

# TUBERCULOSIS 101

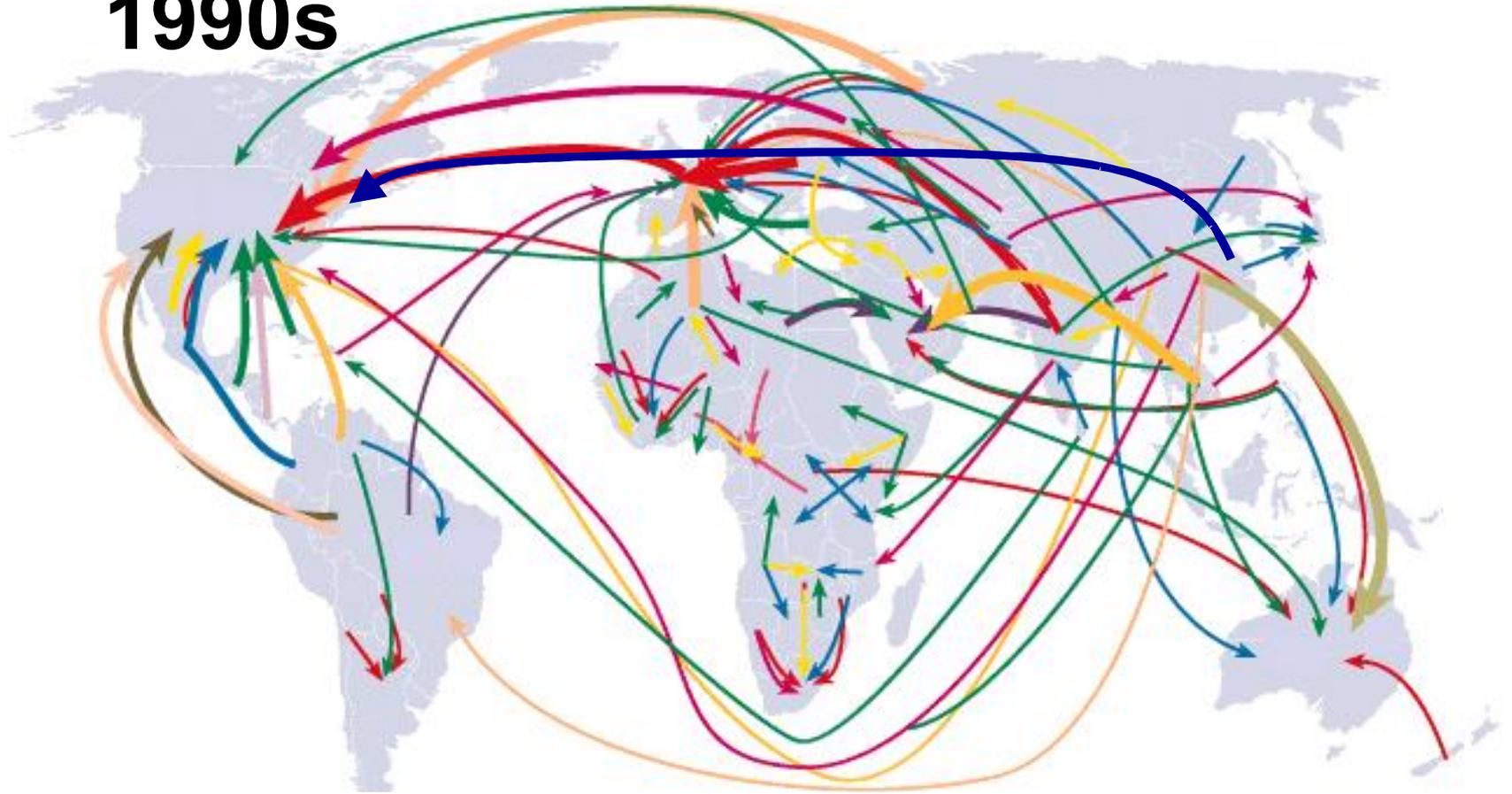
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VDH, Division of Disease Prevention  
TB Control



# Have germs, will travel...

## Migrating populations in the 1990s

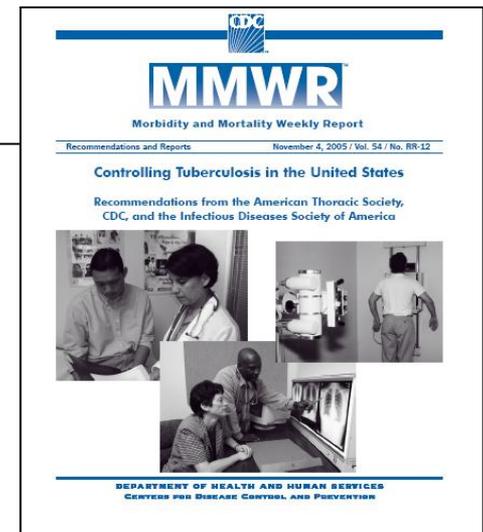
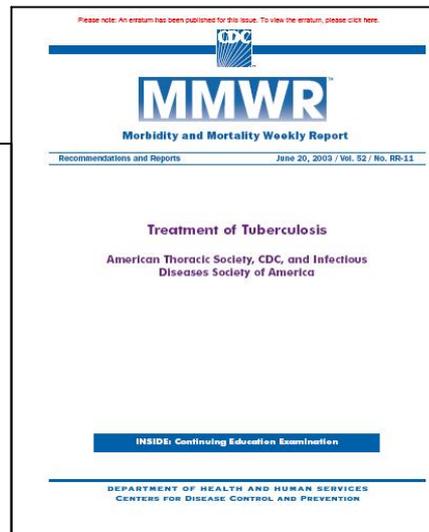
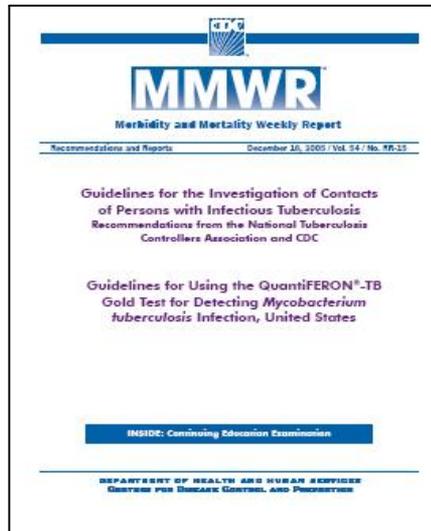


