# TB Infection Diagnosis Recommendations

Megan Devine, MD

Associate Professor of Pulmonary and Critical Care Medicine
University of Texas HSC at Tyler

Screening and Treating Tuberculosis Infection
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Tyler, Texas

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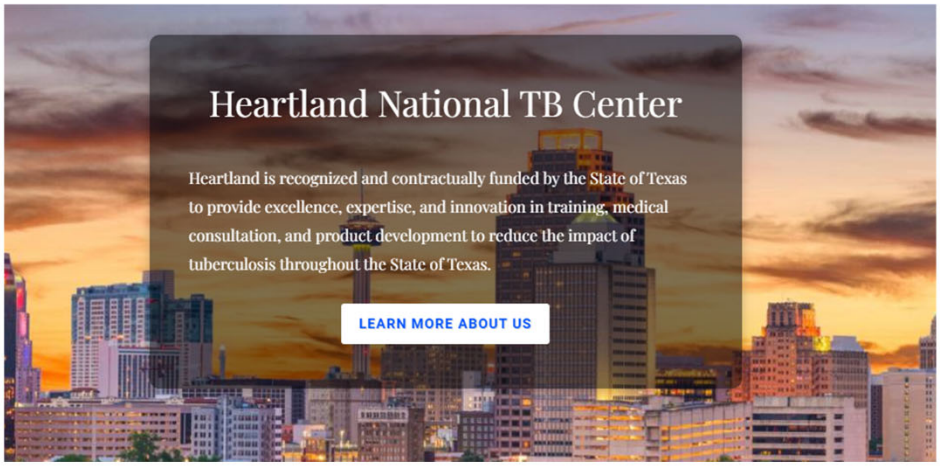
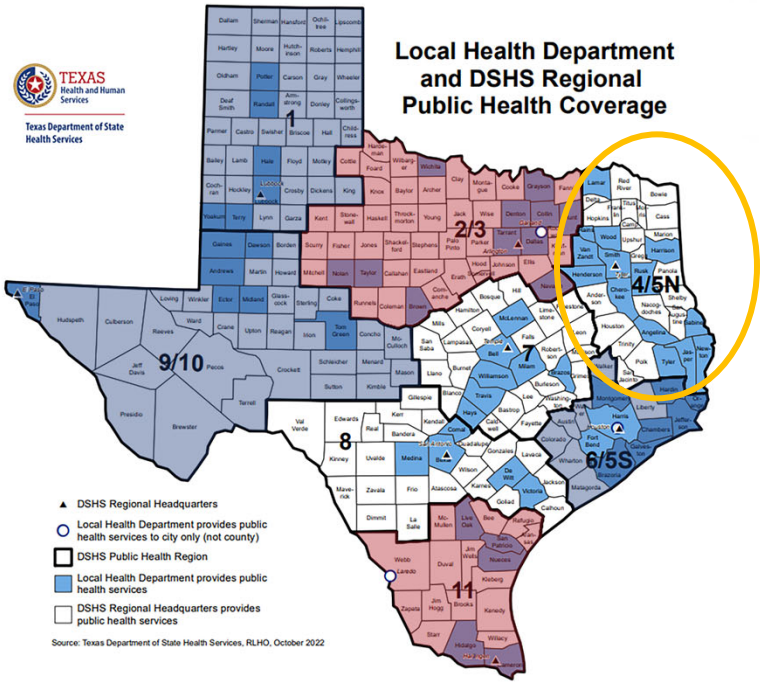
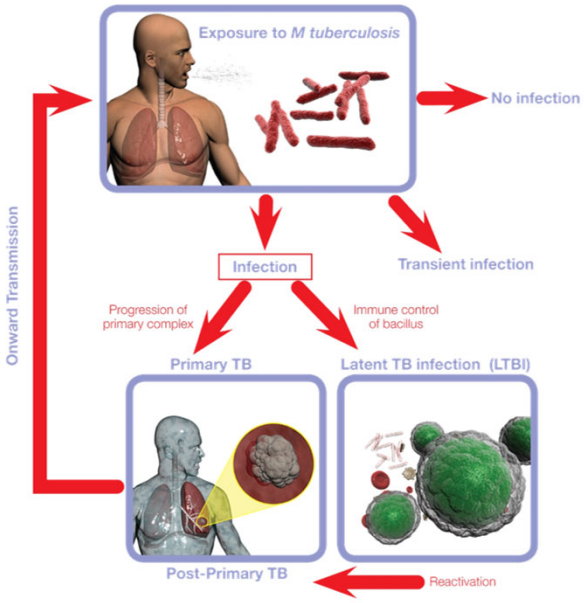
## Texas Center for Infectious Disease (TCID)

