TB Basics

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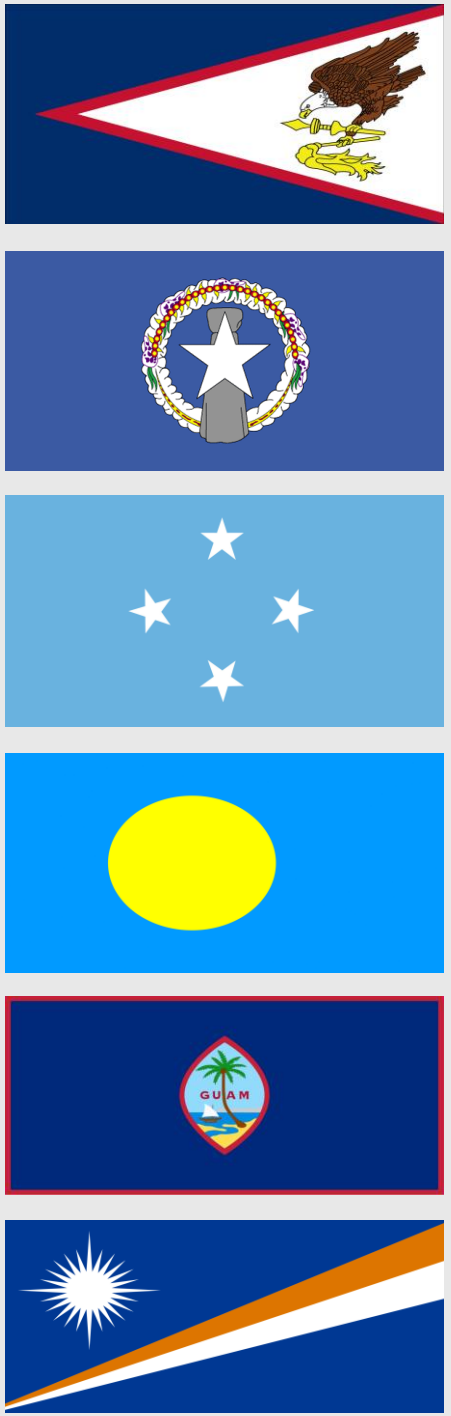
USAPI Regional TB Training 2024



Objectives

- Discuss the relevance of past and present TB
- Explain pathogenesis of mycobacterium tuberculosis infection
- Discuss the spectrum of tuberculosis infection and disease
- Review screening for TB infection
- Review basic workup of TB disease

Terminology

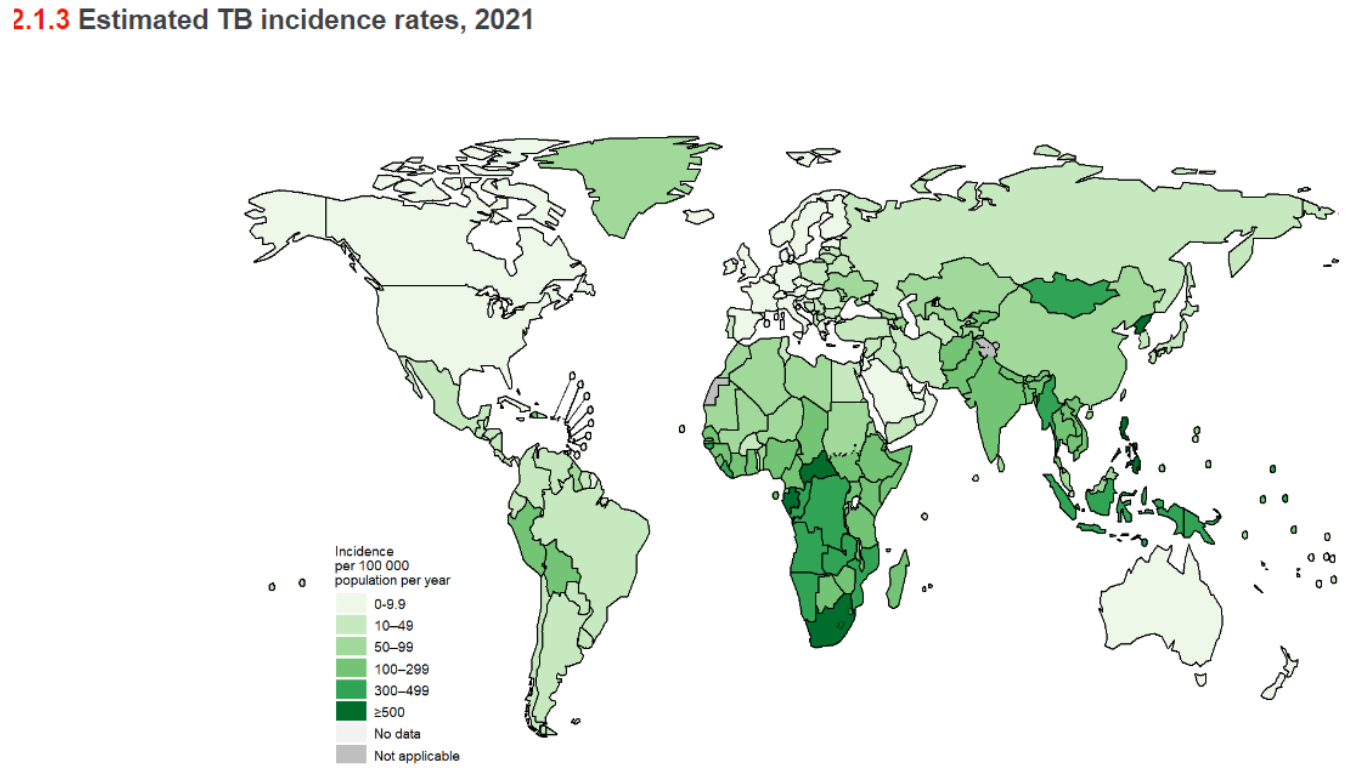
- Latent TB = LTBI = sleeping TB = TB infection = sleeping TB
- Active TB = TB disease

TB in History

- One of the oldest pathogens known to man
- Evidence of TB disease in ancient Egyptian mummies
- Called “consumption”
- Romanticized and thought of as a creative disease
- TB influences many parts of day-to-day life, language, and culture
  - To “inspire” is to breathe in; inspire creativity
  - To “expire” to breathe out; synonym for death
  - Beauty standards
  - Stethoscopes