*Compared to 1960-75, four-fold increase in migration*

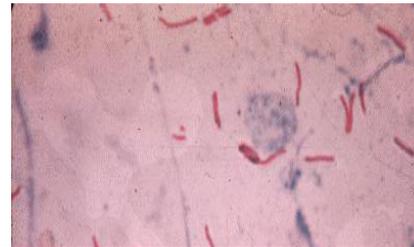
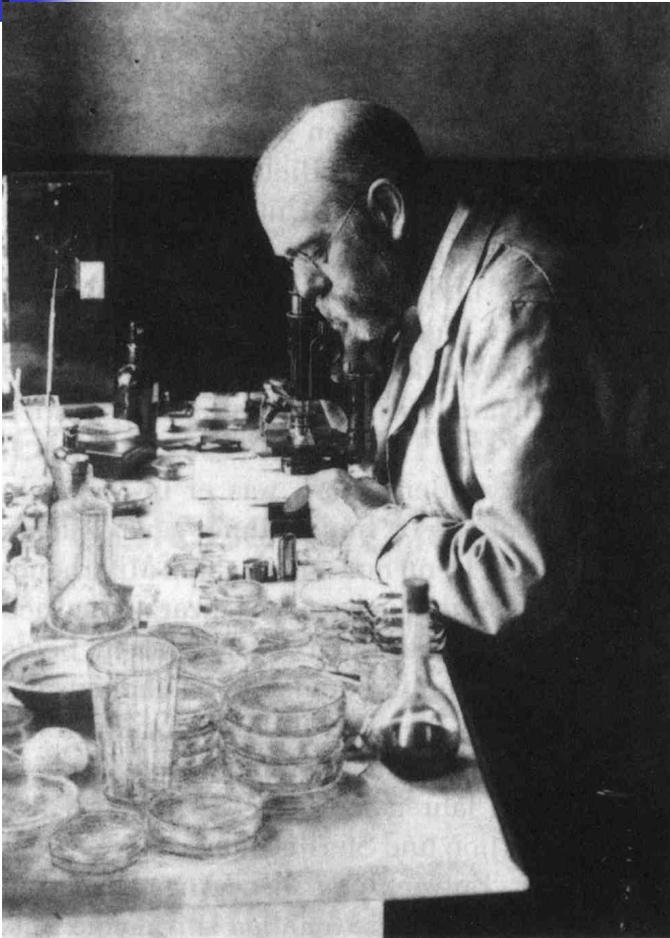
*Source: Population Action International 1994*

# VDH TB Prevention and Control Policies and Procedures

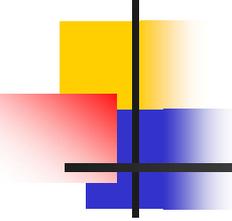
- Based on USPHS/CDC, ATS, IDSA and Pediatric “Red Book” guidelines
- Adapted to address uniquely Virginia issues



*M tuberculosis* as causative agent for tuberculosis



Robert Koch ~ 1882



# The Mycobacteria

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## Human pathogens

### *M. tuberculosis* Complex

(*M. tuberculosis*, *M. bovis*, *M. microti*,  
*M. africanum*, *M. canettii*)

*M. leprae*

# Transmission of TB

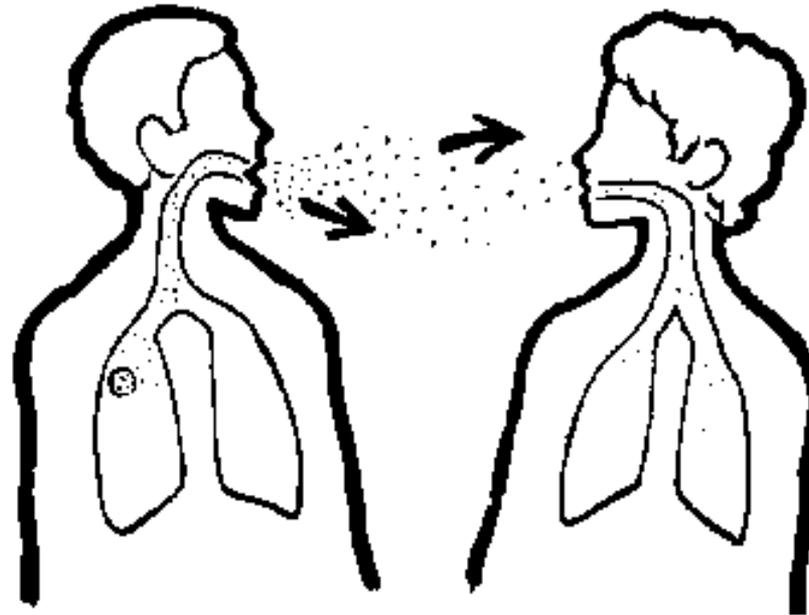
- Spread person to person through the air



# TB: Airborne Transmission

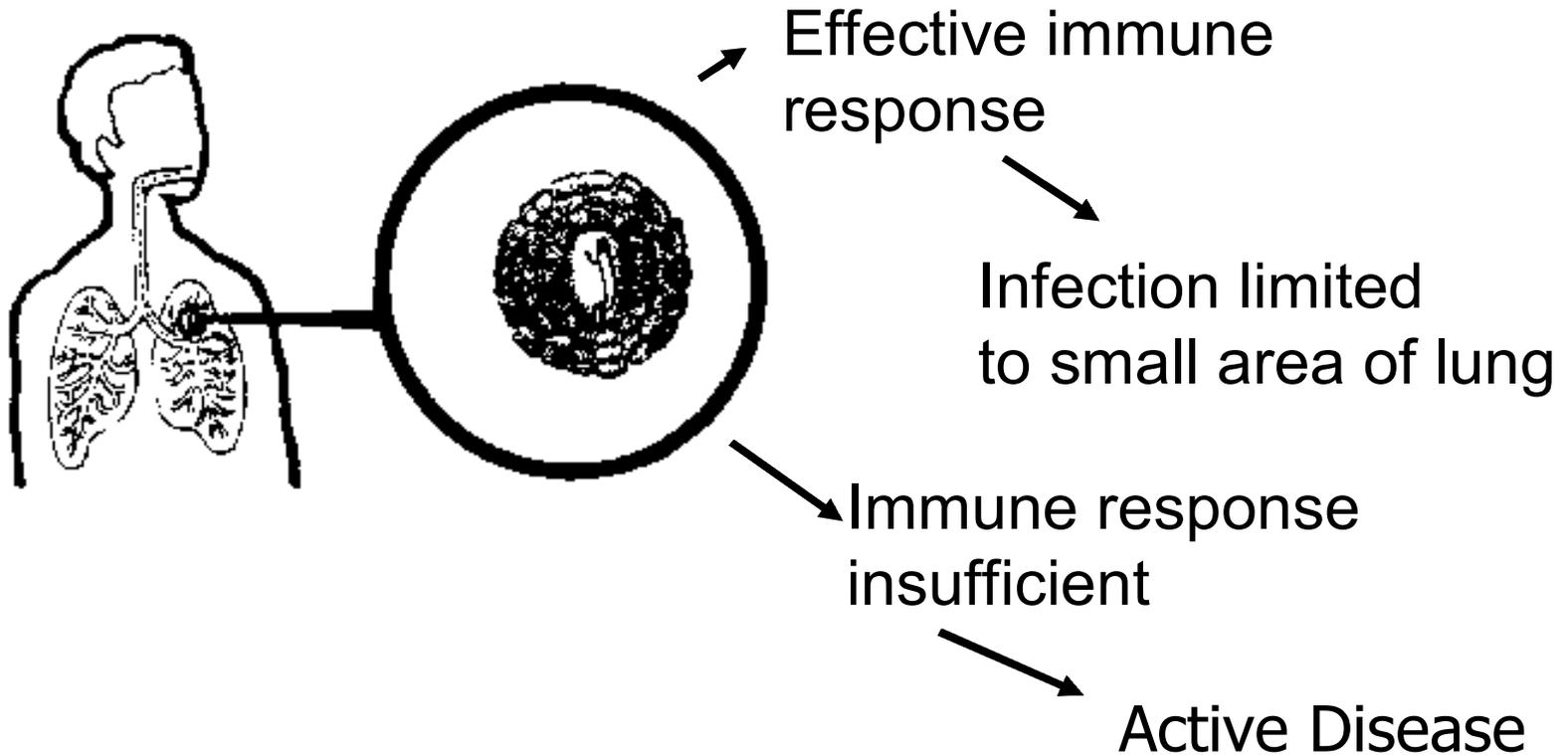
TB bacteria airborne

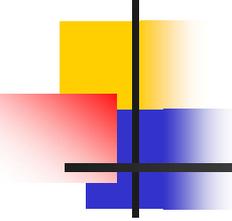
Person with  
active  
pulmonary TB



Person breathing  
TB bacteria

# TB Invades/Infects the Lung

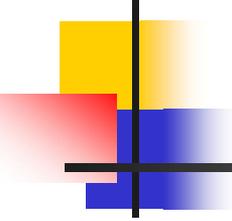




# Probability of TB Transmission

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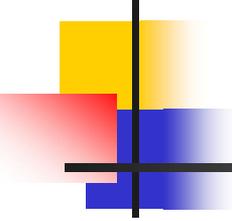
- Transmission dependent on these factors
  - Infectiousness of the person with TB
  - Environment in which the transmission occurs
  - Duration of the exposure to TB bacteria
  - Virulence of organism
  - Immune system of person exposed