- 75-bed capacity, 50-acre secure campus
- Joint Commission accredited as acute care hospital
- Each bed and bath are private with the ability to maintain a negative air-pressure space
- Eligible patients
  - Difficult to treat TB due to comorbid medical conditions, psychiatric disease and/or social determinants
  - Drug resistant TB
  - Court-ordered treatment


Heartland National TB Center
Heartland is recognized and contractually funded by the State of Texas to provide excellence, expertise, and innovation in training, medical consultation, and product development to reduce the impact of tuberculosis throughout the State of Texas.
LEARN MORE ABOUT US


TEXAS
Health and Human Services
Texas Department of State Health Services
Local Health Department and DSHS Regional Public Health Coverage
1
2/3
4/5N
7
9/10
8
6/5S
11
DSHS Regional Headquarters
Local Health Department provides public health services to city only (not county)
DSHS Public Health Region
Local Health Department provides public health services
DSHS Regional Headquarters provides public health services
Source: Texas Department of State Health Services, RLHO, October 2022

# What is TB Infection?

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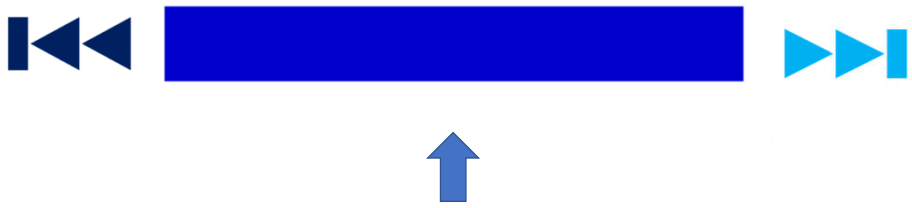
# LATENT TB INFECTION

- We used to think the bacteria were in a resting state or dormant but
  - TB Bacteria are metabolically **active and dividing**, but **infection is controlled by the immune system**.

"…a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB"

**- WHO Guidelines on the management of Latent Tuberculosis Infection 2015**

# TB Can Be Considered a Continuum



**Latent** | **Incipient/Subclinical** | **Active**

**Active TB may develop when immune response is weakened**

# LATENT TB INFECTION

- Persons with LTBI are NOT infectious
- 90 +% chance of never getting Active TB Disease
- But the TB organism is in your body!

# Latent TB Infection

- Persons are infected with *Mycobacterium tuberculosis* but:
  - No Active TB Symptoms
  - Chest X-ray may be normal, or show granuloma, **stable** pleural or parenchymal scarring
  - Positive TST or IGRA

**The TST, the T Spot and the QuantiFERON -**
**All miss > 10 % of those with active TB; % of those with true LTBI with negative tests unknown**

## Latent TB Infection (LTBI)

- Persons are **infected** with *Mycobacterium tuberculosis* but:
  - No Active TB Symptoms
  - Chest X-ray may be normal, or show small granuloma, **stable** pleural or parenchymal scarring
  - Positive TST (Tuberculin Skin Test) or IGRA (Blood Test)
  - **Not infectious – Do not transmit TB**

## Active TB Disease

- Persons are **sick** and usually have at least one of the below
  - Abnormal CXR
  - Symptoms and or findings consistent with TB disease
  - Specimen grows MTB or is PCR positive
  - **Usually are infectious**

# Persons at Risk of (**Exposure**) MTB Infection or Disease

- People who have spent time with someone who has TB disease
- People from a country where TB disease is common.
- People who **live or work** in high-risk settings:
  - correctional facilities, long-term care facilities or nursing homes, and homeless shelters
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children and adolescents exposed to adults who are at increased risk for latent tuberculosis infection or TB disease

## Percent Risk of Disease by Age

| Age at Infection | Risk of Active TB |
|---|---|
| Birth – 1 year* | 43% |
| 1 – 5 years* | 24% |
| 6 – 10 years* | 2% |
| 11 – 15 years* | 16% |
| Healthy Adults | 5-10% lifetime risk |
| HIV Infected Adults+ | 30-50% lifetime |

