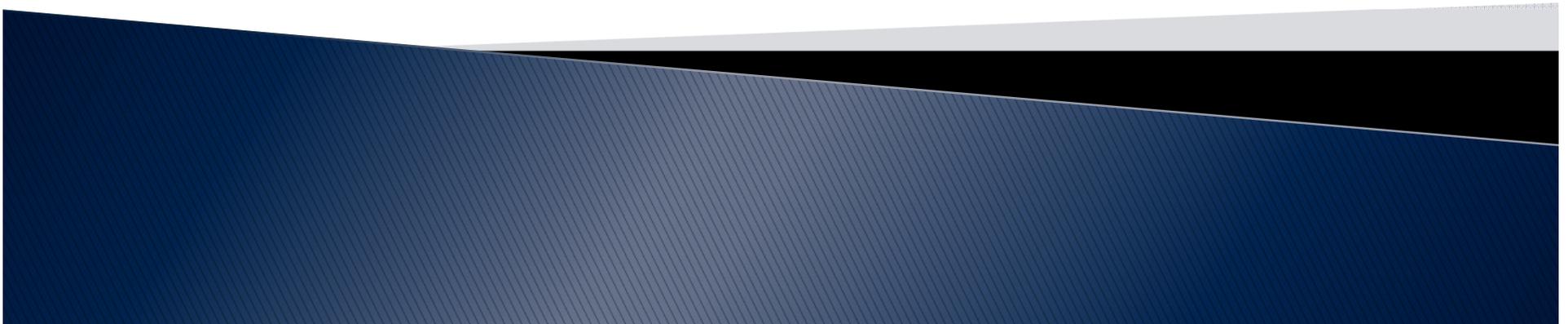


# TB: Interpretation of Tests and Risk Assessment

Dee Pritchet, TB Controller –  
North Dakota Department of Health



# Objectives

Participants will be able to:

- ❑ 1) define the cause of tuberculosis (TB), progression and management of the disease
- ❑ 2) describe TB Screening procedures for healthcare workers
- ❑ 3) identify populations at risk for TB



# What is tuberculosis?

- » a) A virus
- b) A bacteria
- c) A fungus

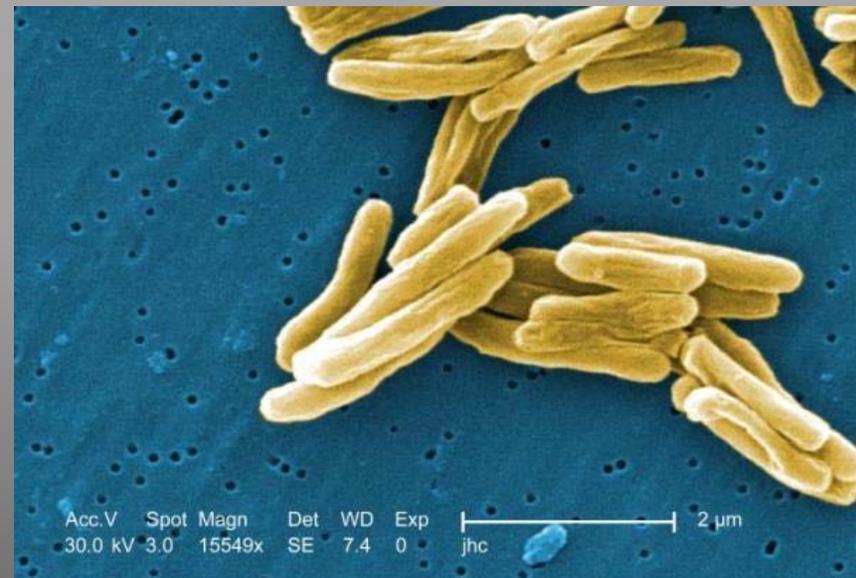
# Tuberculosis (TB)

- ▶ TB is caused by a bacteria – *Mycobacterium tuberculosis*
- ▶ Other names for TB are:
  - consumption
  - wasting disease
  - the white plague
  - Koch's disease

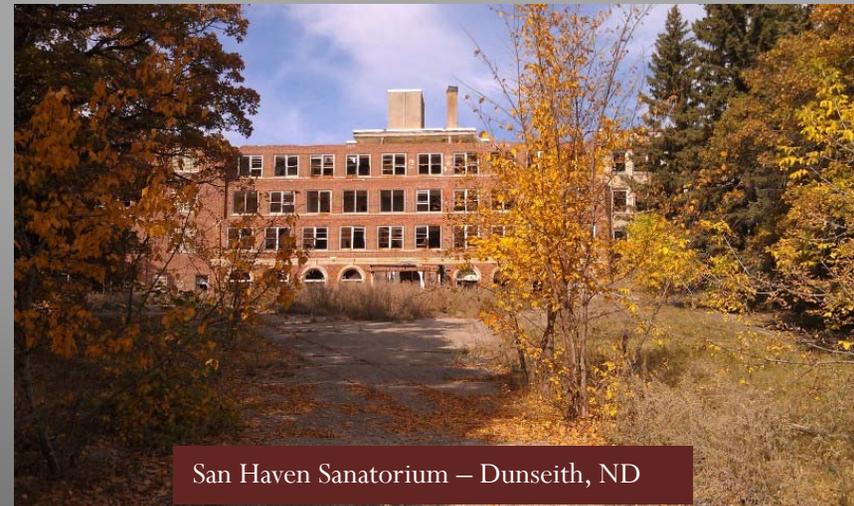


# History of TB Disease

- ▶ This organism has been documented as early as 1000 BC
- ▶ Until mid-1800s, many believed TB was hereditary
- ▶ 1865 Jean Antoine-Villemin proved TB was contagious
- ▶ 1882 Robert Koch discovered *M. tuberculosis*, the bacterium that causes TB



- ▶ Before TB antibiotics, many patients were sent to sanitariums
- ▶ Patients followed a regimen of bed rest, open air and sunshine
- ▶ TB patients who could not afford sanatoriums often died at home