TB Today: common, curable, preventable

- TB is common
  - 1.7 billion people worldwide have latent TB infection
  - Estimated 13 million people in the US have latent TB infection
  - 10.8 million people became ill with active TB in 2023
  - 1.25 million people died from TB disease in 2023



TB Today: common, curable, preventable

- TB is curable
  - WHO reported:
    - with first line regimens treatment success rate was 88%
    - <1% of individuals had treatment failure
    - 4% of people died

TB Today: common, curable, preventable

- TB is preventable
  - Globally, LTBI treatment is 60%-90% efficacious depending on the region
  - Early detection of TB disease reduces transmission

TB stigma

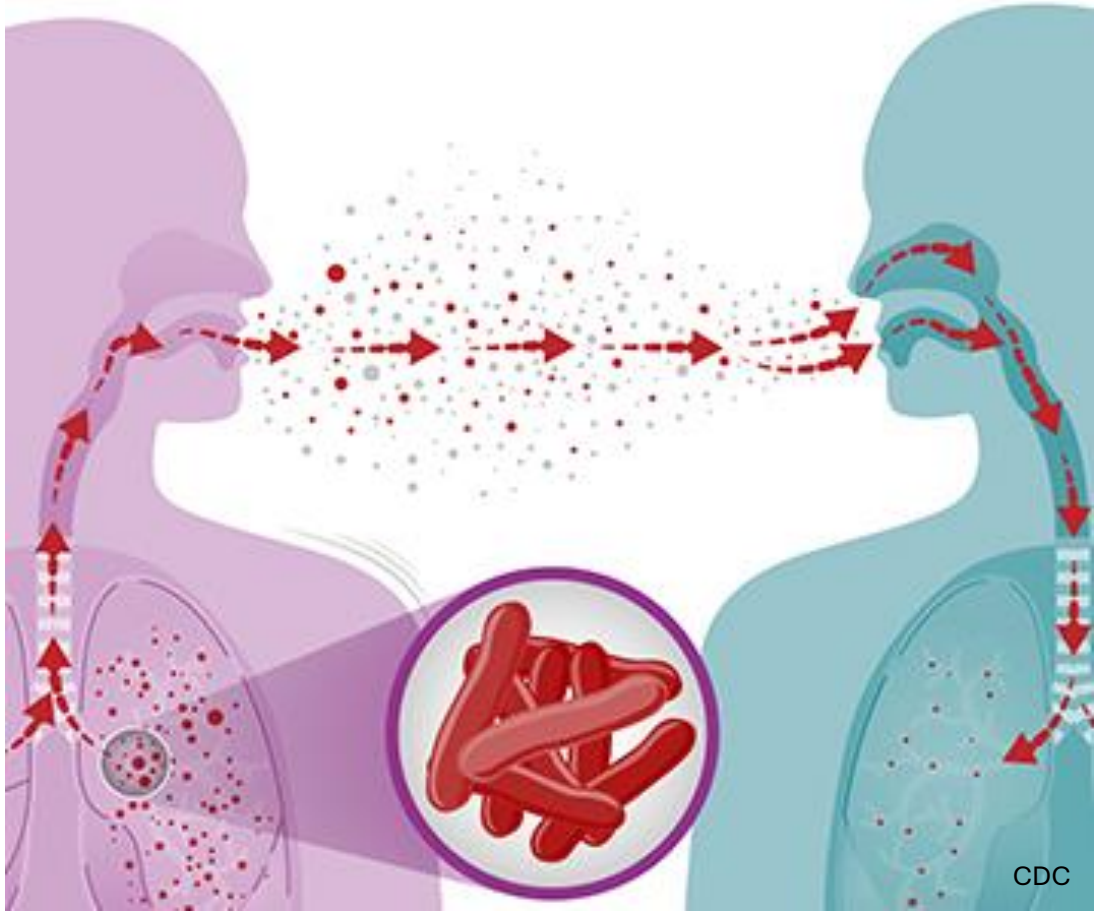
- Societal symptom of TB disease that allows for continued disease life cycles and delays in diagnosis
- Isolation can make people feel like the person themselves is dangerous
- In low incidence settings, patients may be less likely to the seek care of those with unfamiliarity with TB for fear of being judged

TB stigma

- Reducing stigma on an individual level when working with patients requires very intentional acts and statements
- DOT is imperative, but can be viewed as punitive by patients
- Contact assessments feel invasive
- Humanity – fighting the pathogen that has infected our patients. Not fighting our patients.