*Miller, Tuberculosis in Children Little Brown, Boston, 1963

+WHO, 2004

## Persons at Risk of **Progression** from Latent TB Infection to Active TB Disease

- HIV infection
- Chronic kidney disease
- Silicosis
- **Recent exposure**
- Diabetes
- Chest x-ray abnormality consistent with previous inadequately treated TB
- Intravenous drug use
- Smoking – active and passive
- Underweight by >10%

ATS-CDC. Am J Respir Crit Care Med 2000;161:S221

## Persons at Risk of **Progression** from Latent TB Infection to Active TB Disease

- Immunosuppression
  - Pregnancy and first three months post partum
  - Organ transplant recipients
  - Hematologic cancers and head and neck cancers
  - Medications
    - TNFα inhibitors
    - Prednisone >15 mg, > 4 weeks
    - Chemotherapy
    - Other immunosuppressive drugs

## Tests for Tuberculosis

……are still not awesome

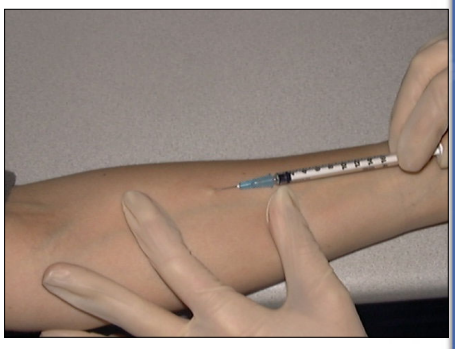
**The TST, the T Spot and the QuantiFERON -**
**All miss > 10 % of those with active TB; % of those with true LTBI with negative tests unknown**

# TB Infection Diagnostics

- TB Skin Test (TST)
- Interferon Gamma Release Assays (IGRA)

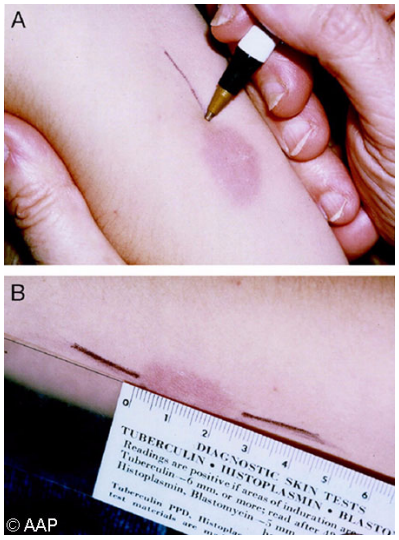
# The Tuberculin Skin Test (TST)

- 0.1 ml of 5 TU PPD tuberculin injected intradermally
- **Induration** in millimeters read 48-72 hours after injection



# Reading the TB Skin Test

Measure **induration**, not erythema!!!




# TB Skin Test (TST)

- Pros:
  - Inexpensive
  - Simple to perform (if you know what you are doing)
- Cons:
  - Must return in 48-72 hrs
  - Interpretation is somewhat subjective
  - False Negatives:
    - Elderly
    - Immunosuppressed
  - False Positives:
    - Low risk populations
    - Non-tuberculous mycobacteria
    - BCG vaccination

# Classifying the Tuberculin Reaction

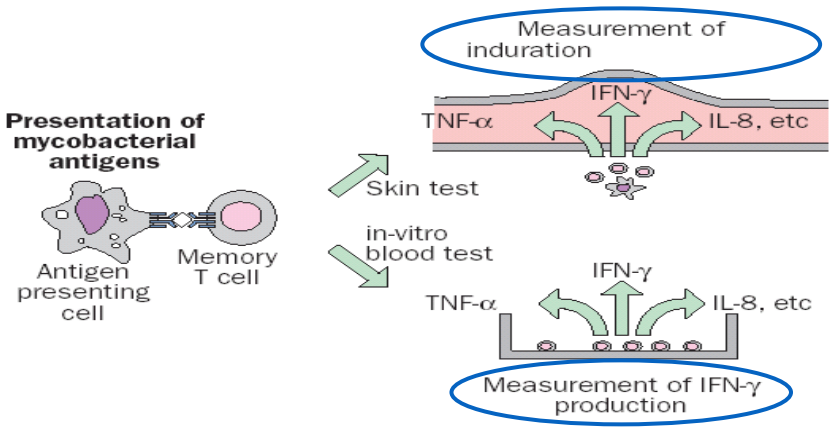
- You must know something about your patient!
- ≥ 5 mm is positive in 'high risk people'
- ≥ 10 mm is positive in 'people from high-risk environments"
- ≥ 15 mm is positive……period
- Targeted skin testing programs should only be conducted among high-risk groups