# Pathogenesis of TB

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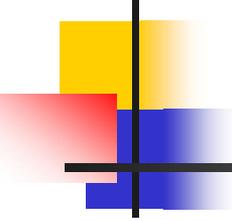
- Infection begins when the inhaled droplets reach the lungs
- Tubercle bacilli multiply
- A small number of tubercle bacilli may enter the bloodstream and spread throughout the body (lungs, kidneys, brain, bone)
- Within 2-10 weeks, the immune system produces a capsule that surround the tubercle bacilli



# Sites of TB Disease

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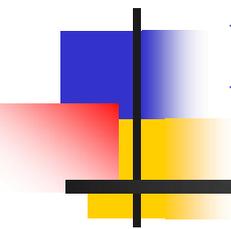
- Pulmonary TB (TB of the lungs)
  - 80% of cases
  - Potential for transmission – infectious until proven otherwise
- Extrapulmonary TB (outside the lungs)
  - Can occur anywhere in body
  - Portal of entry through lungs
  - Typical sites include larynx, lymph nodes, the pleura, brain, kidneys, bones, or joints
  - Usually not infectious – always rule out pulmonary!



# Likelihood of Developing TB Disease

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- Once infected with tubercle bacilli
  - 90% chance of never developing the disease
  - 10% life time chance that TB disease will develop
    - Half the risk within the first 2 years
    - Risk lower after the first 2 years
  - Other personal health factors can influence risk
    - HIV infection - single highest risk for progress to active disease
      - 10% annual risk



# Diagnosis of TB Infection and Disease

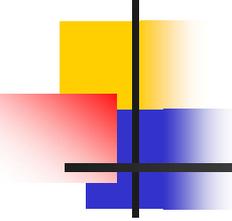
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Signs and Symptoms

TST

CXR

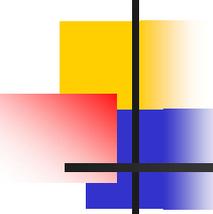
Bacteriology (positive sputa)



# Diagnosis of TB Disease: Symptoms

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- Pulmonary TB Disease
  - Coughing
  - Pain in the chest when breathing or coughing
  - Coughing up sputum or blood
- General TB Disease
  - Weight loss
  - Fatigue
  - Malaise
  - Fever
  - Night sweats
  - Other symptoms specific to the site of the TB disease

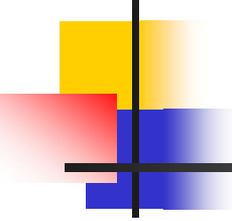


# Latent Infection vs. Active Disease

<b>Latent Infection</b>	<b>Active Disease</b>
Tubercle bacilli in the body	
Tuberculin skin test reaction usually positive	
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB

# Classification System for TB

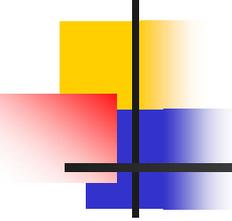
Class	Type	Description
0	No TB exposure Not infected	No history of exposure Negative reaction to tuberculin skin test
1	TB exposure No evidence of infection	History of exposure Negative reaction to tuberculin skin test
2	TB infection No disease	Positive reaction to tuberculin skin test Negative bacteriologic studies (if done) No clinical, bacteriological, or radiographic evidence of active TB
3	TB, clinically active	<i>M. tuberculosis</i> cultured (if done) Clinical, bacteriological, or radiographic evidence of current disease
4	TB Not clinically active	History of episode(s) of TB <b>or</b> Abnormal but stable radiographic findings Positive reaction to the tuberculin skin test Negative bacteriologic studies (if done) <b>and</b> No clinical or radiographic evidence of current disease
5	TB suspected	Diagnosis pending



# Refugees and Immigrants

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- Yellow sheets CDC 75.17 - version 2
- Classifications
  - Class A
  - Class B1
  - Class B2 (TST 10mm or more)
  - Class B3 (Contact)

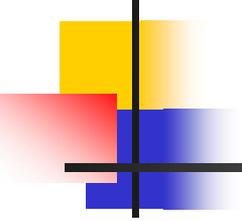


# Persons at Risk for Developing TB Disease

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Persons at high risk for developing TB disease fall into 2 categories

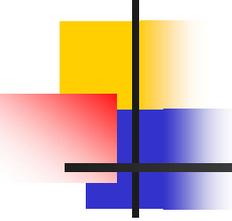
- Those who have been recently infected
- Those with clinical conditions that increase their risk of progressing from LTBI to TB disease



# Recently Infected

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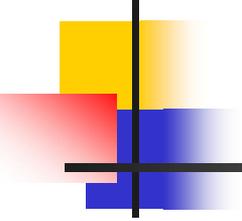
- Close contacts to person with infectious TB
- Skin test converters (within past 2 years)
- Recent immigrants from TB-endemic regions of the world (within 5 years of arrival to the U.S.)



## Recent Infection as a Risk Factor

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- Children  $\leq 5$  years with a positive TST
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, homeless shelters, health care facilities)

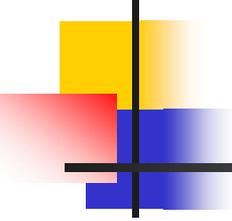


## Increased Risk for Progression to TB Disease

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Persons more likely to progress from LTBI to TB disease include

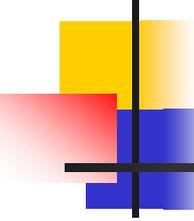
- Immuno-suppressed persons (HIV, TNFa, high doses of steroids)
- Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph



## Increased Risk for Progression to TB Disease

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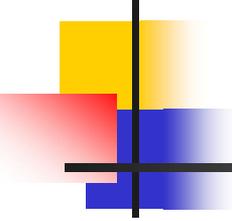
- Underweight or malnourished persons
- Injection drug users
- Those receiving TNF- $\alpha$  antagonists for treatment of rheumatoid arthritis or Crohn's disease



# Increased Risk for Progression to TB Disease

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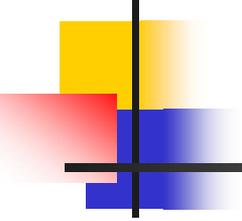
- Persons with certain medical conditions such as
  - Silicosis
  - Diabetes mellitus
  - Chronic renal failure or on hemodialysis
  - Solid organ transplantation (e.g., heart, kidney)
  - Carcinoma of head or neck
  - Gastrectomy or jejunioileal bypass



# TB Skin Testing = TST

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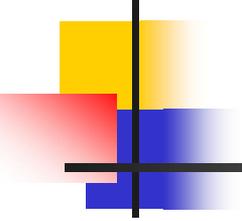
- Screening
- Planting (administration)
- Measurement
- Interpretation
- Follow-up