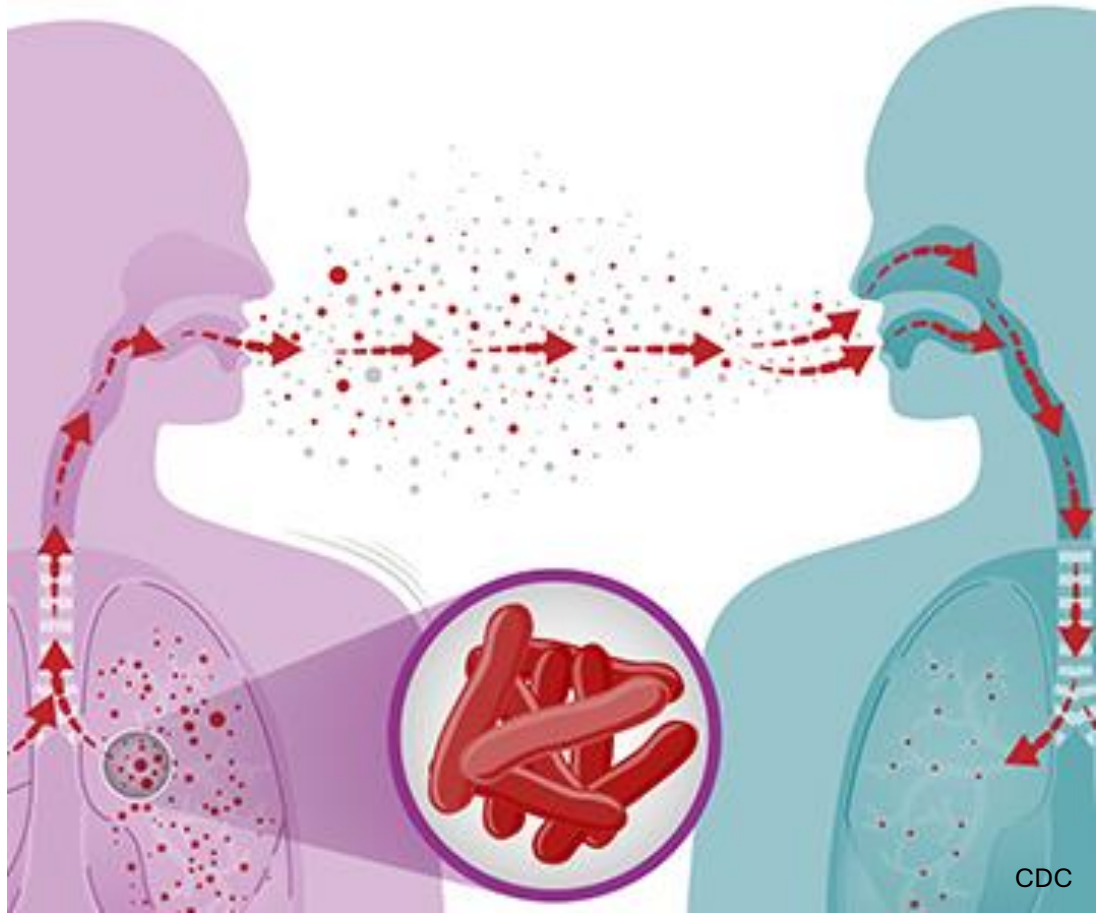
Transmission and pathogenesis

- Caused by mycobacterium tuberculosis (M. tuberculosis)
- Who is contagious?
  - Those with active disease within the respiratory tract who are not yet on anti-TB therapy
  - Extrapulmonary TB is not contagious
  - Latent TB infection is not contagious



Transmission and pathogenesis

- How does it spread?
  - Airborne through a shared airspace via droplet nuclei
  - Expelled when person with infectious TB disease coughs, sneezes, speaks, or sings
- Factors affecting transmission
  - Susceptibility of the host
  - Infectiousness of the patient
  - Environment
  - Exposure



TB is **NOT** spread by:

Shaking someone's hand

sharing food or drink

touching bed linens, toilet seats or tabletops

sharing toothbrushes

kissing

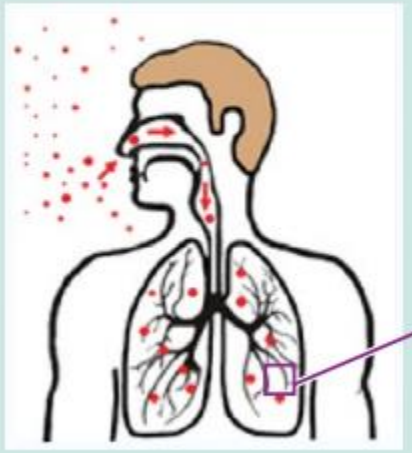
Slide Credit: Shea Rabley, R.N., M.N.

Preventing transmission

- Highest risk for infection are those who spent a lot of time with the patient, especially if it was in an enclosed or poorly ventilated setting
- Generally, repeated daily contact is needed for a healthy adult individual to get infected
- Congregate settings are especially high risk for transmission
- Patients who are still infectious should wear a surgical mask
- Healthcare workers should wear an N-95 or other approved PPE for airborne precautions

Figure 1.3
Pathogenesis of LTBI and TB Disease

1



Area of detail for boxes 2, 4, and 5

Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

2

Bronchiole

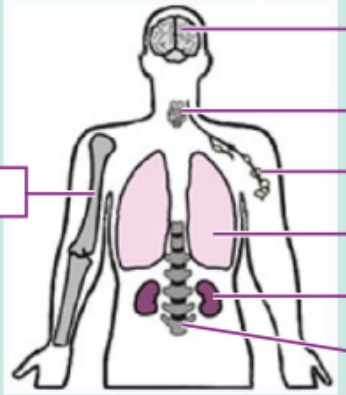
Tubercle bacilli

Alveoli

Tubercle bacilli multiply in the alveoli.

Images from: CDC Core Curriculum on Tuberculosis: What the Clinician Should Know

3



A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is most likely to develop (such as the brain, larynx, lymph nodes, lungs, spine, bone, or kidneys).

Granuloma: cluster of immune cells

4

Within 2 to 8 weeks, special immune cells called macrophages ingest and surround the tubercle bacilli. The cells form a barrier shell called a granuloma that keeps the bacilli contained and under control. (This is known as **latent TB infection**, or **LTBI**.)

A period when PPD or IGRA will be negative, but TB infection is present

5

If the immune system **cannot** keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (**TB disease**). This process can occur in different areas in the body, such as the lungs, kidneys, brain, or bone (see diagram in box 3).