# Interferon Gamma Release Assays (IGRAs)

# Interferon Gamma Release Assays

- Replacing TST in many jurisdictions
- Blood test
  - measures interferon gamma release in response to stimulation by TB antigens
- More specific
- Equally sensitive
- Do not require a patient to return for reading
- Eliminate false positive TST due to BCG
- Can be used in children down to 2 years of age

# TST vs In-vitro Assays




Andersen et al. Lancet 2000;356:1099

# Antigens for Newer Generation IGRAs

- Negative control or nil (e.g., saline, heparin)
- Positive control or mitogen:
  - non-specific immune response stimulator (e.g., phytohemagglutinin)
- *M. tuberculosis*-specific antigens
  - Unlike PPD used in TST, do not cross-react with BCG or NTM (some exceptions)
  - ESAT-6, CFP-10 (actually simulated using overlapping peptides)

# Antigens for Gamma-Release Assays

| Tuberculosis complex | Antigens | |
|---|---|---|
| | ESAT | CFP |
| M tuberculosis | + | + |
| M africanum | + | + |
| M bovis | + | + |
| BCG substrain | | |
| gothenburg | - | - |
| moreau | - | - |
| tice | - | - |
| tokyo | - | - |
| danish | - | - |
| glaxo | - | - |
| montreal | - | - |
| pasteur | - | - |

| Environmental strains | Antigens | |
|---|---|---|
| | ESAT | CFP |
| M abcessus | - | - |
| M avium | - | - |
| M branderi | - | - |
| M celatum | - | - |
| M chelonae | - | - |
| M fortuitum | - | - |
| M gordonii | - | - |
| M intracellulare | - | - |
| M kansasii | + | + |
| M malmoense | - | - |
| M marinum | + | + |
| M oenavense | - | - |
| M scrofulaceum | - | - |
| M smegmatis | - | - |
| M szulgai | + | + |
| M terrae | - | - |
| M xenopi | - | - |

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# FDA-Approved IGRAs

## QuantiFERON®-TB Gold Plus

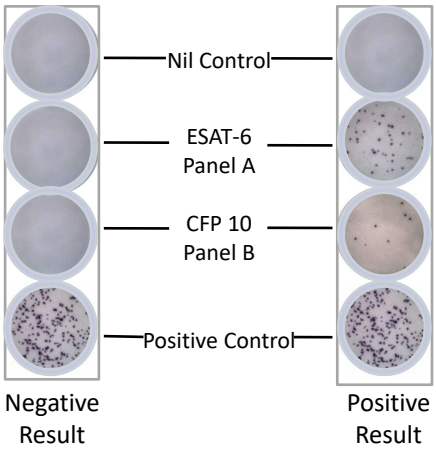
- Mitogen – Positive Control
  Low response may indicate inability to generate IFN-γ
- Nil – Negative Control
  Adjusts for background IFN-γ
- TB1 – Primarily detects CD4 T cell response
- TB2 – Optimized for detection of CD4 and CD8 T cell responses


## TB Spot

# Interpretation Criteria for the QFT-GIT Test

| Nil (IU/mL) | TB Antigen minus Nil (IU/mL) | QFT-GIT (IU/mL) | Mitogen | Interpretation |
|---|---|---|---|---|
| ≤ 8.0 | ≤ 0.35 or < 25% of Nil value | Negative | ≥ 5.0 | *M. tuberculosis* infection unlikely |
| ≤ 8.0 | ≥ 0.35 and ≥ 25% of Nil value | Positive | ANY | *M. tuberculosis* infection likely |
| ≥ 8.0 | ANY | Indeterminate | ANY | Indeterminate |
| ≤ 8.0 | ≤ 0.35 and or < 25% of Nil value | Indeterminate | < 5.0 | Indeterminate |

# Interpretation of Results



## Interpretation Criteria for the T-Spot.TB

| Result | Nil* | TB Response# # | Mitogen++ | Interpretation+ |
|---|---|---|---|---|
| Positive | ≤ 10 spots | ≥ 8 spots | Any | *M.tuberculosis* infection likely |
| Borderline | ≤ 10 spots | 5, 6, or 7 spots | Any | Uncertain likelihood of *M. tuberculosis* infection |
| Negative | ≤ 10spots | ≤ 4 spots | | M Tb infection unlikely |
| Indeterminate | > 10<br>≤ 10 | Any<br>< 5 spots | Any<br>< 20 spots | Uncertain likelihood of *M. tuberculosis* infection |