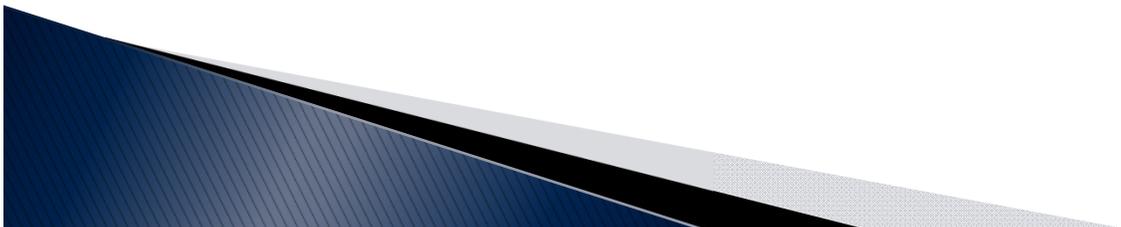


Ghosts of North Dakota –  
San Haven Sanatorium

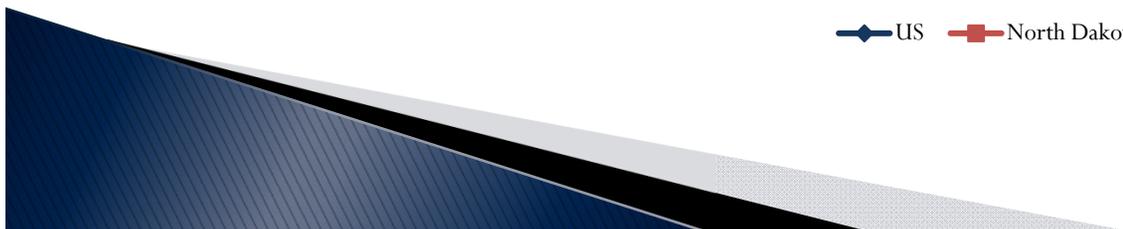
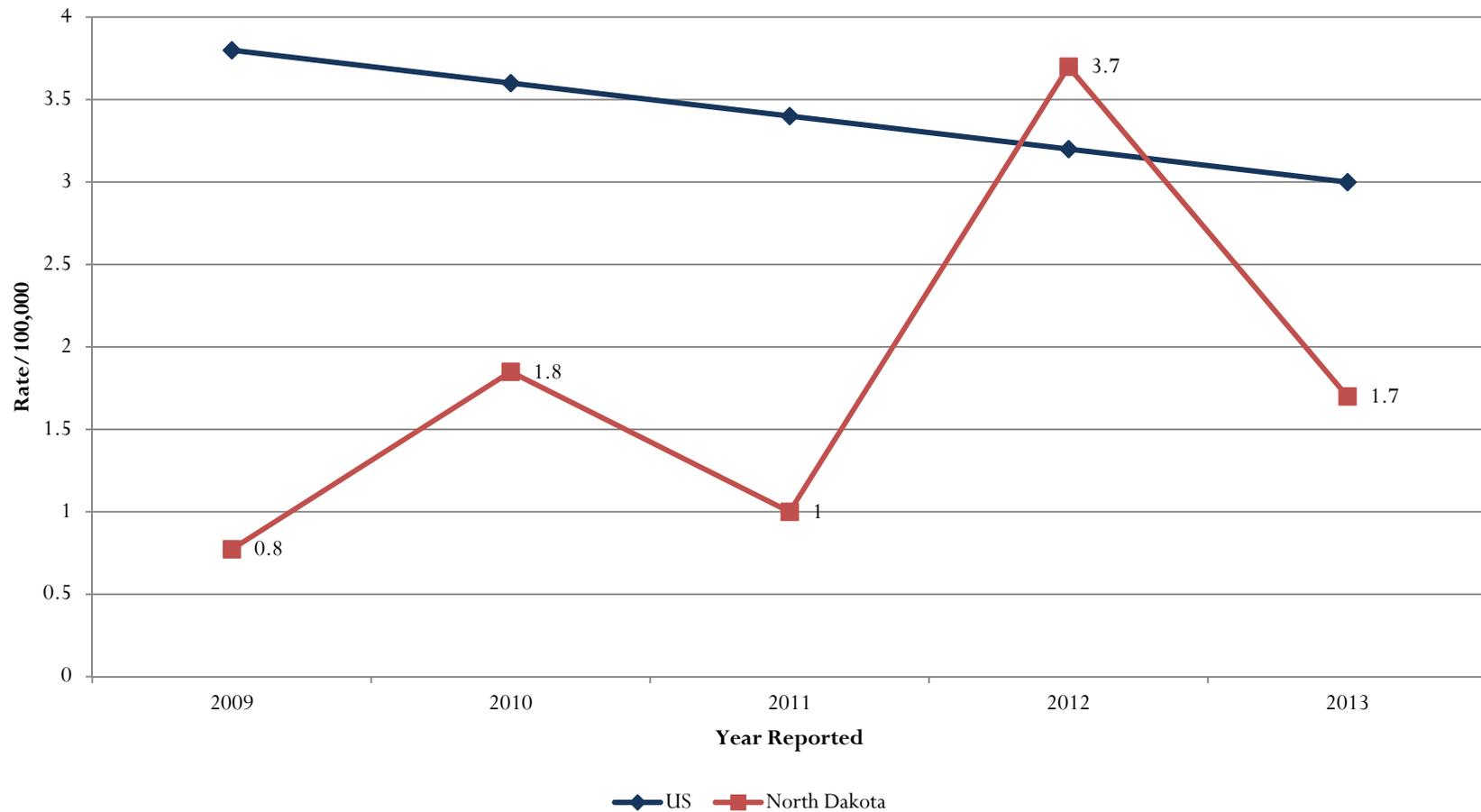
<http://www.ghostsofnorthdakota.com/2011/01/12san-haven-sanatorium/>

# TB Disease in the United States

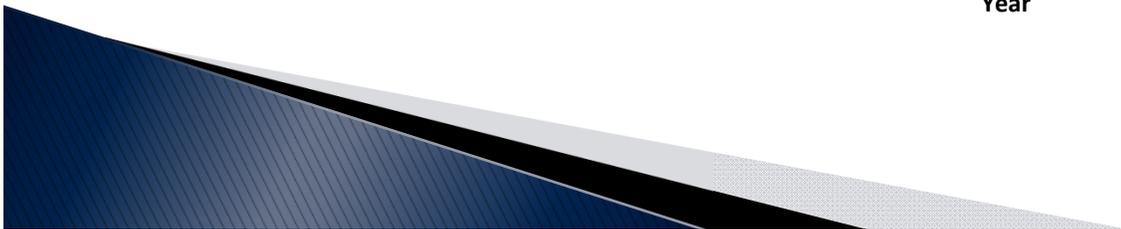
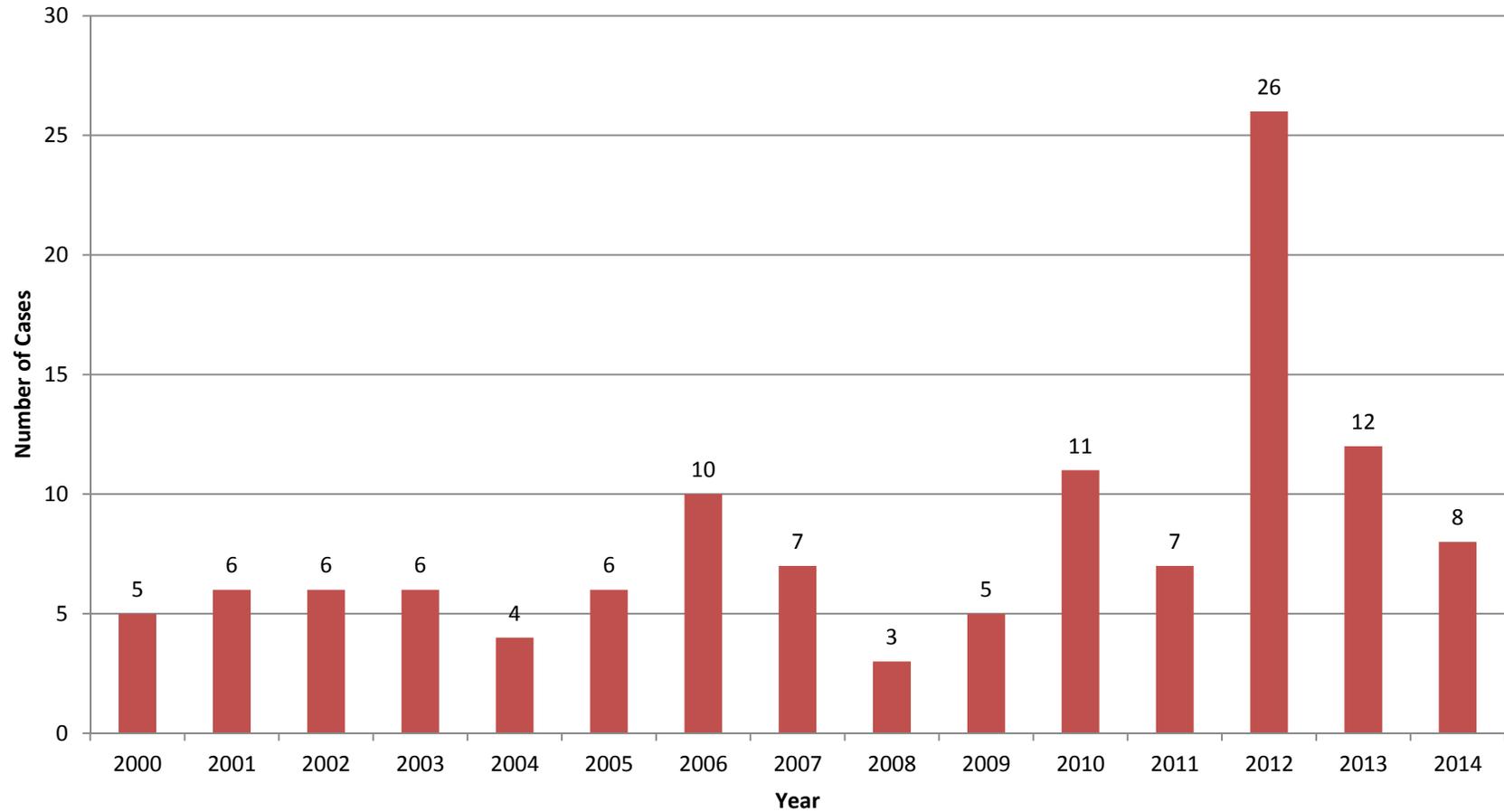
- ▶ 64.6% of the cases of active TB in the US in 2013 were foreign born persons
- ▶ In order to control the spread of TB, one must identify those that have been infected
- ▶ Once identified those same individuals need to be treated to reduce their risk of developing active disease