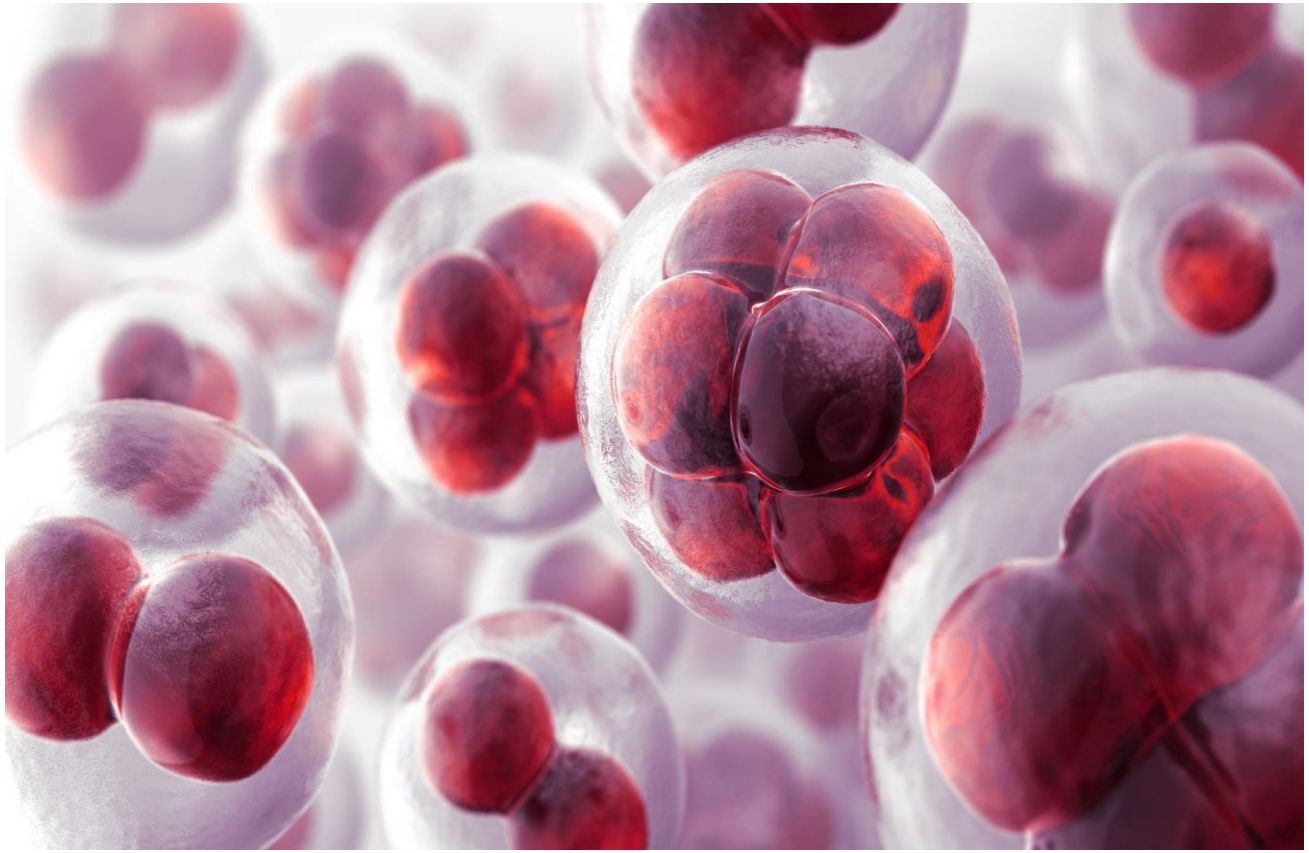
Images from: CDC Core Curriculum on Tuberculosis: What the Clinician Should Know

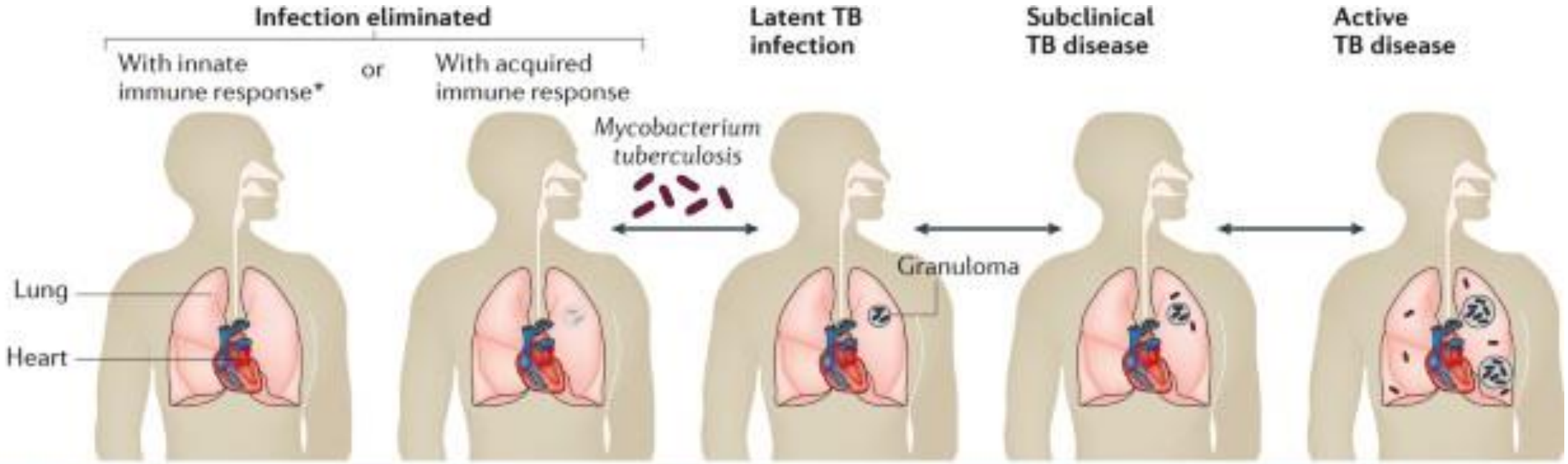
Disease

- 2021 WHO reported pulmonary TB accounted for 83% of disease
- Can affect any organ
  - Lymph nodes
  - Gastrointestinal tract
  - CNS (TB meningitis)
  - Bones

Rethinking what latent and active TB look like

- Traditionally thought of as a binary for disease presentation
- The binary is really treatment: LTBI vs multidrug therapy
- MTB doubling time is 24 hours
  - 20-60 minutes for many common bacteria
  - This will affect how TB presents compared to many other bacterial infections we commonly think of





TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therapy	Multidrug therapy	Multidrug therapy

Pai et al., M. (2016, October 27). *Tuberculosis*. Nature. https://www.nature.com/articles/nrdp201676

