

Introduction to Tuberculosis (TB) for the IHS Provider

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Indian Health Service

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Presentation Outline

- What is Tuberculosis (TB)?
- How TB spreads and infection prevention
- Inactive/Latent TB Infection and TB Disease
- Risk Factors
- TB Testing
- Treatment
- TB in the AI/AN/IHS Context
- TB Elimination
- *I have no conflicts of interest to report

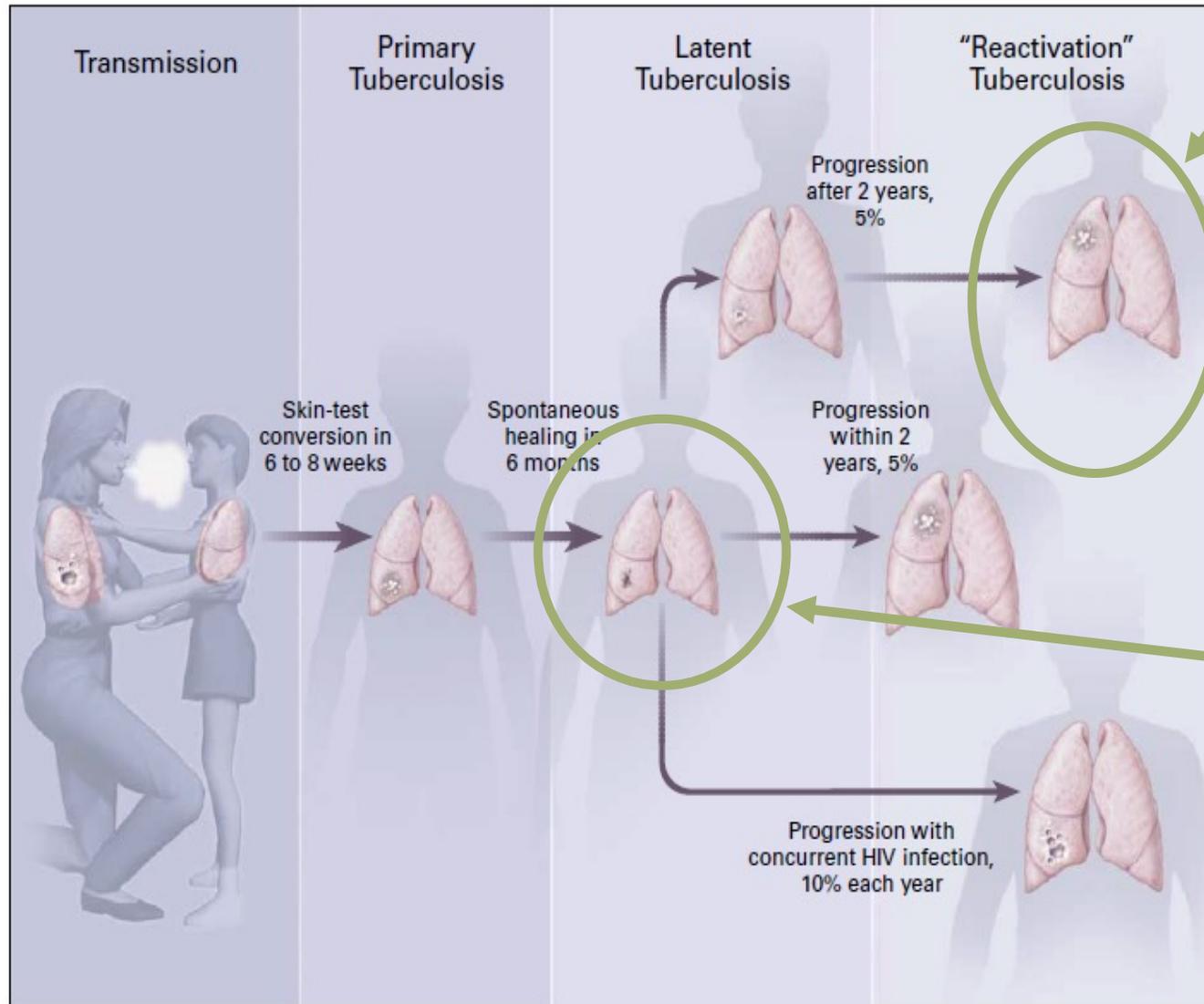


Tuberculosis (TB)