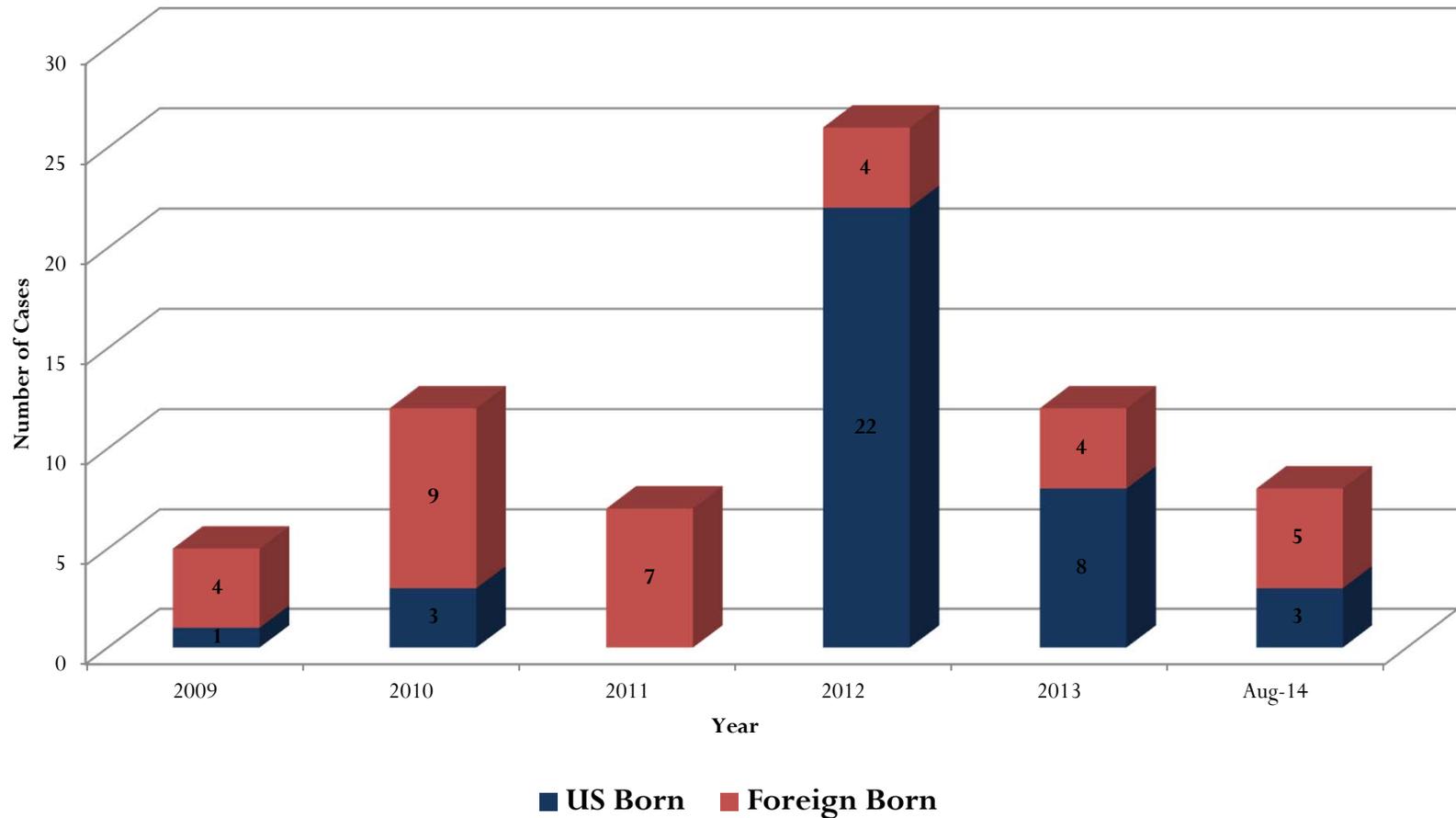
# United States and North Dakota TB Disease Rates, 2009 - 2013



# Number of TB Cases in North Dakota – 2000 - 2014

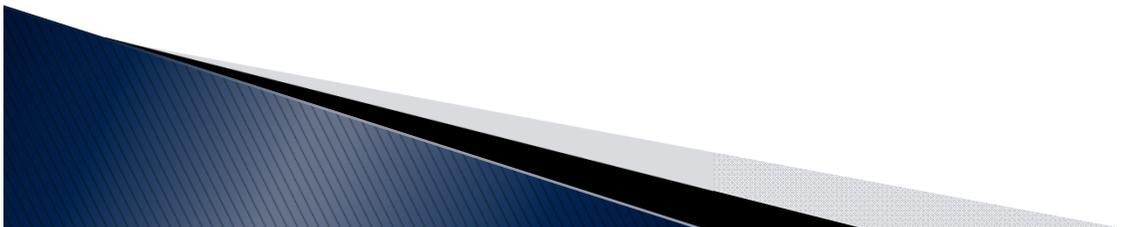


# US Born vs. Foreign Born TB Cases in North Dakota



# What is the TB Risk for my facility?

- ▶ Due to the low number of cases each year, county information cannot be published
- ▶ To do your risk assessment, please call me at 701.328.2377
- ▶ The 2012 epi-profile can be found here:  
[http://www.ndhealth.gov/HIV/HIV%20Data/HIV\\_TB\\_STD\\_HEP\\_EPI\\_2012.pdf](http://www.ndhealth.gov/HIV/HIV%20Data/HIV_TB_STD_HEP_EPI_2012.pdf)
- ▶ The 2013 Quarterly HIV and TB report can be found here:  
<http://www.ndhealth.gov/Disease/NewsLetters/EpiArchives/QTR1-14.pdf>



# Mycobacteria

*Mycobacterium tuberculosis*

*Mycobacterium bovis*

*Mycobacterium africanum*

*Mycobacterium microti*

*Mycobacterium canetti*

*Mycobacterium avium*

*Mycobacterium fortitum*

*Mycobacterium chelone*

*Mycobacterium gordonae*

*Mycobacterium kansasii*

In the United States, most TB is caused by *Mycobacterium tuberculosis*

Mycobacteria that cause TB disease

Mycobacteria that do not cause TB disease

# Common Symptoms of TB include:



- a) Cough
- b) Fever
- c) Unexplained weight loss of 10 pounds or more
- d) All of the above

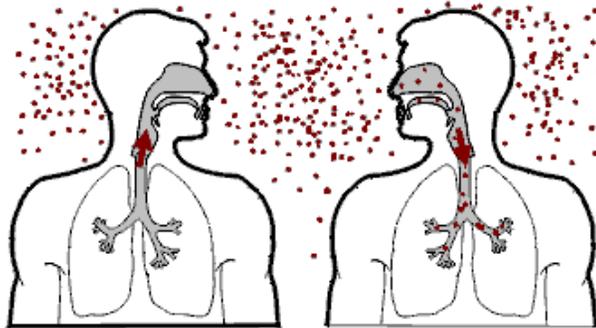
# How is TB Spread?

- ▶ TB is spread person to person through the air via droplet nuclei
- ▶ *M. tuberculosis* may be expelled when an infectious person:
  - Coughs
  - Sneezes
  - Speaks
  - Sings
- ▶ Transmission occurs when another person inhales droplet nuclei



# Transmission

- ▶ Transmitted through airborne droplets
- ▶ Large infectious dose needed
- ▶ Must be in close contact



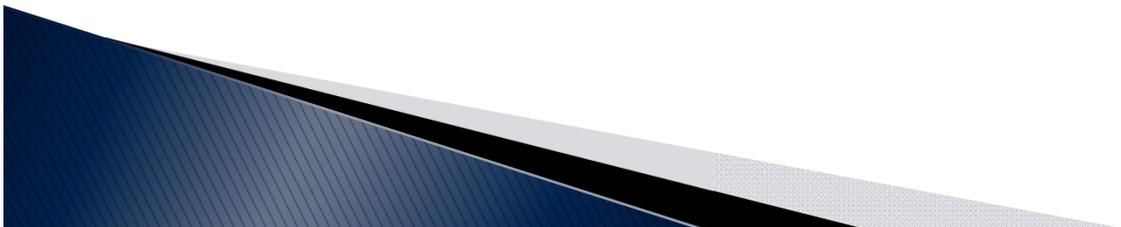
# Pathogenesis

- ▶ Infection begins when the inhaled droplets reach the alveoli of lungs
- ▶ Tubercle bacilli multiply
- ▶ A number of tubercle bacilli enter the bloodstream and spread throughout the body (lungs, kidneys, brain, bone)
- ▶ Within 2-10 weeks, the immune system produces an immune response which encapsulates the bacteria, and is detectable with a TST or IGRA blood test