Nature Reviews | Disease Primers

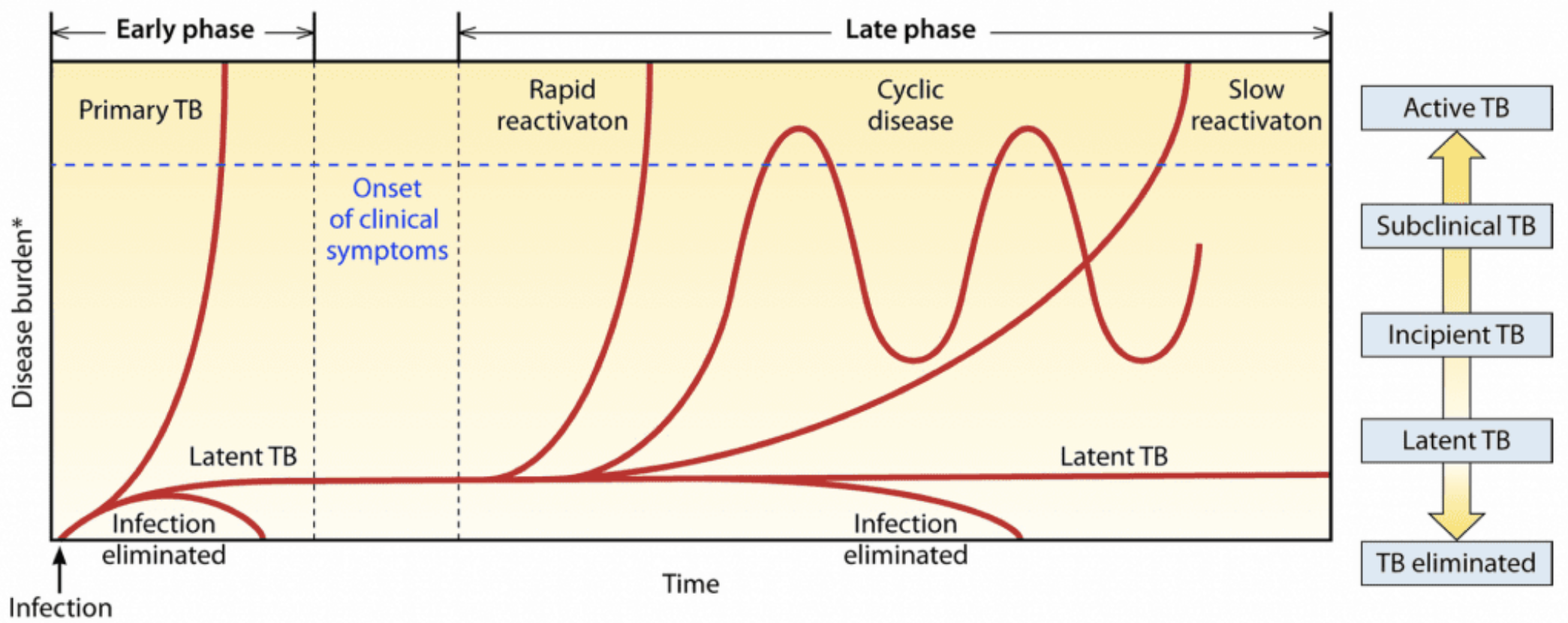


FIG 1 Pathways of tuberculosis disease progression. After initial exposure, *M. tuberculosis* may be eliminated by the host immune response, persist as a latent infection, or progress to primary active disease. Following the establishment of latent infection, disease may persist in a latent form, naturally progress in a slow or rapid fashion to active tuberculosis, or cycle through incipient and subclinical states before developing into symptomatic disease or eventual disease resolution. Although not all possibilities for regression of disease burden are depicted, spontaneous recovery may occur in any of these clinical trajectories.

Drain et al. Incipient and Subclinical Tuberculosis: a Clinical Review of Early Stages and Progression of Infection. Clin Microbiol Rev. 2018 Jul 18;31(4):e00021-18.

Progressing to TB Disease

- Who can progress from LTBI to TB disease?
  - Anyone
    - Healthy individuals:10% lifetime risk of progressing to active disease
    - 5% of risk is within the first 2 years
      - This is why contact assessments are so important

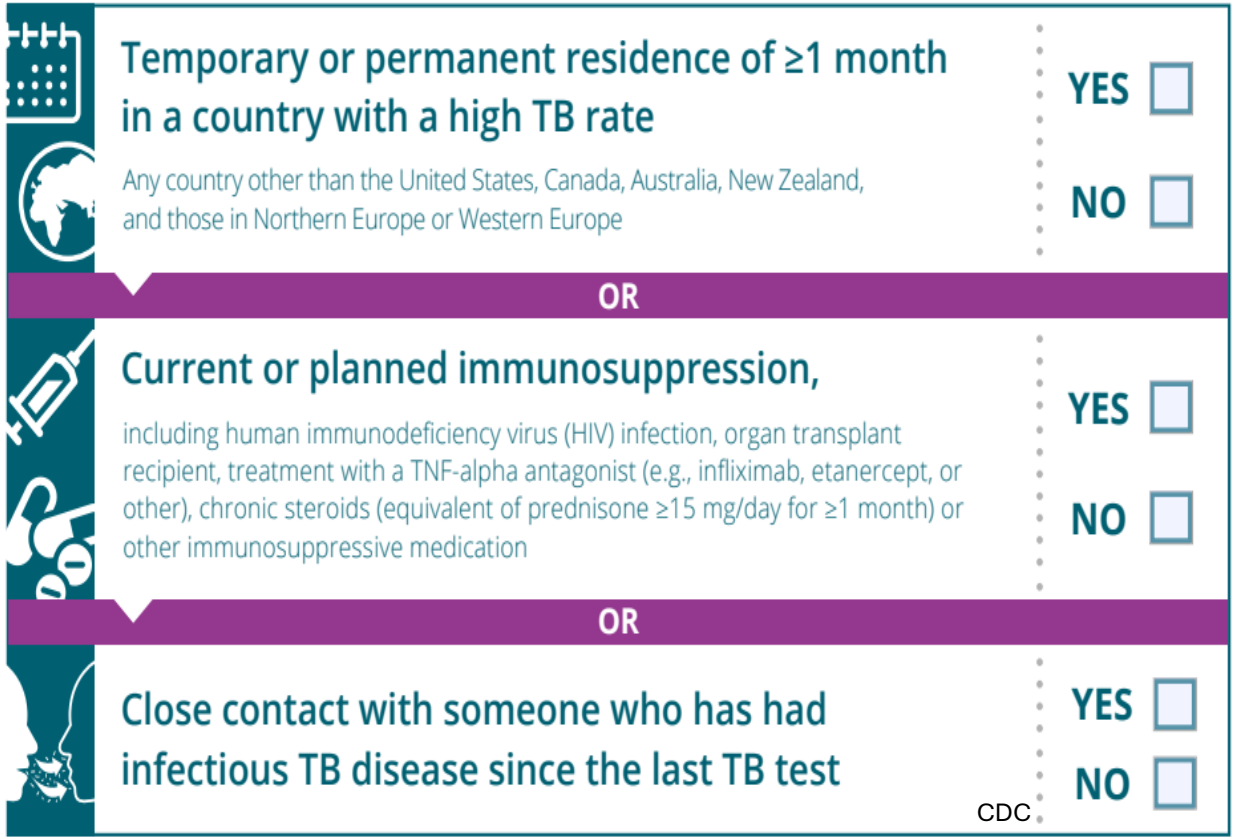
Progressing to TB Disease

- Who is at *higher* risk of progressing to TB disease?
  - Diabetics: 30% lifetime risk of progressing to active disease
  - Untreated HIV infection: have roughly 10% risk per year
  - Children (especially those under 5)
  - immunosuppressive drugs
  - immunosuppressing health conditions

Does BCG prevent progression to active disease?

