ATS, CDC, and Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; 52 (No. RR-11).

www.cdc.gov/MMWR/PDF/rr/rr5211.pdf

CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000; 49 (No. RR-6).

www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm

CDC. Multidrug-Resistant Tuberculosis (MDR TB). <http://www.cdc.gov/tb/pubs/tbfactsheets/mdrtb.htm>

CDC. Extensively Drug-Resistant Tuberculosis (XDR TB). <http://www.cdc.gov/tb/pubs/tbfactsheets/xdrtb.htm>