# Why Screen?

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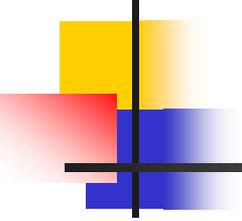
- Assess for symptoms
- Assess risk for acquiring ltbi
- Assess risk factors for developing tb disease
- Need to know risk to determine results



# Screening

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- Screening is a must before administering the TST



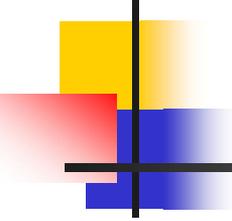
# Purpose of TB Screening

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- Identify individuals with TB infection and TB
- Provide appropriate treatment

## Overall goals

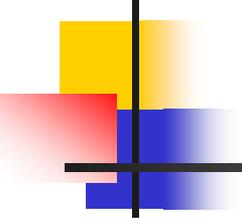
- Reduce morbidity in community
- Reduce transmission



# Diagnosis of TB Infection: Mantoux TB Skin Test (TST)

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- Is the preferred type of skin test
- Determines if a person has TB infection
- Is useful in:
  - Screening people for TB infection (contacts and targeted testing)
  - Examining a person who has symptoms of TB disease



# Mantoux Tuberculin Skin Test

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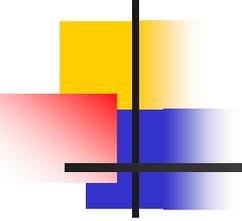
- Multiple puncture test (e.g. Tine Test) are inaccurate and not recommended
- Emergency Box
- QuantiFERON Gold

# Interferon Gamma Release Assays

## IGRAs

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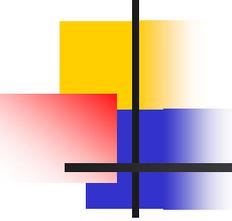
- Measures interferon-gamma (IFN- $\gamma$ ) released from a patient's T cells after stimulation with specific TB antigens
- QuantiFERON - TB Gold (QFT-G) 2005
- QuantiFERON - TB Gold InTube 10/2007
- T-SPOT.TB Test approved 2009



# TST... Who Can Administer?

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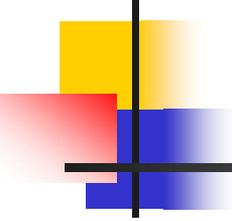
- IN VIRGINIA, only prescribers (MD, NP & PA) RN's and LPN's (working under the direct supervision of an RN ) can legally possess and administer tuberculin which is regulated as a class VI substance.
  - Code 54.1-3408 (G)



# Administering and Reading the Mantoux TST

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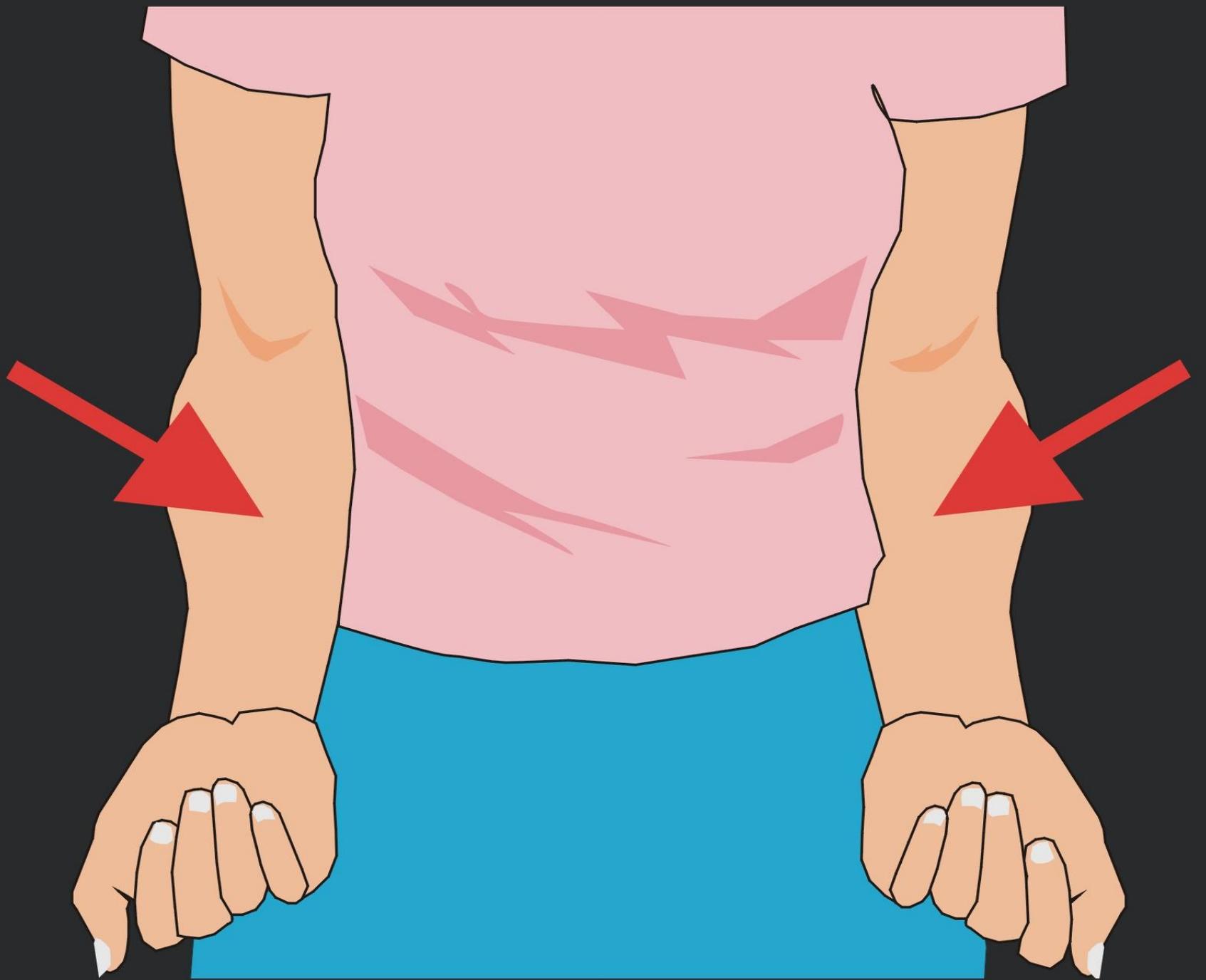
- Inject intradermally 0.1 ml of 5 tuberculin units of liquid tuberculin using a 27 gauge needle
  - Use the forearm whenever possible volar surface
  - Produce a wheal 6 to 10 mm in diameter
- Examine the patient's arm 48-72 hours after the tuberculin is injected
  - Assess the injection site for erythema (redness) and induration (swelling that can be felt)
  - Measure across the forearm the diameter of the indurated area only in millimeters
  - Do not measure the erythema