- TB is a disease caused by bacteria called *Mycobacterium tuberculosis*
- TB is spread from person to person through the air
 - Individuals can develop **Inactive/Latent Tuberculosis**
 - Don't feel sick, non-infectious, reservoir TB germs is alive but inactive
 - Individuals can develop **Active Tuberculosis Disease**
 - Patients feel sick and are infectious, TB germs are active and multiplying
- TB usually attack the lungs. However, TB germs can attack any part of the body such as the kidney, spine, or brain
 - **Pulmonary TB** is TB in the lungs
 - **Extrapulmonary TB** is TB in places other than the lungs
- Without treatment ~1/3 of patients with active TB disease clear it on their own, ~1/3 will die of the disease, ~1/3 of people will develop a chronic infection
 - These are the people who went to TB sanitoriums prior to antibiotics



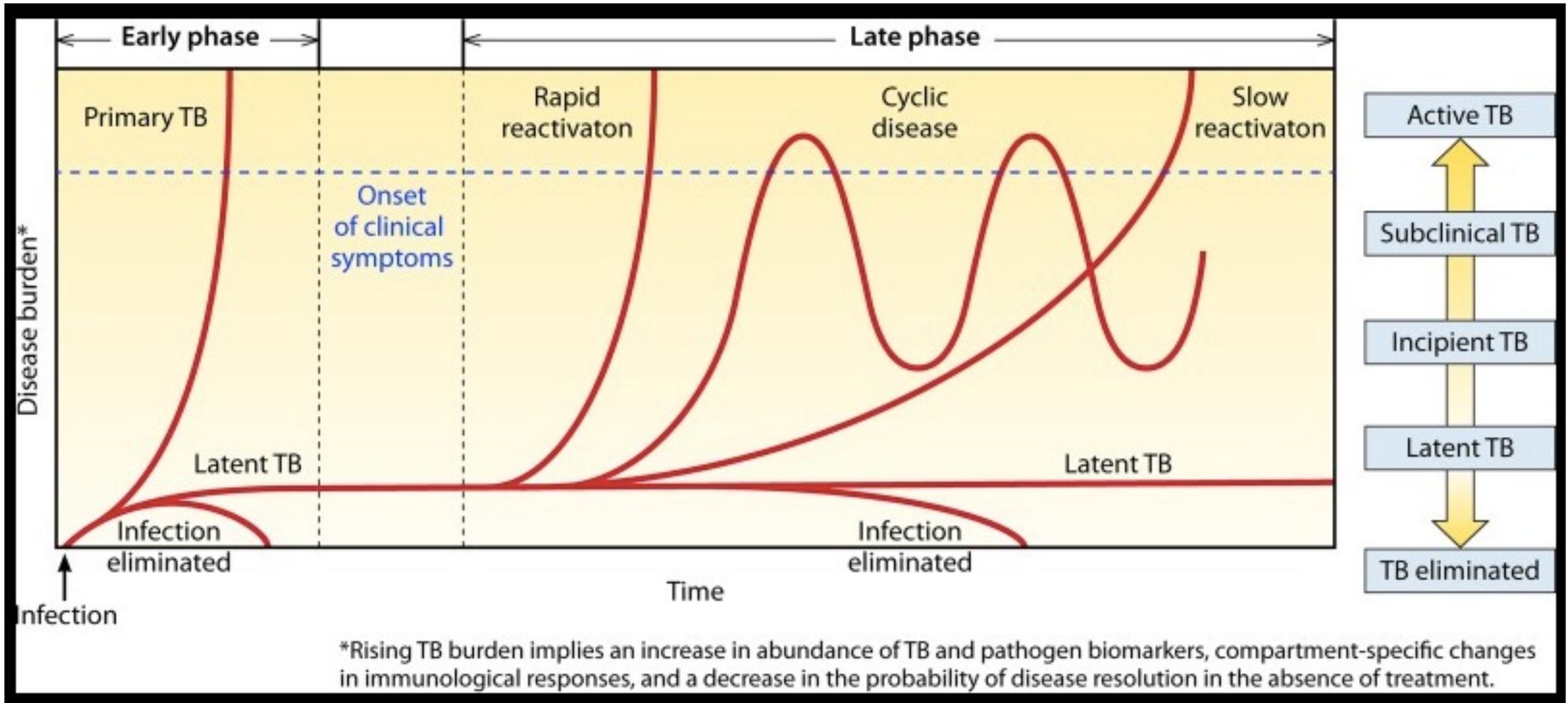
Variability in TB Outcomes



80% of U.S. TB cases due to reactivation: PREVENTABLE

~90% will not progress to TB disease

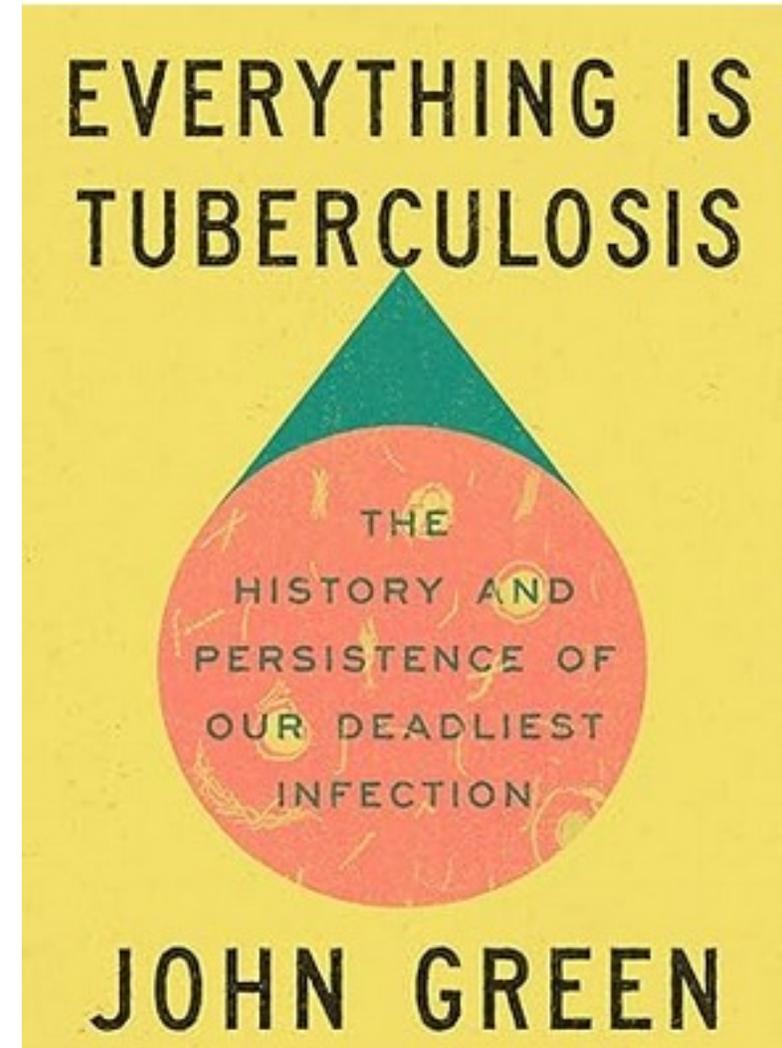
Variability in TB Disease Progression



TB History and Epidemiology



- TB has co-evolved with humans and our predecessors over the last million years
- It is estimated that **TB has killed over 1 billion people** throughout history
- TB was one of the leading causes of death in Europe and North America through the mid-20th century then
 - TB rates declined with advent of antibiotics and reductions in poverty
 - TB is a disease of poverty
- **Globally TB remains the leading infectious cause of death.** Per the WHO:
 - 2 billion people estimated to have latent TB
 - 10.8 million people develop active TB disease each year
 - 1.3 million people die from TB each year
 - 400,000 people develop drug-resistant TB each year



Does TB only infect humans?

- TB also infects animals and is a zoonotic disease
- Other non-tuberculous mycobacteria (NTM) are an important source of infection in humans and animals
 - *M. bovis*
 - *M. marinum*
 - *M. leprae*
 - *M. kansasii*
 - *M. abscessus*
 - Mycobacterium avium complex (MAC)
- AFB smear and culture help identify NTM, not just TB