# Risk of Infection

- ▶ How infectious is the person with TB
- ▶ Length of exposure
- ▶ Environment in which transmission occurs
  - Close proximity
  - Indoors, Outdoors



# Likelihood of Developing TB Disease

- ▶ Once infected with tubercle bacilli
  - 10% life time chance that TB disease will develop
    - Half the risk within the first 2 years
    - Gradually decreasing risk after the first 2 years
  - 90% chance of never developing the disease
  - Other personal health factors can influence risk
    - HIV infection - single highest risk for progress to active disease, at 10% risk annually
    - Diabetes – 30% risk over lifetime



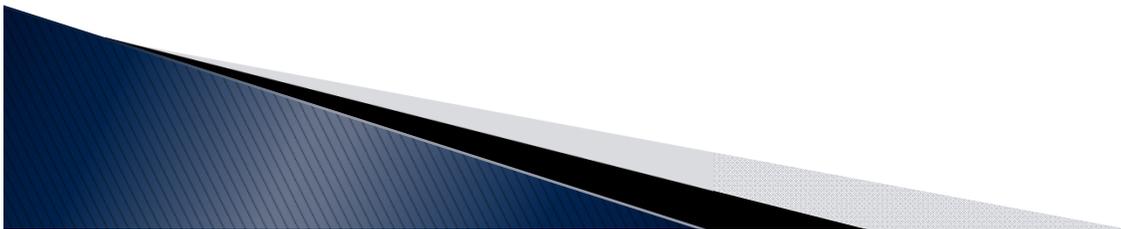
# Sites of TB Disease

- ▶ Pulmonary TB – lungs, 80-85% of TB cases
- ▶ Extra-pulmonary TB– outside of the lungs
  - Can occur anywhere in body
  - Typical sites include larynx, lymph nodes, the pleura, brain, kidneys, bones, or joints
  - Usually not infectious – always rule out pulmonary!
  - Laryngeal TB is extremely contagious – hoarseness
  - Found more often in those that are HIV infected, immunosuppressed person or young children
- ▶ Miliary TB – carried to all parts of the body, through the bloodstream



# Why Screen for TB

- ▶ Tuberculosis is one of the world's deadliest diseases
- ▶ Once identified, treatment can begin
- ▶ Once treatment begins, the spread of disease can be halted



An individual diagnosed with latent TB is infectious and can transmit TB to others

- » a) True
- b) False

# Active Disease vs. Latent Infection

- ▶ Positive TST or IGRA
- ▶ Cough, fever, unexplained weight loss, chest pain, fatigue, loss of appetite
- ▶ Abnormal CXR
- ▶ Positive sputum smears
- ▶ Positive sputum cultures
- ▶ **Infectious** prior to treatment

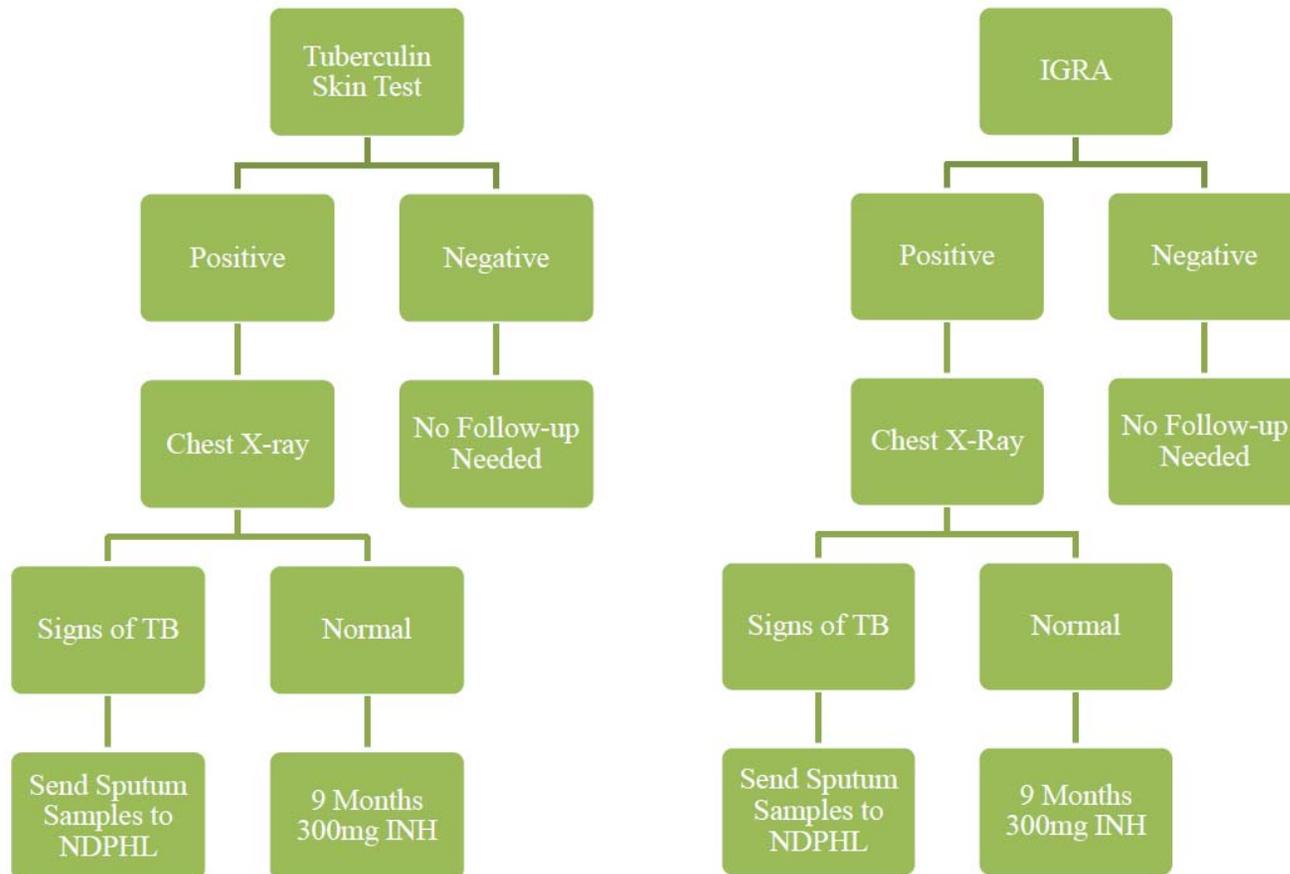
May have a negative sputum smear &/or culture

- ▶ Positive TST or IGRA
- ▶ Normal CXR
- ▶ Negative sputum smear
- ▶ Negative sputum culture
- ▶ **Not infectious**

Active TB Disease

Latent TB Infection (LTBI)

# TB Screen Algorithm



# Who can Receive a TST

- ▶ Almost everyone can receive a TST, including: infants
- ▶ Children
- ▶ Pregnant women
- ▶ People living with HIV
- ▶ People who have had a BCG shot

\*People who had a severe reaction to a previous TST *should not* receive another TST



- Developed by Charles Mantoux in 1908
- The standard tuberculin skin test
- Two Purified Protein Derivative (PPD) antigen products licensed by the FDA
  - Tubersol
  - Aplisol



If at all possible do not switch between the two brands of tuberculin antigen



## Mantoux Tuberculin Skin Testing

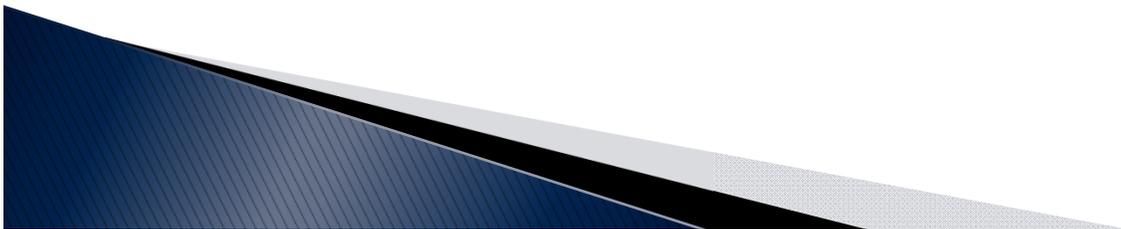


## How to Perform the Tuberculin Skin Test

The TST is performed by injecting 0.1 ml of tuberculin purified protein derivative (PPD) into the inner surface of the forearm.