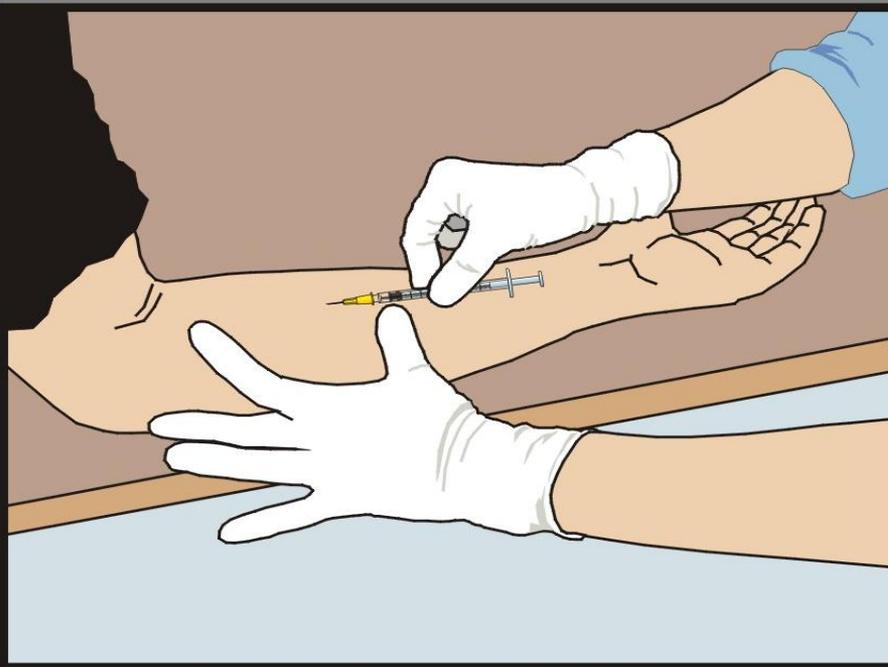
## Reading the TST

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- Educate clients regarding significance of a positive TST result
- Positive TST reactions can be measured accurately for up to 7 days
- Negative reactions can be read accurately for only 72 hours

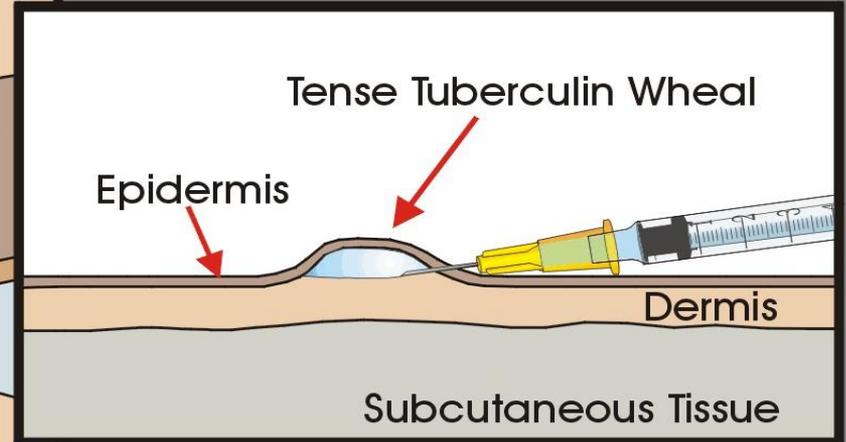
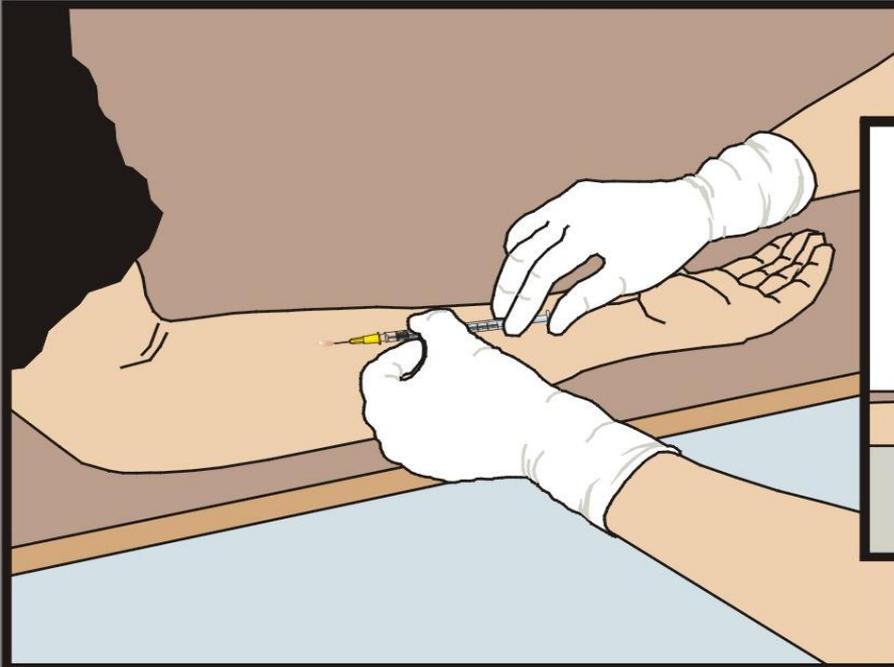


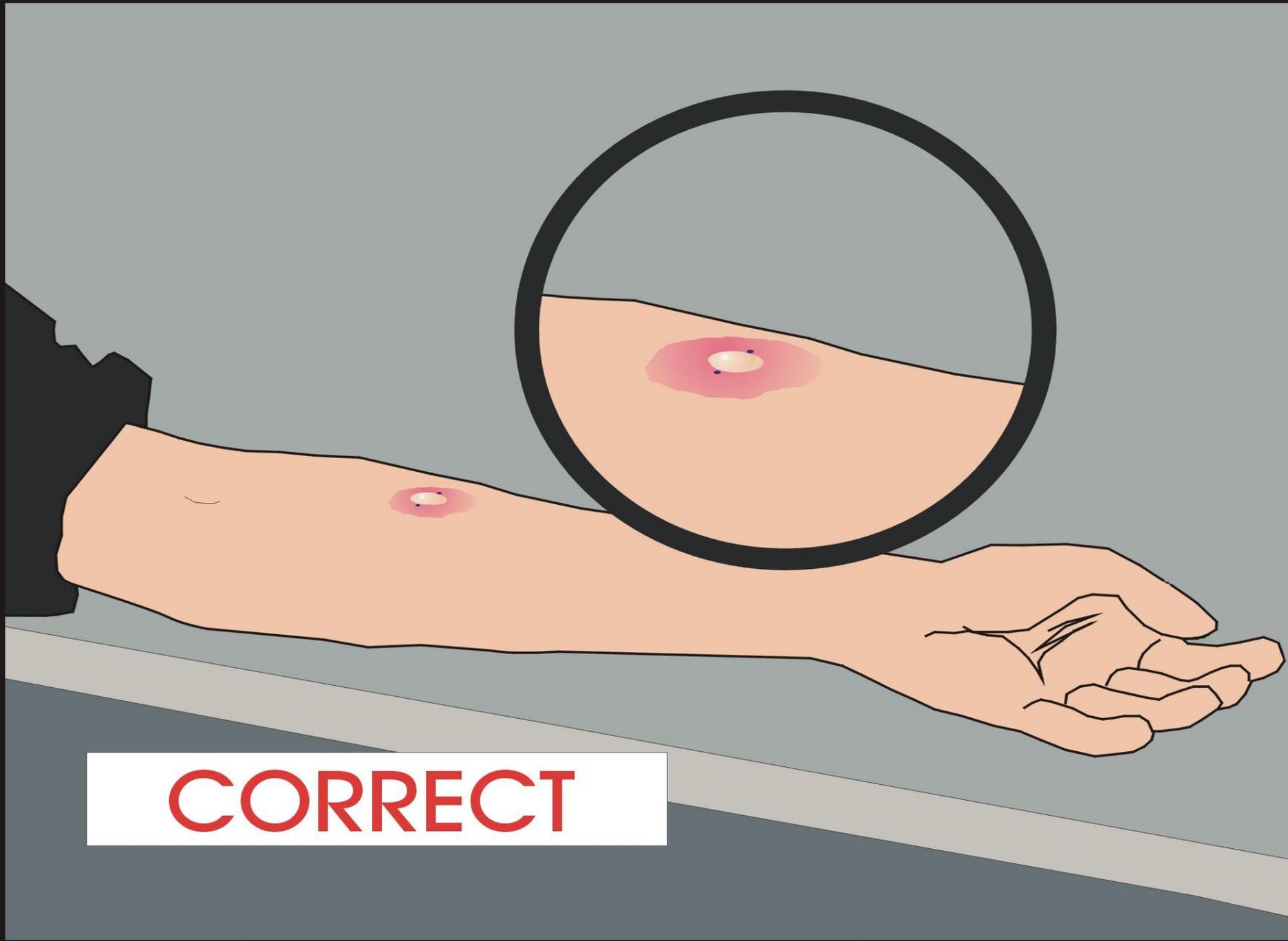
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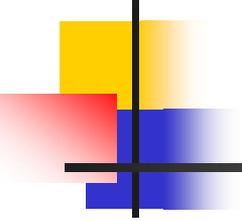
CORRECT