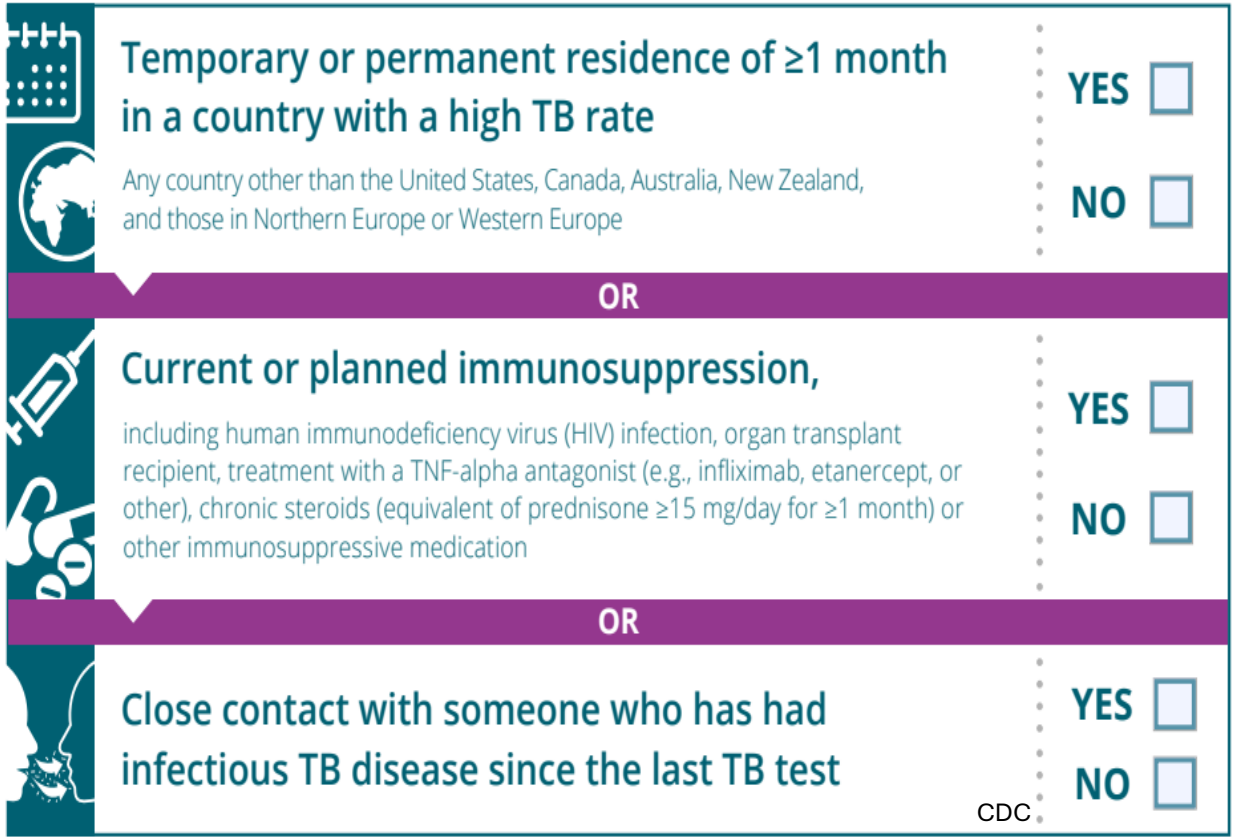
- Suboptimal efficacy and inadequate for TB elimination
- Prevents TB meningitis, disseminated disease, miliary TB in children
- An adult with a positive TST should be considered to have TB infection
- Most pediatric patients with a positive TST should be considered to have a positive

Screening for risk



- Have you ever been tested before
  - If so, what was your result?
  - If positive, did you receive any treatment?
- Other possible questions:
  - Do you recall anyone in your life who was coughing, sick, and losing weight?
  - Have you ever had to isolate from someone that you lived with?
  - Where have you traveled in the US?
    - KC MDR outbreak

Screening for risk



- Symptom screening
- If screening questionnaire identifies a risk for TB, testing is indicated
  - If a patient has symptoms during the risk assessment, they should receive a CXR alongside additional testing – transitioning to active TB workup
  - TST or IGRA are acceptable
- Targeted testing
  - Finds individuals with TB infection who would benefit from treatment
  - Finds individuals with TB disease who would benefit from treatment

Tests for infection

- TST or IGRA
  - Both rely on the body to react to something
  - Once positive it doesn't need to be tested again and is generally going to be positive for life
- A positive test supports your diagnosis
- A negative test does not rule out disease