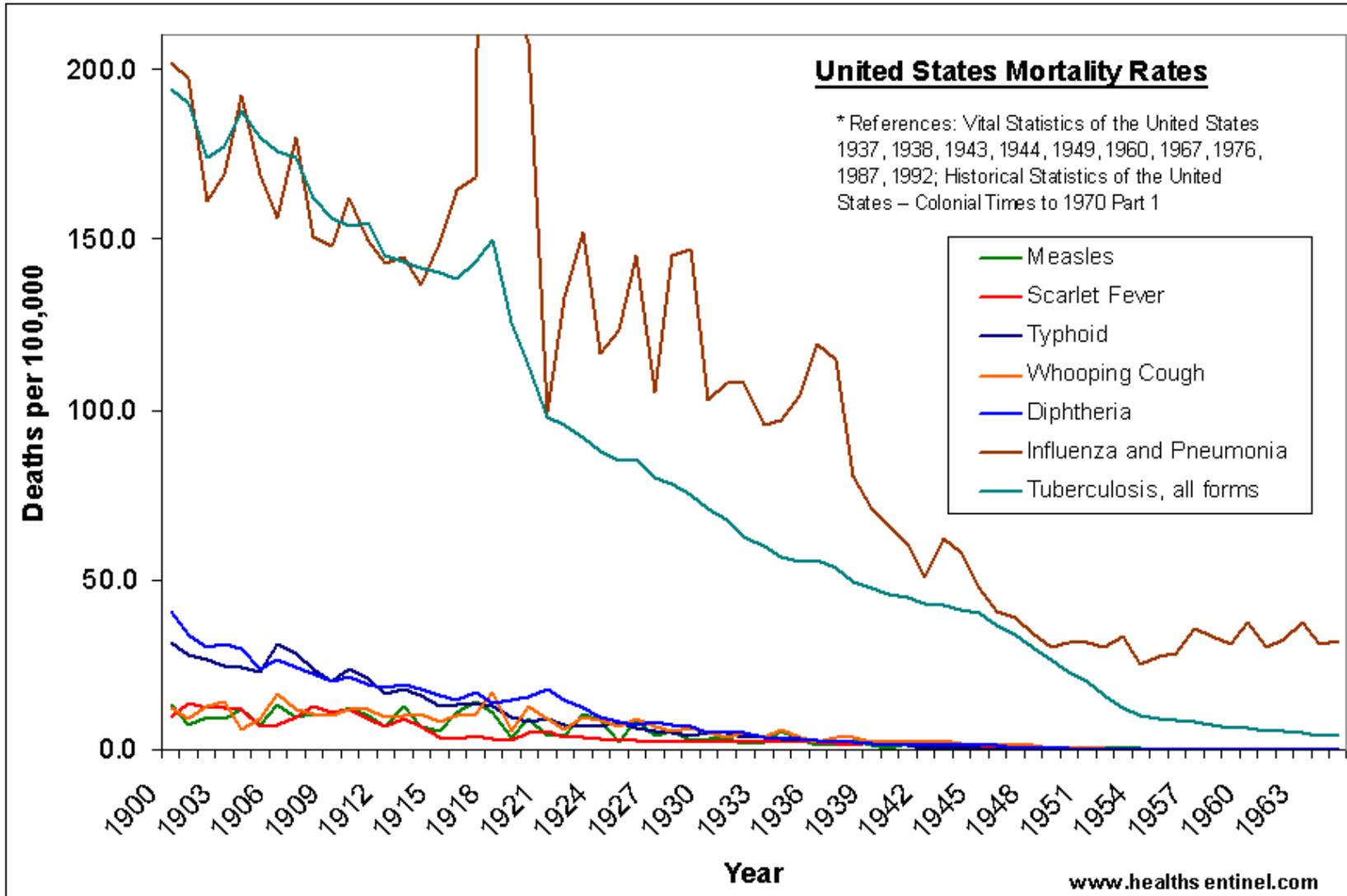


Epidemiol. Infect. (2013), **141**, 1488–1497. © Cambridge University Press 2013
doi:10.1017/S095026881300068X

Transmission of *Mycobacterium tuberculosis* from an Asian elephant (*Elephas maximus*) to a chimpanzee (*Pan troglodytes*) and humans in an Australian zoo