B





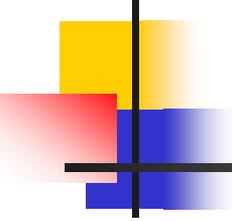
**CORRECT**



## Persons Positive at $\geq 5$ mm

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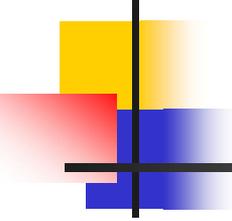
- People with HIV infection
- Close contacts of people with infectious TB
- Persons with chest x-ray findings suggestive of previous TB disease
- Persons on TNF- $\alpha$  drugs (Humaria, Remicaide)
- Persons on high doses of steroids



## Persons Positive at $\geq 10$ mm

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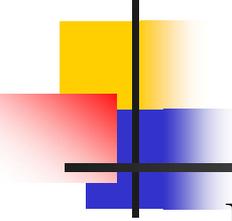
- Persons born/lived in areas of the world with high TB prevalence
- Injection drug users
- Persons who work or reside in high-risk congregate settings
- People with medical conditions that increase the risk for TB ( those listed on risk screen)
- Children younger than 4 years old
- Locally identified groups at higher risk for exposure



## Persons Positive at $\geq 15$ mm

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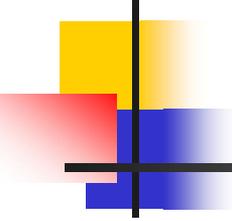
- Persons who have no risk factors for TB
- *Certain individuals may require TST for employment or school attendance*



# TST Result: False Positive

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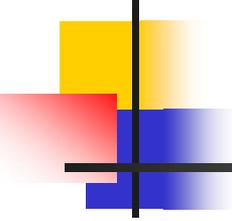
- Possible causes
  - Nontuberculous mycobacteria
  - BCG vaccination
    - Routinely administered to children in countries where TB is prevalent
    - Not a contraindication for the administration of the TB skin test
    - Wanes over time ; if TST is + likely due to TB infection if risk factors present



# TST Result: False-Negative

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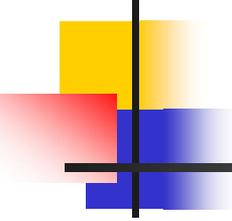
- Causes include
  - Anergy
  - Recent TB infection (within past 10 weeks)
  - Very young age (younger than 6 months old)
  - Incorrect administration and storage of test solution
  - Live-virus vaccination
  - Overwhelming TB Disease
  - Poor TST administration technique



# Other Issues in Skin Testing

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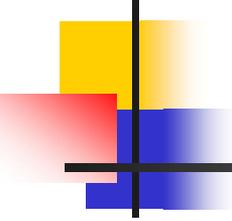
- Booster phenomena
  - Ability to react to tuberculin may wane with time
- Two-step testing    1 to 3 weeks apart
  - Use with groups who will have repeated TSTs as part of infection control programs
  - Use to validate test results



# Diagnosis of Active TB

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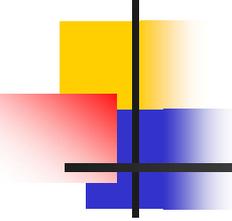
- *Evaluate all patients with symptoms of TB for TB disease, regardless of the patient's skin test reaction*
- *1/4 to 1/3 of all active MTB cases have negative TST at onset of treatment*



# Diagnosis of TB Disease: Chest X-Ray

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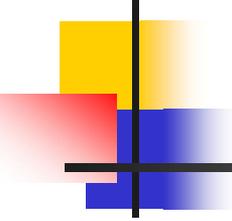
- Check for lung abnormalities suggestive of TB disease
- Typical findings may include cavities, infiltrates, effusions
- *Does not confirm TB disease*
- *May not disprove active TB in immune compromised individuals*



# Diagnosis of TB Disease: Bacteriologic Examinations

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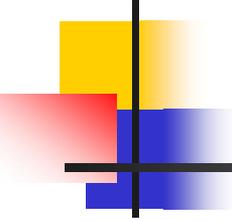
- Sputum collection
  - Spontaneous or induced
  - All symptomatic individuals
  - Abnormal CXR
- *M.tb* can be cultured from any body fluid or tissue
  - Specimen collected depends on the site of potential disease



# Yield Of Smear And Culture From Repeated Sputum Induction For The Diagnosis Of Pulmonary Tuberculosis.

## Induced sputum (% yield)

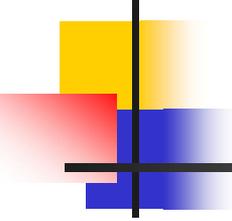
specimen	one	two	three	four
AFB smear	64	81	91	98
AFB culture	70	91	99	100



## Bacteriologic Examination (Cont.)

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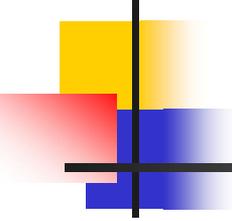
- Microscopy
  - “Smear results”
  - Presence acid-fast bacilli (AFB)
    - AFB are bacteria that remain stained even after they have been washed in an acid solution
    - Tubercle bacilli are only one kind of AFB
    - Results available usually within one day



# Bacteriologic Examination: AFB Smear Interpretation

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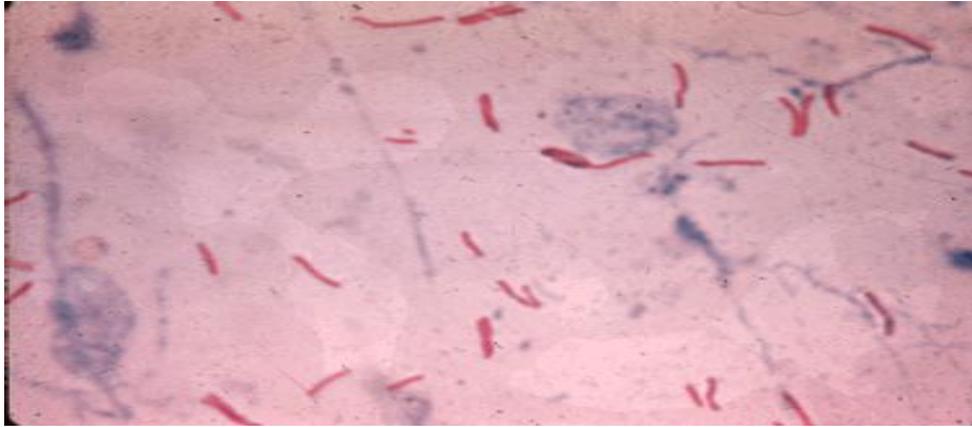
- Classify smear according to the number of AFB seen
  - Measure of number of organisms presented ( negative to 4+ )
  - Helps to determine level of potential infectiousness
- If no AFB seen, result is negative
  - Does not rule out possibility of TB