Symptoms of TB disease

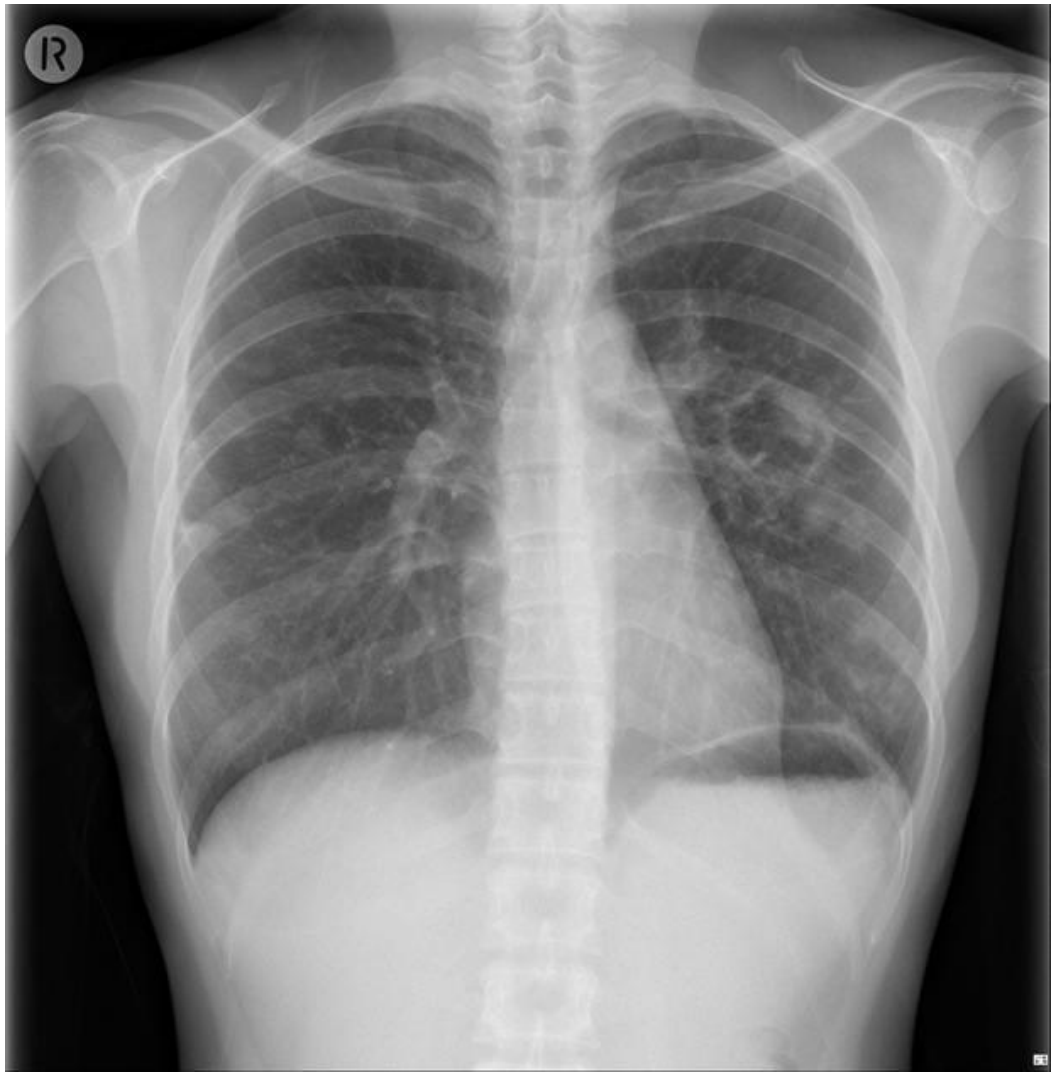
- Traditional classic symptoms:
  - Cough >3 weeks, fever, night sweats, weight loss
- Other symptoms
  - Reduced appetite, fatigue, chest pain
- Site specific symptoms
  - Blood in the urine, abdominal pain, diarrhea, back pain, swelling/lump of lymph nodes in the neck, armpits, or groin

Ruling out active TB disease

- All patients with positive TST or IGRA should get a CXR even if asymptomatic
- Review medical history
- Signs or symptoms of pulmonary and extrapulmonary TB
- Physical examination
- Degree of scrutiny when evaluating for active disease depends on pretest probability (risk) of active disease

Chest radiograph

- Pulmonary TB can present in almost any manner on radiograph
  - TB doesn't follow a textbook
- Typical findings in an adult would include abnormalities in the upper lobes of the lungs and hilar adenopathy in children
- Cavities generally pose a higher risk of transmission
- CXR should guide index of suspicion but is not the end of your workup



Sputum Collection

RESULTS OF ANALYSIS - INTERIM REPORT

TEST	RESULT	MODIFIER
Fluorescent Stain for AFB, Fluorochrome (Auramine-Rhodamine Stain)		
Acid Fast Bacillus	Positive	4+

I see something that looks like TB.

TEST	RESULT	ANALYSIS NOTE(S)
MTB Complex and Rifampin DNA, Nucleic Acid Amplification Cepheid GeneXpert		
Sample Processed At	SHL	
MTB target DNA sequence	Detected	
Rifampin mutation in the rpob gene	Not Detected	

TB has been here.

This TB looks good in red.

PENDING/CANCELLED ANALYSES

TEST	STATUS
Acid Fast Bacillus, Bacterial Culture	Pending

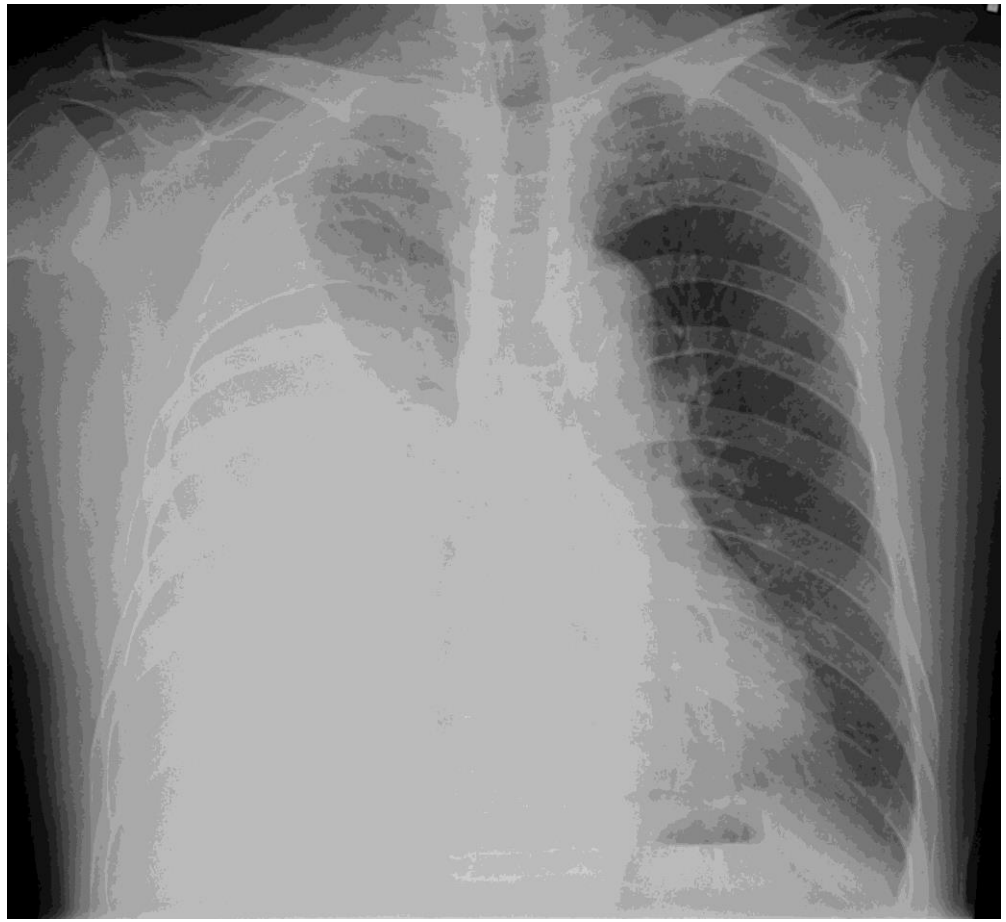
Don't rush me!