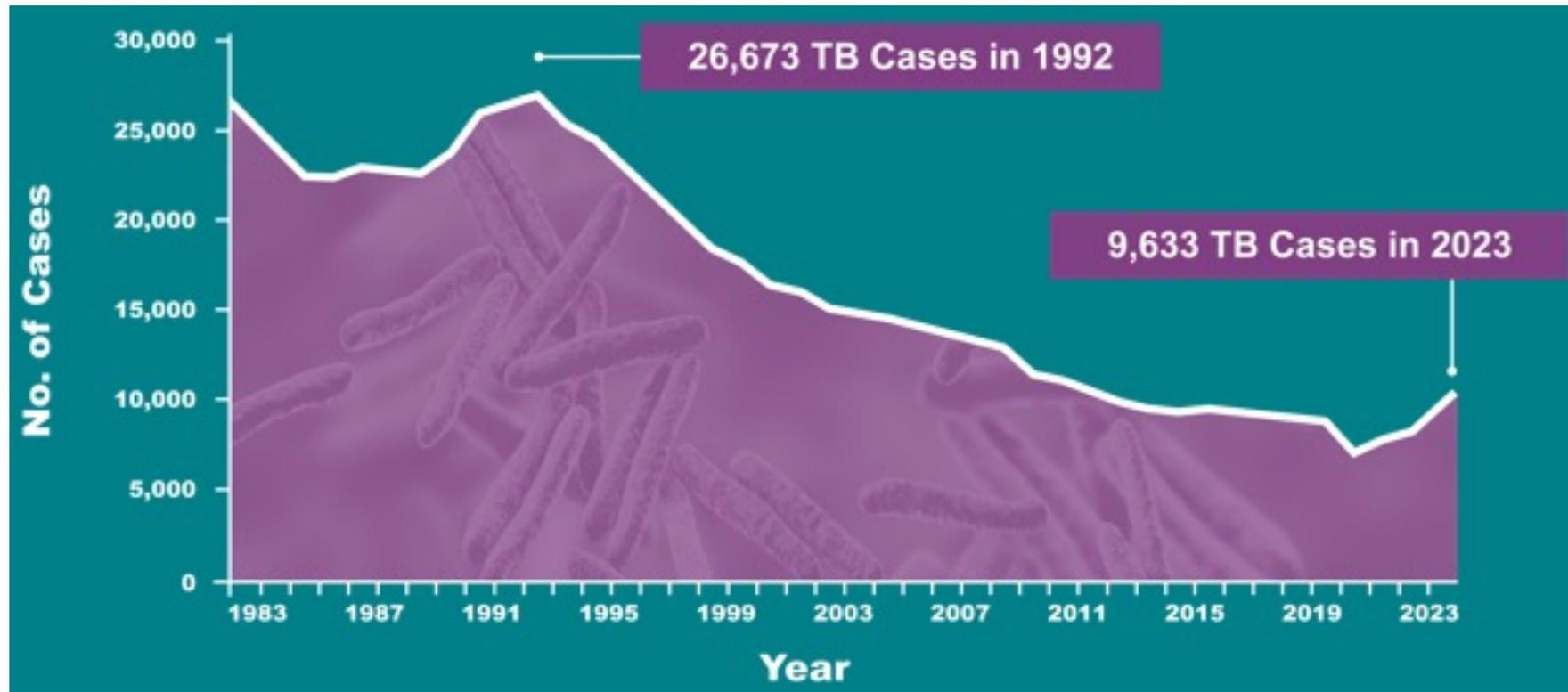
TB Death Rates Plummet in Early 1900s



- TB caused 25% of deaths in 19th Century
- First drugs for TB developed in 1943
- Social Determinants of TB Disease
 - Poverty
 - Malnutrition
 - Over crowding
- USA Stopped most TB funding and drug development in 1960s

Progress Toward TB Elimination

United States, 1982-2023



- To reverse recent increases in TB and reach the goal of TB elimination in the United States, enhanced strategies to diagnose and treat inactive TB and TB disease are needed. The TB elimination threshold is <1 case per 1,000,000 population, which is approximately 335 cases per year for the current U.S. population.

Case Presentation



- An 86-year-old Navajo woman presented with weakness and falling in the spring of 2021. She has a past medical history of Diabetes Mellitus and had received two months of Isoniazid 30 year ago for a positive TST/PPD but never completed treatment.
- On physical exam she had a temperature of 37 degrees C and looked frail but non-toxic. Her lung exam is normal. She is admitted to medicine.
- Laboratory data including white blood count, creatinine and liver function tests are WNL.
- PCR for SARS-CoV-2, RSV, flu is negative
- CXR showed a LUL infiltrate
- **If TB is on the differential diagnosis, what should we do next?**

Management of Presumptive TB



- **Infection Prevention**

- Airborne Infection Isolation (AII): providers/visitors need to wear N95s, negative pressure room if available
- Patients in AII often receive lower quality and less frequent care, can be upsetting for patients

- **Testing for active pulmonary TB disease**

- 3 sputums 8 hours apart, ideally one that is collected early morning
 - Consider induced sputums with respiratory therapy, bronch
- **Send all 3 sputums for AFB smear, AFB culture and TB PCR**
- *At this time there is no role for TST/PPD or IGRA testing if one is evaluating a patient for active pulmonary TB disease
- Evaluate patient for possible extra-pulmonary TB and see if other targeted sample/tissue collection and testing is indicated



Why do we put presumptive TB pts in AII?