## Who Should be Tested for TB Infection?

### Targeted Testing for TB Infection

The simplified version:

- Persons who are at increased risk for *M. tuberculosis* infection
- Persons at increased risk for progression to active disease if infected with *M. tuberculosis* (even if not at increased exposure risk)

And those who tend to be tested in addition:

- Persons tested for administrative reasons (e.g., mandatory employment testing)
- Persons with symptoms of active TB disease (fever, night sweats, cough, and weight loss)

## New in the Diagnosis Guidelines

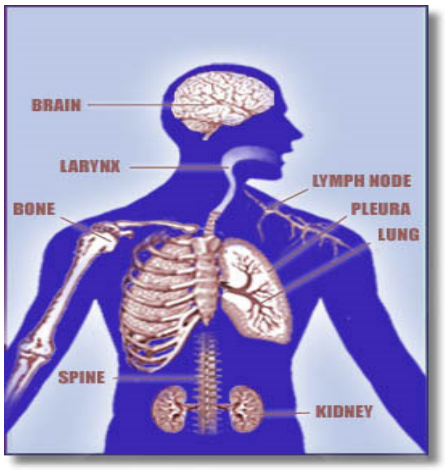
- Decisions to test or treat are based on likelihood of infection and likelihood of progression
- IGRAs are recommended for testing for TB infection in individuals ≥ 2 years old with low or moderate risk if infection or progression
  - Note: IGRAs are a 'better' choice
    - When TST administration is questionable
    - In BCG vaccinated populations (increased specificity)
    - In populations with a poor rate of return
- Testing in low-risk populations is still not recommended. When it is necessary, such as required HCW screenings, use an IGRA
- In populations at high risk for infection or progression, either a TST or IGRA is appropriate

# Diagnosing Tuberculosis

# Sites of TB Disease

Pulmonary:
- Lungs

Extrapulmonary:
- Larynx
- Lymphatics
- Pleural effusion
- Kidneys
- Genito-urinary
- Bones & joints
- Miliary (disseminated)




# Signs & Symptoms Pulmonary TB

Pulmonary Symptoms:

- Prolonged productive cough of over 3 weeks duration
- Chest pain
- Hemoptysis

Systemic Symptoms:

- Fever
- Chills
- Night sweats
- Appetite loss
- Weight loss
- Easy fatigability

## Evaluation for TB

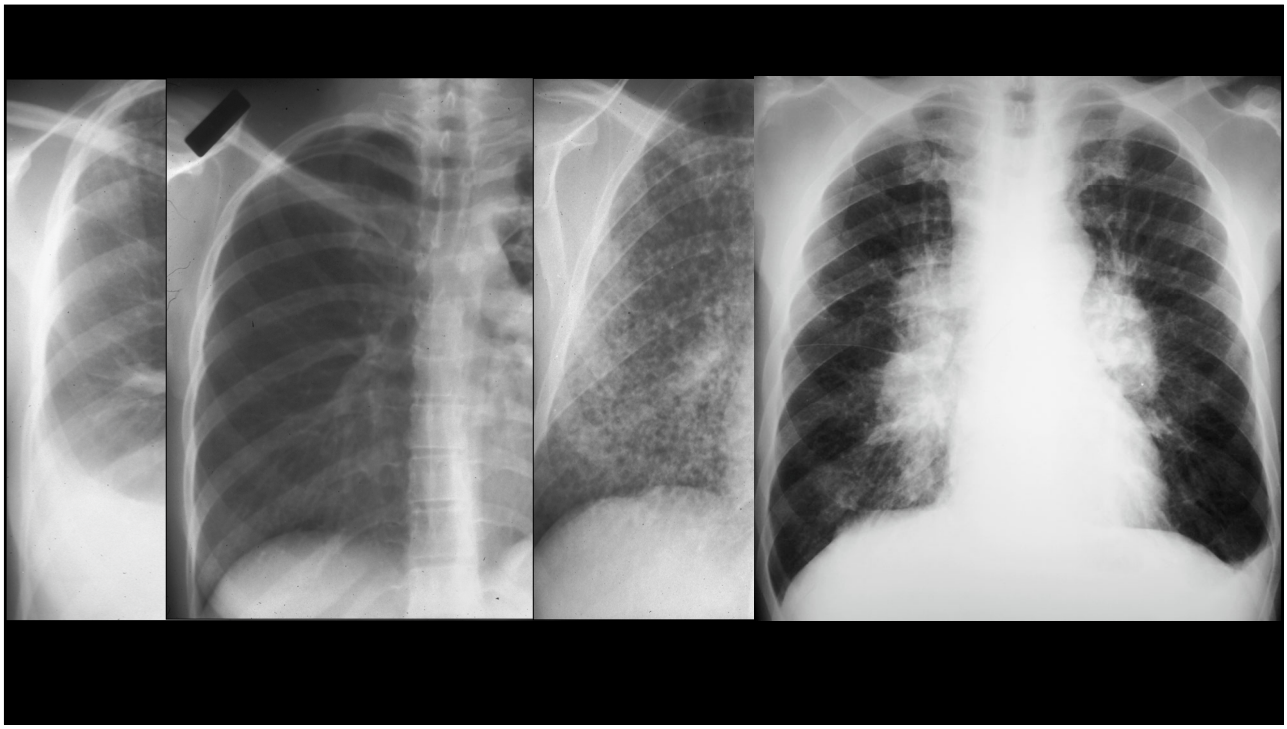
- Medical history
- Physical examination
- Testing for TB infection
- Chest radiograph
- Bacteriologic or histologic exam