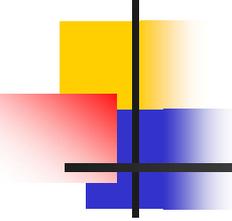


# Other TB Testing

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- DNA probe
  
- NAAT
  - MTD done in Virginia by DCLS
  - PCR
  - MTB
  - HAINES (UF)

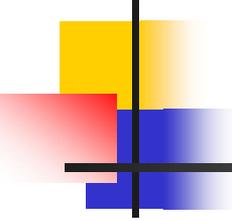




# Bacteriologic Examination: Culturing the Specimen

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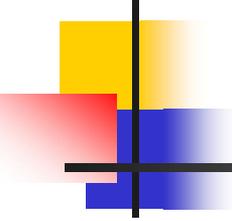
- Grow the mycobacteria on media
  - Several types of media
- All specimens should be cultured, regardless of whether the smear is positive or negative
- Results may take up to 6-8 weeks
- If *M. tuberculosis present*, confirms diagnosis of TB disease



# Bacteriologic Examination: Drug Susceptibility Testing

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- Critical test for appropriate management of active TB disease
- Test mandated by VA TB Control laws
- Determines which drugs will kill the tubercle bacilli that are causing disease in the individual patient
- Done in initial **positive** culture for *M. tuberculosis*
- May need to be repeated later in treatment course
- Drug levels



# Antituberculosis Drugs Currently in Use in the US

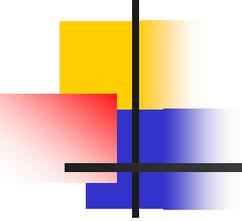
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## ■ First-line Drugs

- Isoniazid
- Rifampin
- Rifapentine
- Rifabutin
- Ethambutol
- Pyrazinamide

## ■ Second-line Drugs

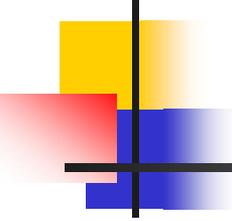
- Cycloserine
- Ethionamide
- Levofloxacin
- Moxifloxacin
- Gatifloxacin
- *P*-Aminosalicylic acid
- Streptomycin
- Amikacin/kanamycin
- Capreomycin
- Linezolid



# Definitions

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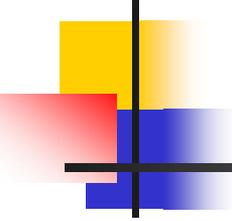
- **Primary drug resistance:**
  - **Infected with TB which is already drug resistant**
- **Secondary (acquired) drug resistance:**
  - **Drug resistance develops during treatment**



# What Causes Secondary Drug Resistance?

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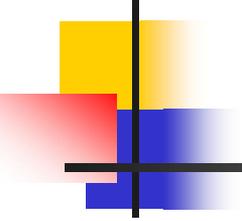
- **TREATMENT  
FAILURE**



# Criteria for Reporting TB Cases

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- All TB cases and suspects are required to be reported in Virginia (EPI 1)
  - Positive smear
  - Positive culture
  - Clinical findings and/or treatment started
- All children under age 4 found to have latent TB infection are required to be reported (EPI 1)
- Discharge Plans approved by Health Department



# Counting Cases

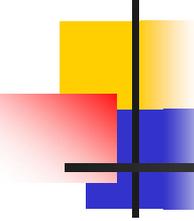
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- Culture confirmed MTB
- Clinical TB Case
  - Keep on medicines for two months and if there is clinical and radiographic improvement and meets other CDC guidelines, can be classified as a clinical case
- ❖ Suspects



# LTBI Treatment Regimens

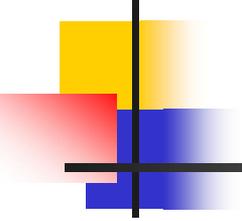
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# Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection

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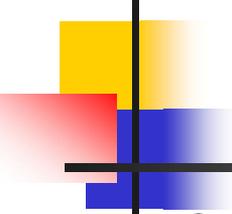
As tuberculosis (TB) disease rates in the United States (U.S.) decrease, finding and treating persons at high risk for latent TB infection (LTBI) has become a priority.



# Before Initiating Treatment

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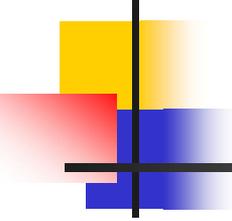
- Rule out TB disease (i.e., wait for culture result if specimen obtained)
- Determine prior history of treatment for LTBI or TB disease
- Assess risks and benefits of treatment
- Determine current and previous drug therapy



# Isoniazid Regimens

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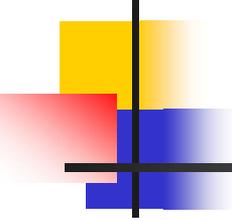
- 9-month regimen of Isoniazid 300mg qd (INH) is the preferred regimen (270 doses in 12 months)
- 6-month regimen is less effective but may be used if unable to complete 9 months(180 doses)
- May be given daily or intermittently (twice weekly)
  - Dosage different 900mg twice weekly
  - 76 doses in 12 months or 52 doses in 9 months
  - Use directly observed therapy (DOT) for intermittent regimen
  - Private sector/HD does not do intermittent INH



## Rifampin Regimens (1)

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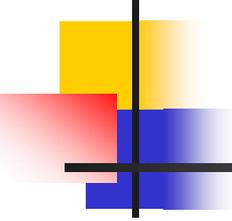
- Rifampin 600mg (RIF) given daily for 4 months is an acceptable alternative when treatment with INH is not feasible.
  - 120 doses in 6 months
- In situations where RIF cannot be used (e.g., HIV-infected persons receiving protease inhibitors), rifabutin may be substituted.



## Regimens ...Suspects

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- RIF daily for 4 months  
*(120 doses within 6 months)*
- RIF and PZA for 2 months should generally not be offered due to risk of severe adverse events