Extrapulmonary TB

- TB lymphadenitis
  - Most common form of EP TB
  - Most commonly cervical, usually unilateral
  - FNA to diagnose may show caseating granulomas and no signs of cancer
  - Sputum samples

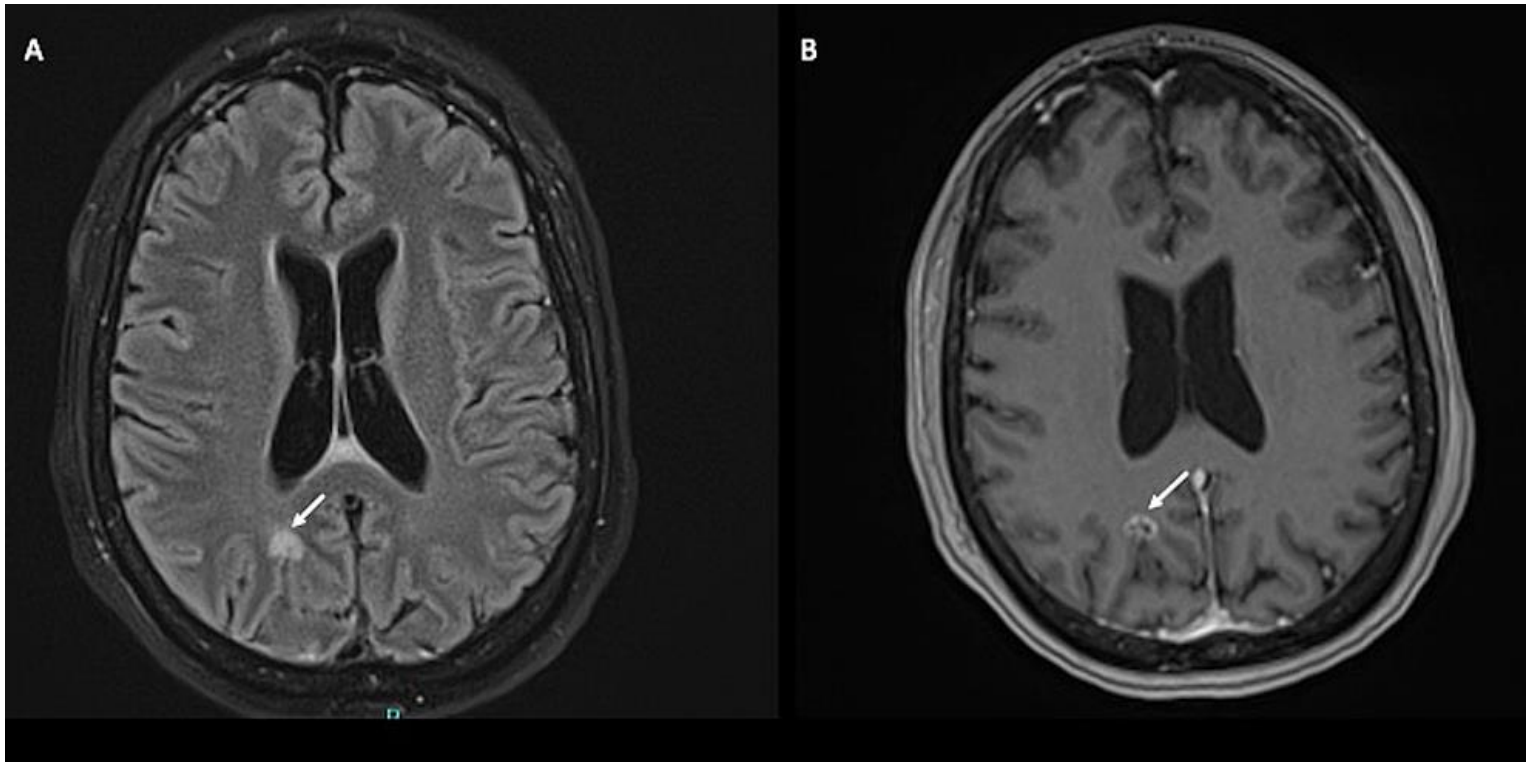
Extrapulmonary TB

- TB pleural effusion
  - Second leading presentation of EP TB
  - Usually unilateral
  - Pleural fluid likely has lymphocytic predominance
  - Adenosine deaminase (ADA) usually elevated
  - AFB stain and cultures are often negative
  - Consider pulmonary TB



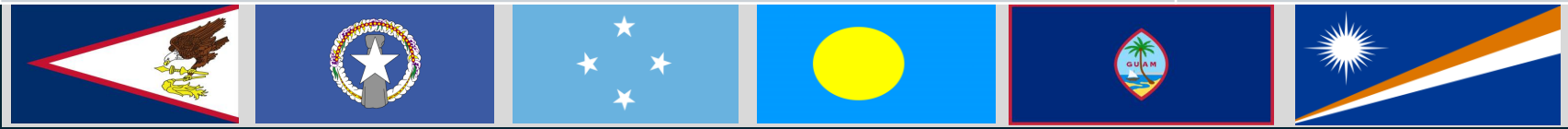
Extrapulmonary TB

- CNS TB
- Can present at TB meningitis or TB of the brain and accounts for 1% of EP cases
- Varying clinical presentation: meningitis, tuberculoma
- CSF in TBM is usually lymphocytic with elevated protein and low glucose
- May cause seizures or altered mental status
- AFB stain and culture are often negative



In summary: TB is everyone's (least*) favorite toddler.

TB	My Children
Slow	Takes 13094948 years (per child) to get ready for school in the morning
Can't predict how it will present	Either perfect angels or acting like a cat in a bathtub in the morning
Can easily be missed and may have subtle symptoms	Constantly trying to find whatever they put down 10 minutes ago, a lot better at hiding than seeking their own things. Very good at seeking things I've hidden from them.
Doesn't always seem to make sense	My son told me he had a cold, so he needed a "human fire." … He meant humidifier.
Long complicated treatment when compared to other infections	Takes 13094948 years (per child) to get to sleep.



Thank you!

- "…most American doctors are so unfamiliar with this old but now resurgent disease that they wouldn't recognize if a TB patient coughed in their face."
- Your work prevents TB from consuming people, families, communities, and cultures.