# How is the TST Administered?

- ▶ 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.



# Reading the TST



- ▶ Must be read 48-72 hours after the test is placed

A patient who does not return within 72 hours will need to be rescheduled for another skin test.

- ▶ Measure the induration in mm – not erythema

- ▶ If test is not read by 72 hours, repeat the test – no waiting time is required

# 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.



# Key Definitions

- ▶ An individual with a positive skin test reaction (size interpreted as “positive” based on risk factors) with no clear documentation or history of being skin tested in the last two years
- ▶ Any individual with a negative skin test documented as baseline but who developed positive reaction with increase in reaction size of  $\geq 10$  mm within the past two years or a change from negative to positive on an IGRA

Reactor

Convertor

# Storage and Handling of PPD

- ▶ Date and initial when vial is opened
- ▶ Discard 30 days after opening
- ▶ Draw up just prior to injection
- ▶ Store at **35-46 degrees Fahrenheit** in a refrigerator or cooler with ice packs and **keep out of direct light** (antigen is sensitive to light and heat; these elements can affect antigen's stability and potency)



# 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 vaccine or 4-6 weeks after the administration of the live-virus vaccine
  - At least one month after smallpox vaccination



# PPD Shortage – Is it over?

- ▶ Storage Problem of testing solution
- ▶ More testing being done
- ▶ Blood test may be done to replace TST testing
- ▶ The NDDoH continues to receive allotments of Tubersol



# Classification of the TB Skin Test

Induration of $\geq 5$ mm is considered positive in	Induration of $\geq 10$ mm is considered positive in	Induration of $\geq 15$ mm is considered positive in
<ul style="list-style-type: none"> <li>• Human immunodeficiency virus (HIV)-positive persons</li> <li>• Recent contacts of TB case patients</li> <li>• Persons with fibrotic changes on chest radiograph consistent with prior TB</li> <li>• Patients with organ transplants and other immunosuppressed patients (Receiving the equivalent of <math>\geq 15</math> mg/d of prednisone for 1 month or more. Risk of TB in patients with corticosteroids increases with higher dose and longer duration.)</li> </ul>	<ul style="list-style-type: none"> <li>• Recent immigrants (i.e., within the last 5 years) from high-prevalence countries</li> <li>• Injection drug users</li> <li>• Residents and employees<sup>†</sup> of the following high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health care facilities, residential facilities for patients with acquired immunodeficiency syndrome (AIDS), and homeless shelters</li> <li>• Mycobacteriology laboratory personnel</li> <li>• Persons with the following clinical conditions that place them at high risk: silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head, neck, or lung), weight loss of <math>\geq 10\%</math> of ideal body weight, gastrectomy, and jejunioileal bypass</li> <li>• Children &lt; 4 years of age, or infants, children and adolescents exposed to adults at high-risk</li> </ul>	<ul style="list-style-type: none"> <li>• Persons with no known risk factors for TB</li> </ul>

# IGRA

Interferon Gamma Release Assay (IGRA) measure the cell-mediated response to specific TB antigen in whole blood. WBC's in TB infected person release INF-g when mixed with antigens derived from Mycobacteria Tuberculosis (MTB).

Currently there are two IGRA's in use: Quantiferon (Cellestis) and T-Spot (Oxford)



Quantiferon



T-Spot

# Advantages of IGRA's

- ▶ Requires a single patient visit
- ▶ Results not subject to reader bias and error
- ▶ Greater sensitivity and specificity – not affected by BCG or most nontuberculous mycobacteria
- ▶ Results are usually available within 24-48 hours
- ▶ Does not “boost” responses measured by subsequent tests as a TST may
- ▶ More costly than a TST\*
- ▶ Not recommended for use in children  $\leq 5$  years of age
- ▶ Blood must be processed in 8-30 hours
- ▶ Can have false positive, false negative and indeterminate test results

Advantages of IGRA's

Disadvantages of IGRA's

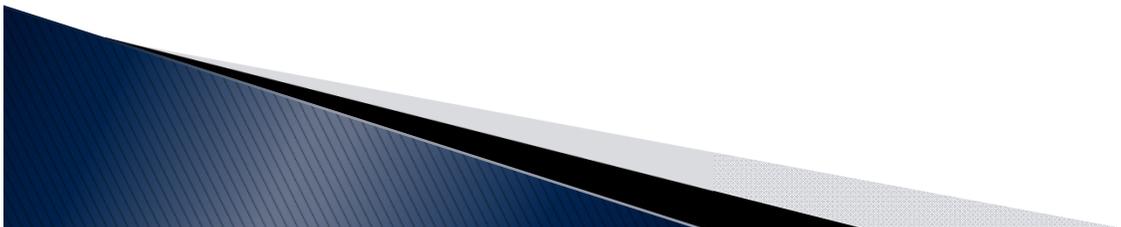
# LTBI Treatment

- ▶ To prevent active TB disease, treatment for latent TB is very important
- ▶ 9 months isoniazid (INH) – 270 doses
  - May be given daily or twice a week
- ▶ Rifampin (RIF) – 4 months
- ▶ Isoniazid-Rifapentine - 12 week course, must be given DOT
- ▶ In situations where RIF cannot be used (HIV-infected persons receiving protease inhibitors – rifabutin may be substituted