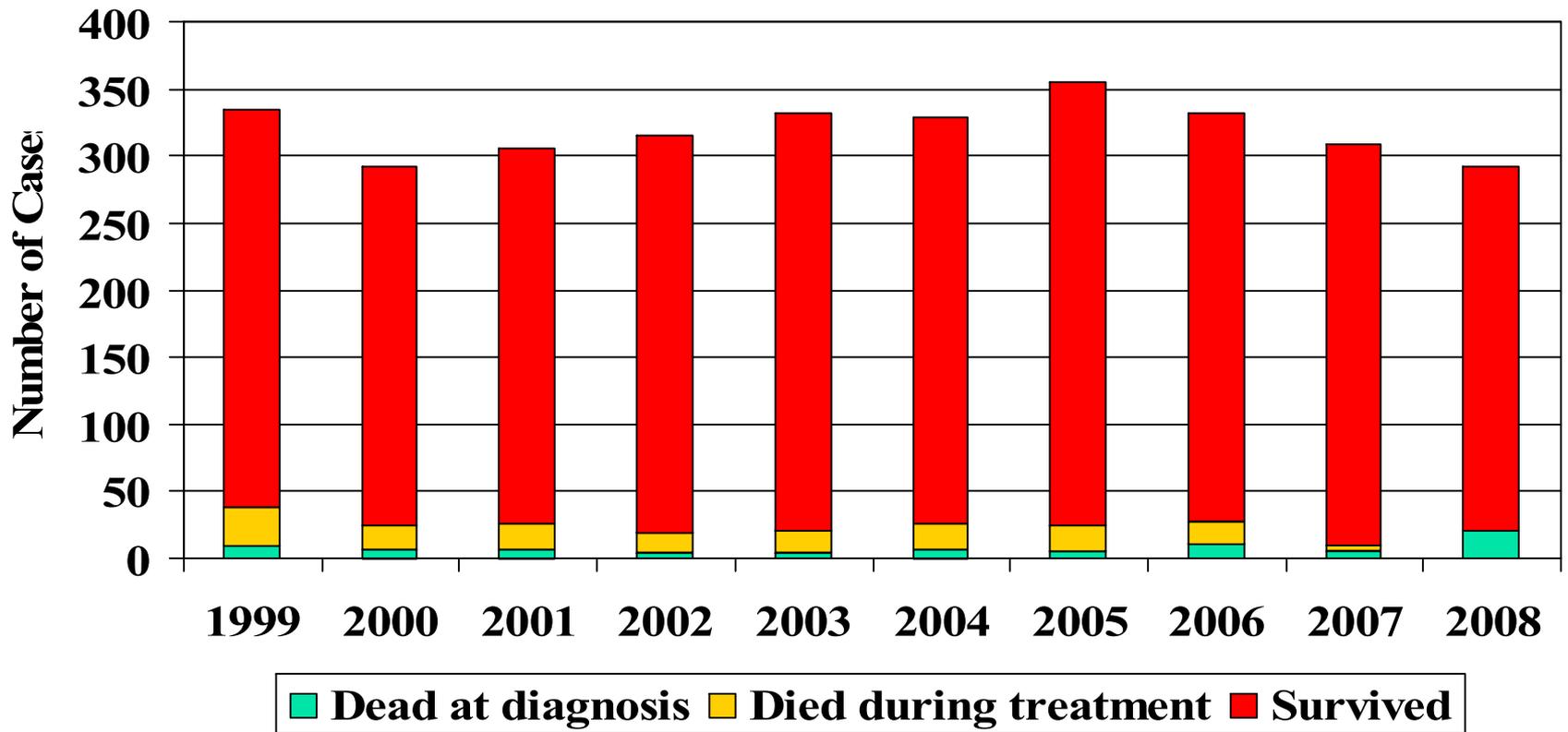


# Completion of Therapy

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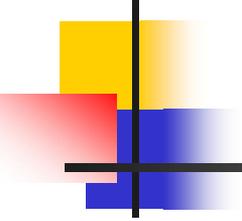
Completion of therapy is based on the total number of doses administered, not on duration alone.

# Tuberculosis Mortality VA 1999-2008

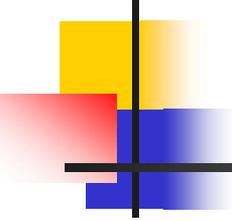


# TB in Selected Risk Factors 2008

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■ Health care workers	6
■ Expired from TB	17
■ LTC	5
■ Corrections	5
■ Homeless	1
■ HIV	9
■ Pediatric ( 0-14)	10

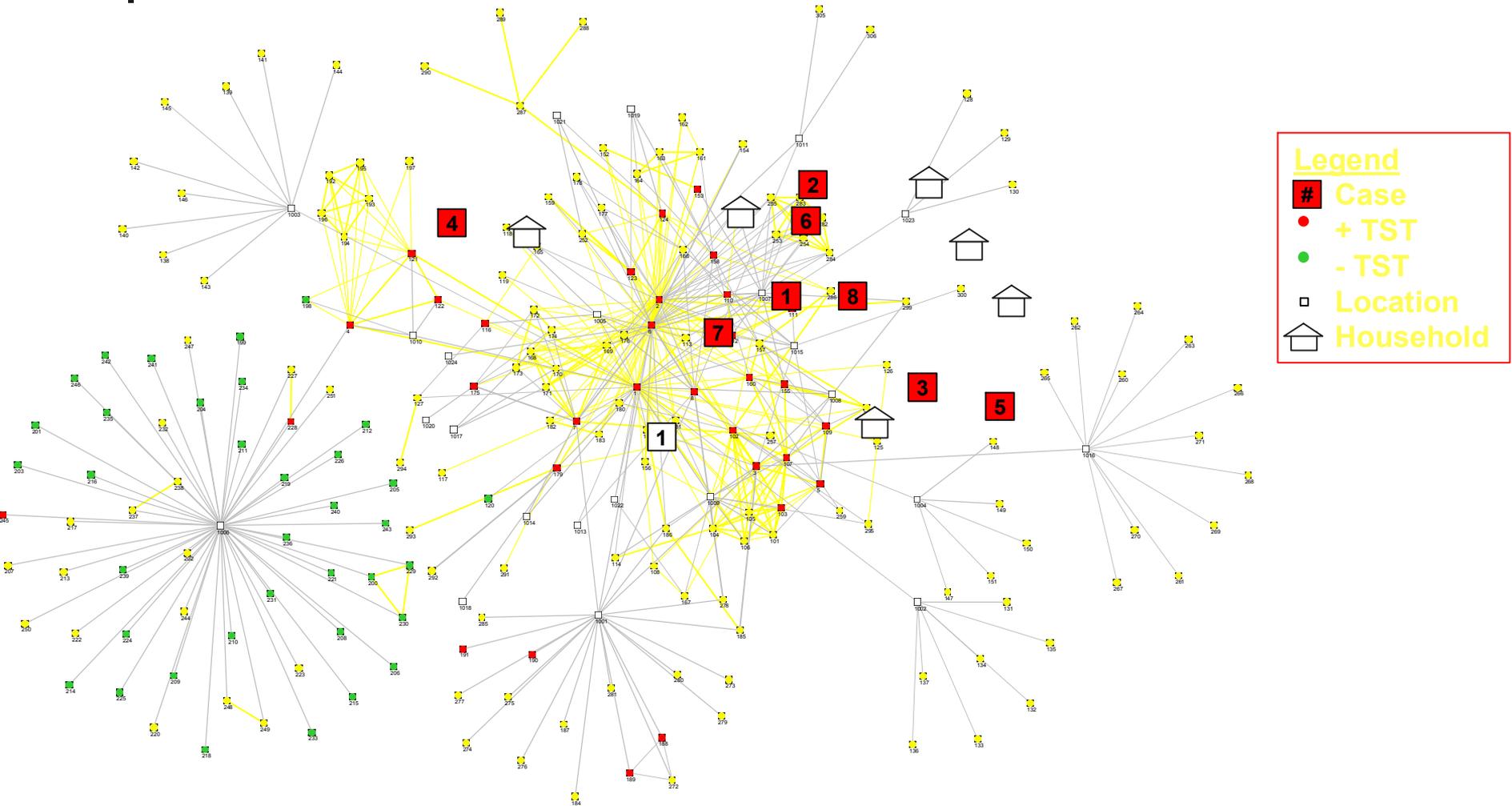


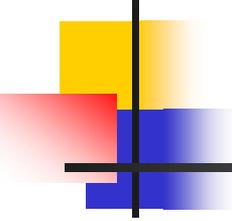
# CONTACT INVESTIGATION

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- MTD Testing

# WHAT ARE WE TRYING TO PREVENT?

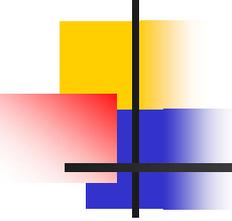




# What Can You Help Prevent?

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- By providing DOT?



# Who to Call

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## VDH DIVISION OF DISEASE PREVENTION TB PROGRAM

Jane Moore (804) 864-7920

Brenda Mayes (804) 864-7968