## No CXR study shows findings SPECIFIC for TB

Cavitary process are more likely to be TB

Common mimics of TB =

- Non-tuberculous mycobacteria (NTM)
- Fungal infection
- Bacterial abscesses
- Necrotic neoplasm (especially lung neoplasm)

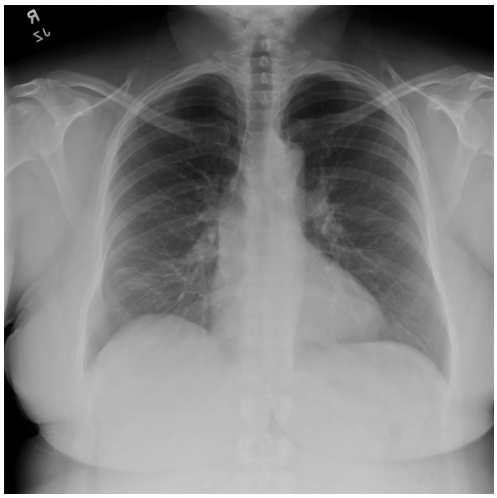


# Example Evaluations

# Patient # 1

40yo woman undergoing evaluation for immunosuppressant therapy
- Feels well, has no respiratory symptoms or concerns
- No substance abuse
- Hx = chronic iritis
- Physical exam is normal
- TB QFT 4.15 / 3.64

Latent TB Infection



# Patient # 2

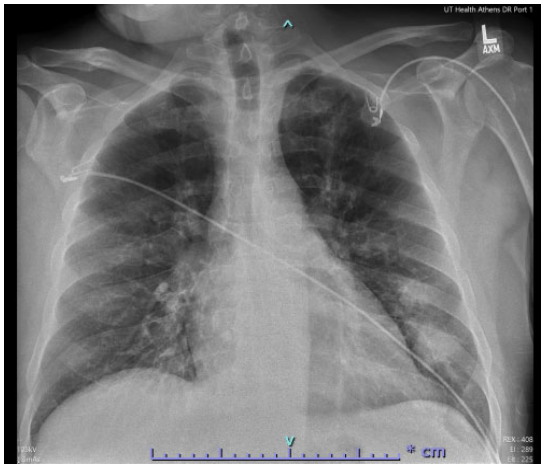
58yo man undergoing evaluation for immigration
- Feels well, has no symptoms or concerns
- No substance abuse
- No chronic medical problems
- Physical exam is normal
- TB QFT 4.53 / 5.52

Sputum AFB culture + MTB

# Patient # 3

58yo man has a CXR as part of an evaluation in the ED for nausea. He reports no respiratory symptoms.
- Hx of prior IV drug use
- Hx of untreated Hep C
- Chronic hemolytic anemia treated with chronic prednisone for 2 months followed by Rituxan
- TB QFT 0.13 / 0.028

Sputum AFB culture + MTB




# Thank you