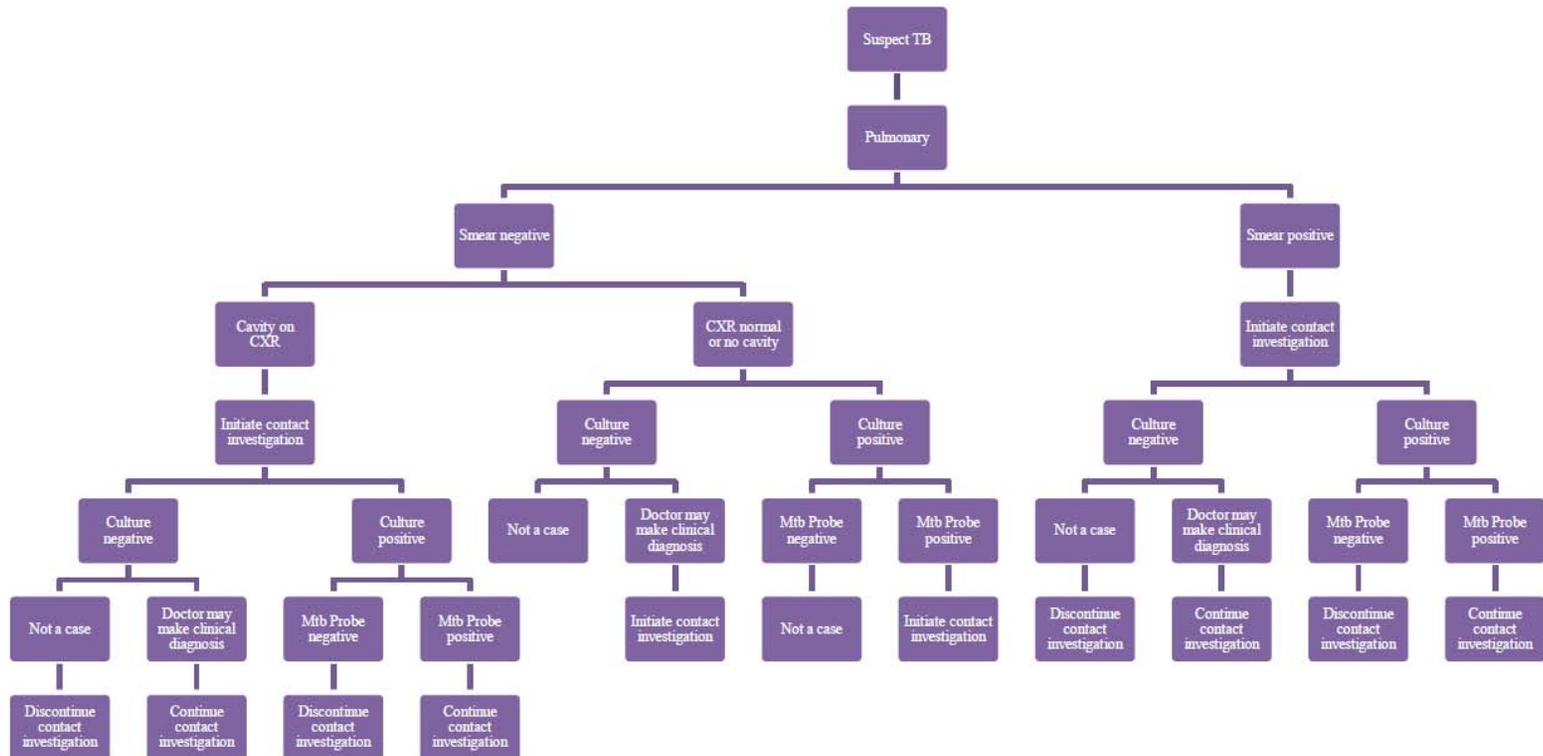


# Chest X-Ray

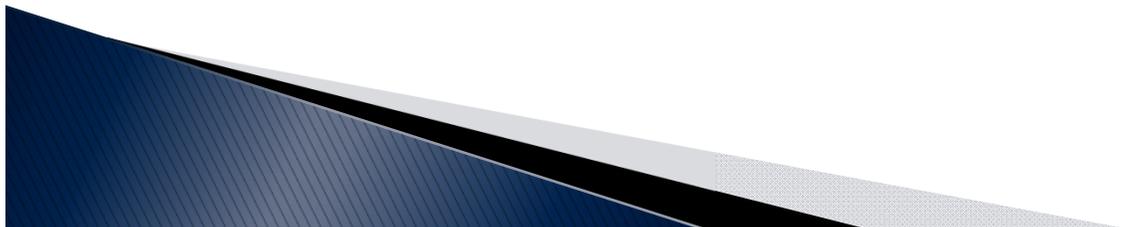
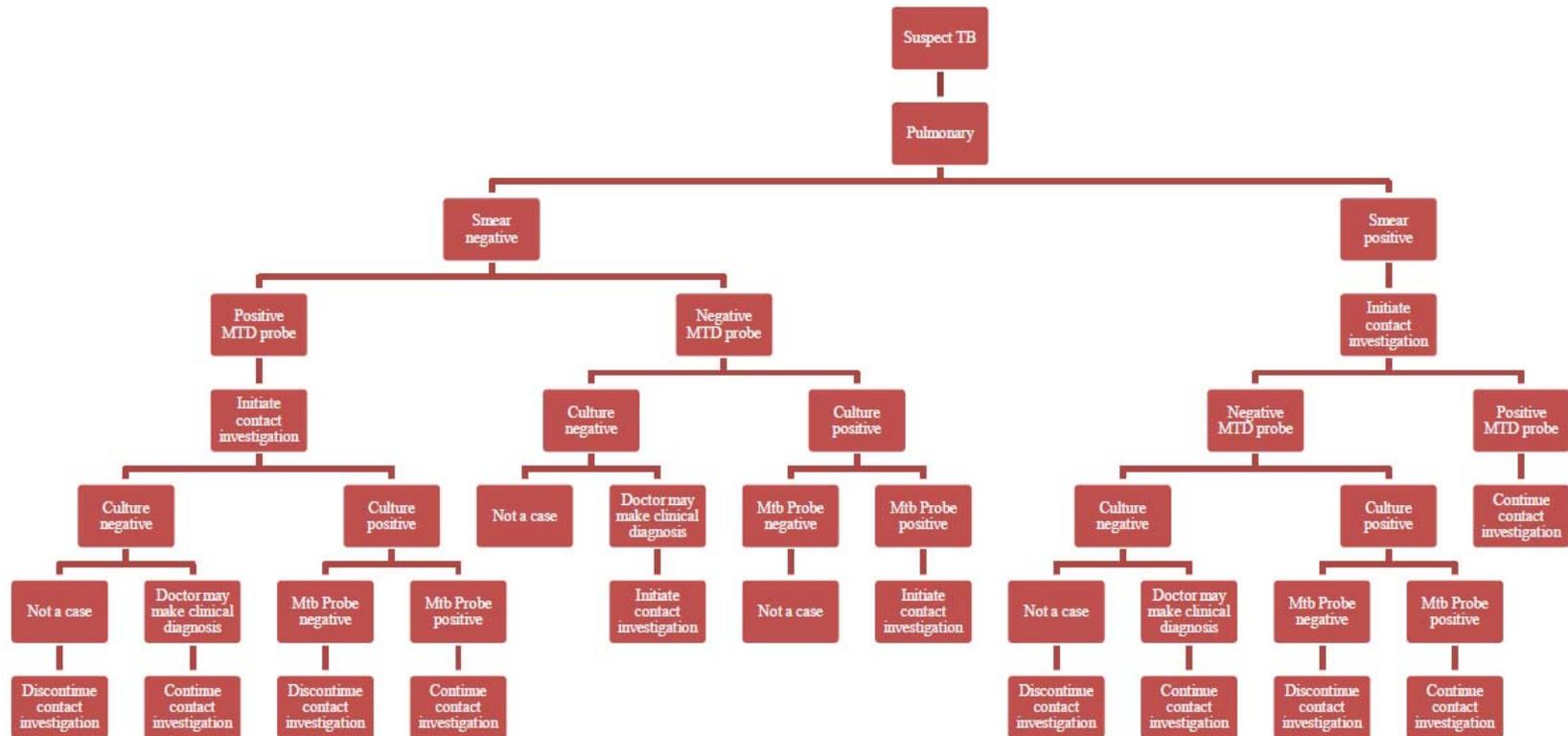
- ▶ Check for lung abnormalities suggestive of TB disease
- ▶ Typical findings may include cavities, infiltrates, effusions, opacities
- ▶ A chest x-ray does not confirm TB disease
- ▶ A chest x-ray does not rule out active TB in immune compromised individuals and children



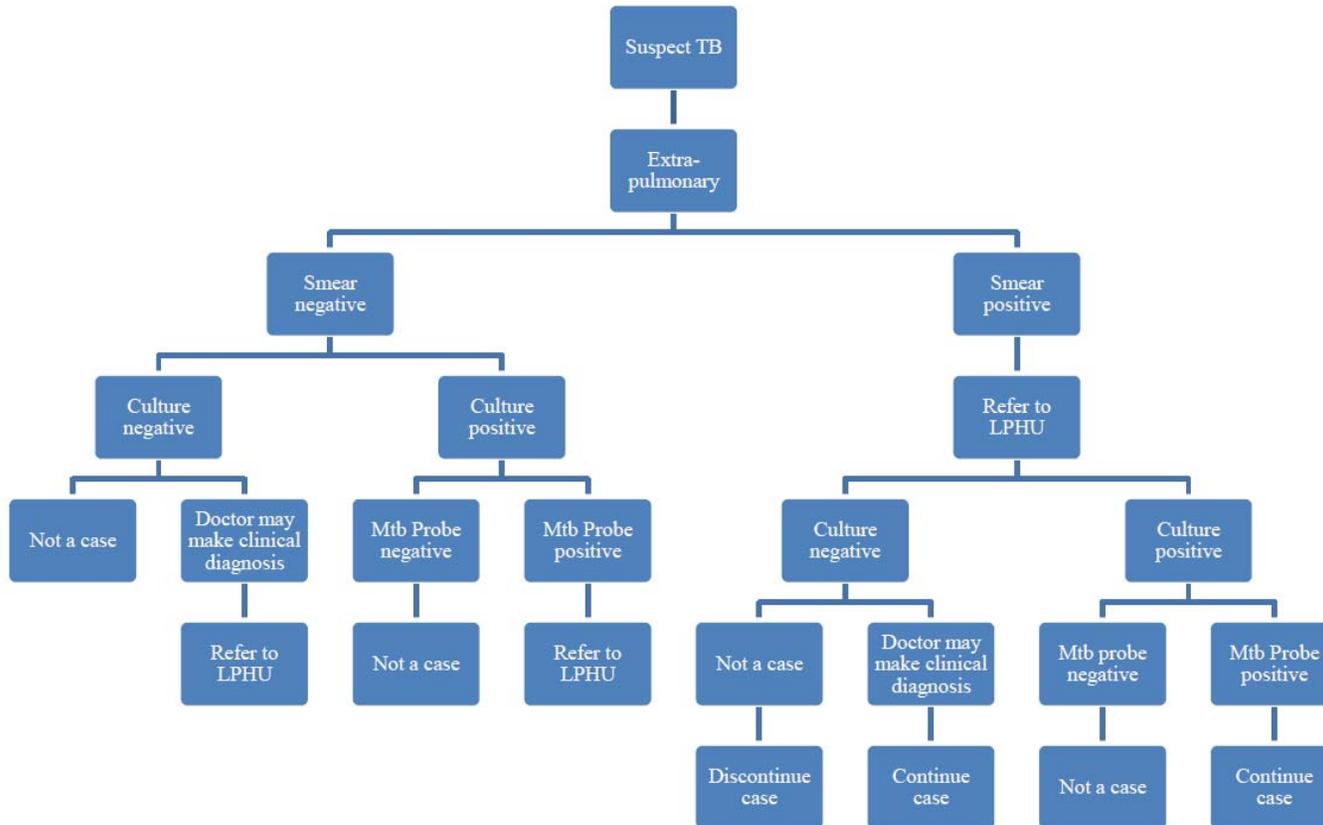
# Suspect Pulmonary TB: AFB Smear and Chest X-ray



# Suspect Pulmonary TB: AFB Smear and MTD Probe



# Suspect Extra-Pulmonary TB: AFB Smear



# MTD - Direct Tests for TB

Mycobacterium tuberculosis direct or TB PCR – results in 1-2 days

- ▶ These rapid tests are done directly on raw respiratory samples; culture growth is not needed
- ▶ Very sensitive on samples with higher smear positivity
- ▶ A negative test does not rule out TB, especially with negative smear results
- ▶ A negative does not provide enough evidence to release from isolation

Gene Xpert – results in 6-8 hours

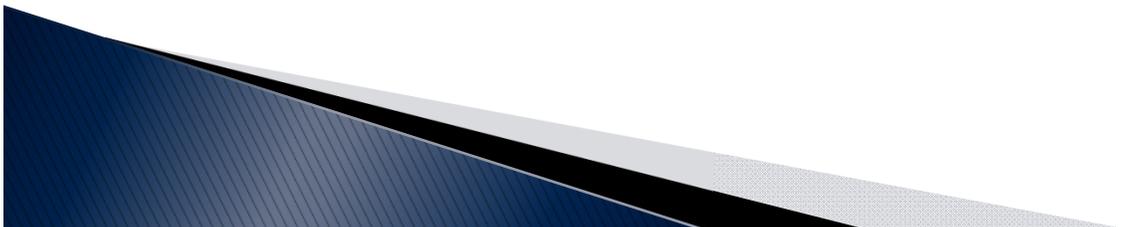


A person with a negative TST or IGRA cannot have TB disease

- » a) True
- b) False

# Diagnosis

- ▶ Evaluate all patients with symptoms of TB for TB disease, regardless of the patient's skin test reaction
- ▶ 1/4 to 1/3 of all active MTB cases have negative TST at onset of treatment



# Symptoms of TB Disease

- ▶ Cough
- ▶ Pain in the chest when breathing or coughing
- ▶ Coughing up sputum or blood
- ▶ Fatigue/malaise
- ▶ Decreased appetite
- ▶ Unexplained weight loss usually  $> 10$  pounds
- ▶ Fever
- ▶ Night sweats
- ▶ Other symptoms specific to the site of the TB disease

Pulmonary Symptoms

Systemic Symptoms

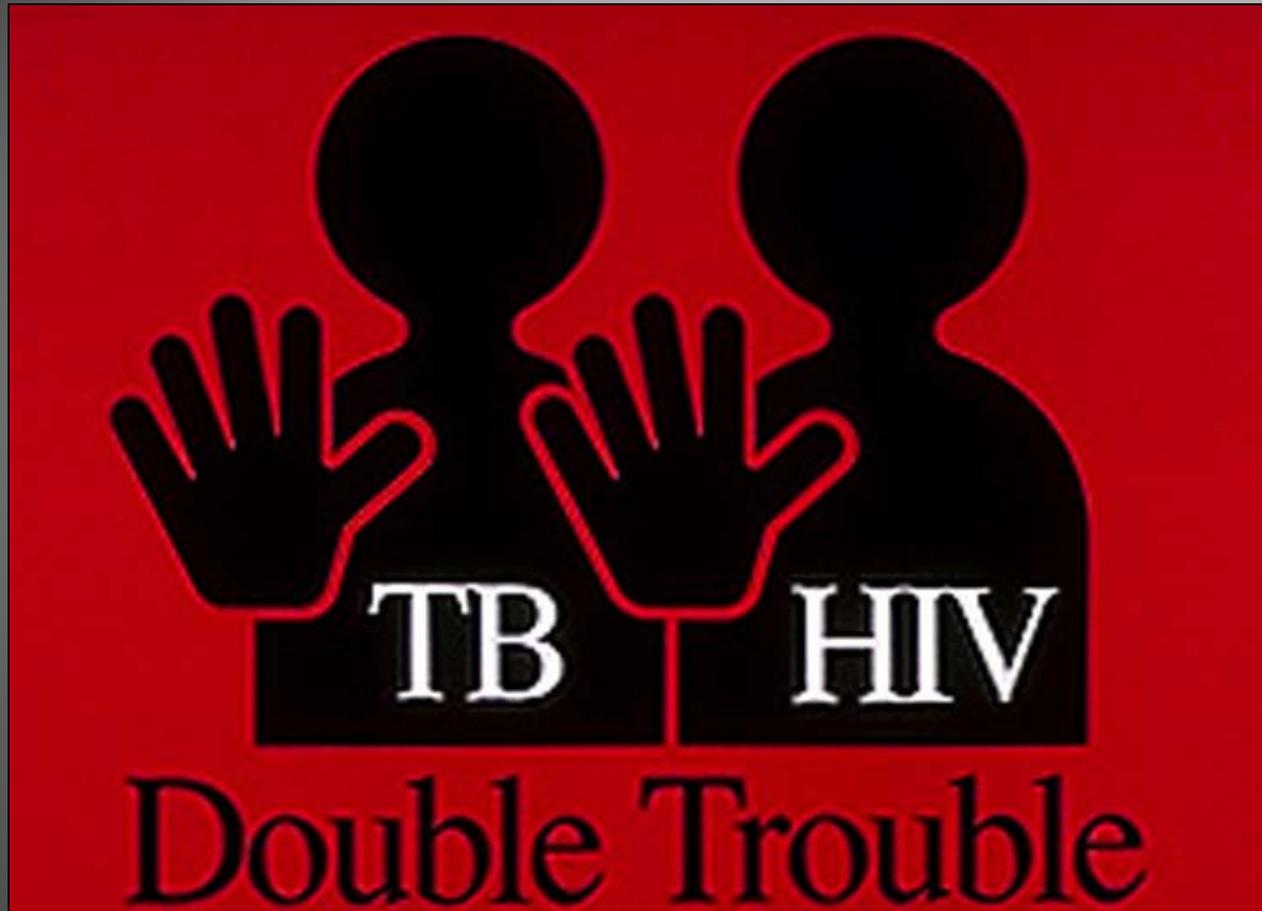
The infectious period for someone diagnosed with active TB is how many months prior to symptom onset?

- a) 1 month
  - b) 3 months
  - c) 6 months
  - d) 12 months
- 

# Who is at Greatest Risk for developing disease in North Dakota?

- ▶ Contacts to known TB cases
- ▶ Persons with HIV or other immunosuppressed diseases
- ▶ Persons from countries where TB is common (Latin America, the Caribbean, Asia, Africa, Eastern Europe and Russia)
- ▶ People who work in or live in facilities where TB is common: homeless shelters, correctional facilities, hospitals and clinics, nursing homes
- ▶ Diabetics
- ▶ Homeless





TB is the leading killer of people who are HIV infected >>>

# Links between TB and Diabetes

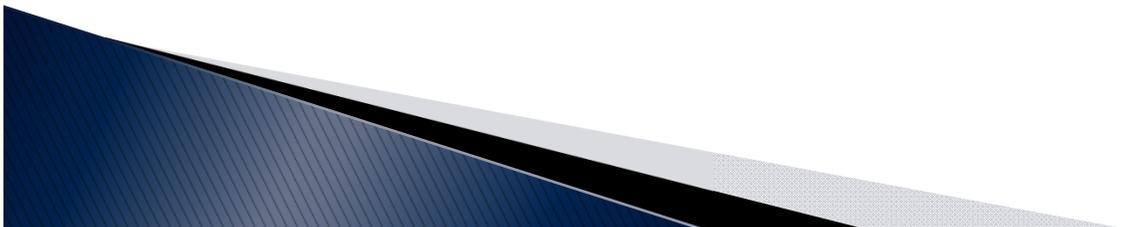
- ▶ People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB
- ▶ People with diabetes have a 2-3 times higher risk of TB compared to people without diabetes
- ▶ About 10 – 15 % of TB cases globally are linked to diabetes
- ▶ A large proportion of people with diabetes as well as TB is not diagnosed, or is diagnosed too late. Early detection can help improve care and control of both



# TB in the Healthcare Setting

# Positive Case – What do I Do?

- ▶ Notify the North Dakota Department of Health
- ▶ Place in isolation until no longer infectious
  - Repeat sputum smear and culture X 3 specimens
- ▶ Contact Investigation
  - How infectious of the person with TB
  - Length of exposure
  - Environment in which transmission occurs
    - Close proximity
    - Indoors, Outdoors
- ▶ DOT (Direct Observed Therapy)



# Environmental Factors That Increase the Risk for Probability of Transmission of *M. tuberculosis*

- ▶ Exposure to TB in small, enclosed spaces
- ▶ Inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplet nuclei
- ▶ Recirculation of air containing infectious droplet nuclei
- ▶ Inadequate cleaning and disinfection of medical equipment
- ▶ Improper procedures for handling specimens



# Healthcare Associated Transmission of TB

- ▶ Bronchoscopy
- ▶ Endotracheal Intubation
- ▶ Suctioning
- ▶ Other Respiratory Procedures
- ▶ Open Abscess Irrigation
- ▶ Autopsy
- ▶ Sputum Induction
- ▶ Aerosol Treatment that Induce Coughing



# TB Risk Assessment

- ▶ Every health-care setting should conduct initial and ongoing evaluations of the risk for transmission of *M. tuberculosis*, regardless of whether or not patients with suspected or confirmed TB disease are expected to be encountered in the setting
- ▶ The TB risk assessment determines the types of administrative, environmental, and respiratory-protection controls needed for a setting and serves as an ongoing evaluation tool of the quality of TB infection control and for the identification of needed improvements in infection-control measures



# TB Screening Risk Classifications

- ▶ Low risk – Setting in which persons with TB disease are not expected to be encountered
- ▶ Medium risk – HCW will or will possibly be exposed to persons with TB disease or to clinical specimens that might contain *M. tuberculosis*
- ▶ Potential ongoing transmission - The classification of potential ongoing transmission should be temporarily applied to any setting (or group of HCWs) if evidence suggestive of person-to-person (e.g., patient-to-patient, patient-to-HCW, HCW-to-patient, or HCW-to-HCW) transmission of *M. tuberculosis* has occurred in the setting during the preceding year.
- ▶ If uncertainty exists regarding whether to classify a setting as low risk or medium risk, the setting typically should be classified as medium risk.



# TB Screening Procedures for Settings (or HCWs) Classified as Low Risk

- ▶ All HCWs should receive baseline TB screening upon hire, using two-step TST or a single BAMT to test for infection with *M. tuberculosis*.
- ▶ After baseline testing for infection with *M. tuberculosis*, additional TB screening is not necessary unless an exposure to *M. tuberculosis* occurs.
- ▶ HCWs with a baseline positive or newly positive test result for *M. tuberculosis* infection or documentation of treatment for LTBI or TB disease should receive one chest radiograph result to exclude TB disease (or an interpretable copy within a reasonable time frame, such as 6 months). Repeat radiographs are not needed unless symptoms or signs of TB disease develop or unless recommended by a clinician



# TB Screening Procedures for Settings (or HCWs) Classified as Medium Risk

- ▶ All HCWs should receive baseline TB screening upon hire, using two-step TST or a single BAMT to test for infection with *M. tuberculosis*.
- ▶ After baseline testing for infection with *M. tuberculosis*, HCWs should receive TB screening annually (i.e., symptom screen for all HCWs and testing for infection with *M. tuberculosis* for HCWs with baseline negative test results).
- ▶ HCWs with a baseline positive or newly positive test result for *M. tuberculosis* infection or documentation of previous treatment for LTBI or TB disease should receive one chest radiograph result to exclude TB disease. Instead of participating in serial testing, HCWs should receive a symptom screen annually. This screen should be accomplished by educating the HCW about symptoms of TB disease and instructing the HCW to report any such symptoms immediately to the occupational health unit. Treatment for LTBI should be considered in accordance with CDC guidelines



## TB Screening Procedures for Settings (or HCWs) Classified as Potential Ongoing Transmission

- ▶ Testing for infection with *M. tuberculosis* might need to be performed every 8–10 weeks until lapses in infection control have been corrected, and no additional evidence of ongoing transmission is apparent
- ▶ The classification of potential ongoing transmission should be used as a temporary classification only. It warrants immediate investigation and corrective steps. After a determination that ongoing transmission has ceased, the setting should be reclassified as medium risk. Maintaining the classification of medium risk for at least 1 year is recommended



# TB Airborne Precautions

- ▶ Within health-care settings, TB airborne precautions should be initiated for any patient who has symptoms or signs of TB disease, or who has documented infectious TB disease and has not completed antituberculosis treatment.
- ▶ Initiate Airborne Infection Isolation – negative pressure room if available
- ▶ Use of N95 mask by HCWs
- ▶ Airborne precautions may be discontinued when infectious TB disease is considered unlikely and either
  - Another diagnosis is made that explains the clinical syndrome
  - The patient has three consecutive, negative AFB sputum smear results



# TB Prevention

- ▶ Early detection
- ▶ If LTBI, take medication to treat the infection
- ▶ Education and Screening
- ▶ Personal hygiene
- ▶ Isolation



# Risk Classification Examples

## ▶ **Inpatient Settings with More Than 200 Beds**

- If less than six TB patients for the preceding year, classify as low risk. If greater than or equal to six TB patients for the preceding year, classify as medium risk.

## ▶ **Inpatient Settings with Less Than 200 Beds**

- If less than three TB patients for the preceding year, classify as low risk. If greater than or equal to three TB patients for the preceding year, classify as medium risk.

## ▶ **Outpatient, Outreach, and Home-Based Health-Care Settings**

- If less than three TB patients for the preceding year, classify as low risk. If greater than or equal to three TB patients for the preceding year, classify as medium risk.



**An inpatient setting (a hospital) with more than 200 beds and less than six TB patients for the preceding year would be classified as low risk according to the criteria in the guidelines; however, the infection-control team for our setting prefers to continue screening nurses annually.**

**Is that acceptable?**

Yes, the infection-control team may determine that a higher risk classification is warranted for a specific setting or for a specific group of health-care workers (HCWs). Low-risk settings are free to select recommendations for medium-risk settings, if desired.

# How should HCWs in low-risk settings who have positive test results for *M. tuberculosis* infection (positive TST or QFT/T-Spot for *M. tuberculosis* result) be managed?

- ▶ Perform a CXR
  - ▶ If CXR is normal , recommend treatment for LTBI
  - ▶ If CXR is abnormal, collect sputum samples
- ▶ If Normal CXR, perform annual symptom assessment for disease.

- ▶ **If a HCW with a newly positive TST or QFT/T-Spot result has documentation of a recent (1 month ago) negative CXR result would they need an additional CXR?**

If the HCW has symptoms of TB, a CXR would be recommended. If the HCW is immunocompromised, a CXR might be considered. If not, another CXR is not needed

# Guidelines for Preventing the Transmission of *M. tuberculosis* in Health-Care Settings



[http://www.cdc.gov/tb/publications/slidesets/  
InfectionGuidelines/slides.ppt](http://www.cdc.gov/tb/publications/slidesets/InfectionGuidelines/slides.ppt)

Thank you for attending

TB: Interpretation of Tests and Risk Assessment

Please take post-test to receive CEU's for this presentation,  
you must score at least 70% to receive credit.

Dee Pritschet, TB Controller >>

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NORTH DAKOTA  
DEPARTMENT of HEALTH