Why do we put presumptive TB pts in AII?



 **The Seattle Times**

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150 Harborview staff, 45 patients may have been exposed to tuberculosis

Originally published January 26, 2017 at 10:36 am | Updated January 26, 2017 at 3:15 pm



When to Discontinue AI



- **How to Safely Remove Airborne Infection Isolation in Patients with Presumptive TB**
 - Historically 3 negative AFB smears but can take 8 days with send out lab testing
 - *New gold standard: 2 negative sputum TB PCRs, Xpert MTB/RIF*
 - *TB PCR is more sensitive than smear, results in 70 minutes, can "rule out" infectious TB in 24-48 hrs, very cost effective*

Observational Study > Clin Infect Dis. 2014 Jul 15;59(2):186-92. doi: 10.1093/cid/ciu212.

Epub 2014 Apr 11.

Xpert MTB/RIF assay shortens airborne isolation for hospitalized patients with presumptive tuberculosis in the United States

Christopher K Lippincott¹, Melissa B Miller², Elena B Popowitch³, Colleen F Hanrahan⁴,
Annelies Van Rie⁴

Affiliations + expand

PMID: 24729506 PMCID: [PMC4133562](#) DOI: [10.1093/cid/ciu212](#)

Case Presentation



- **Two of three sputum samples come back with PCR positive for MTB**
 - Xpert also tests for drug resistance to rifampin
 - Fortunately, no molecular drug resistance to rifampin is detected
- **What should we do next?**

Pulmonary TB Management



- Keep patient in Airborne Infection Isolation
- Baseline laboratory testing
 - HIV testing, Hep serologies, baseline CBC and CMP, A1c
 - Evaluate for any other infections, cocci/fungal, bacterial, STIs
 - Evaluate other sites of TB infection that would change management, especially in CSF, bone, joints
- Obtain social history, substance use, especially ETOH
- Review other medications and their interactions with pharmacy
- Review prior TB treatment, TB exposure/risk for drug-resistant TB
- Notify state DOH, request additional laboratory testing, WGS, TB Drug Resistance Testing both molecular and phenotypic (culture)
- If needed get expert support from DOH, infectious disease specialists, USA regional TB Centers of Excellence like Curry Center in San Francisco
- Work with IHS TB techs, PHNs to plan logistics of Directly Observed Treatment (DOT), household and community contact screening
- Discuss treatment/plan with patient and answer questions
- Initiate treatment

Pulmonary DS-TB Treatment

- **2 months of 4 drugs (RIPE or HRZE)**
 - Rifampin – drug interactions and turns urine/tears orange
 - Isoniazid – peripheral neuropathy and hepatotoxicity
 - Daily B6/pyridoxine to decrease risk of peripheral neuropathy
 - Pyrazinamide – hepatotoxicity
 - Ethambutol – optic neuritis and color discrimination
- **4 months of 2 drugs**
 - Rifampin
 - Isoniazid
- **Alternative:** 4 month RPT-MOX (rifapentine, isoniazid, pyrazinamide, Moxi)
- **Monitoring**
 - Monthly CBC and LFTs
 - Monthly sputum for AFB smear and culture to document conversion
 - TB drug resistance testing
 - Side effects including N/V, rash, drug interactions
 - DOT or if available Video Observed Treatment (VOT)



Who Is at Risk for Developing TB?

People at higher risk for developing TB infection/disease generally fall into a few categories:

- Those who have been recently or remotely been exposed/infected with TB
- HCW, h/o incarceration, homelessness, poverty, NI/AN, foreign born high incidence TB country
- Those with medical conditions that weaken the immune system, such as:



•HIV infection



•Diabetes



•Specialized treatment for rheumatoid arthritis, Crohn's disease etc



•Organ transplants



•Severe kidney disease



•Cancer



•Substance use



•Medical treatments such as corticosteroids



•Silicosis

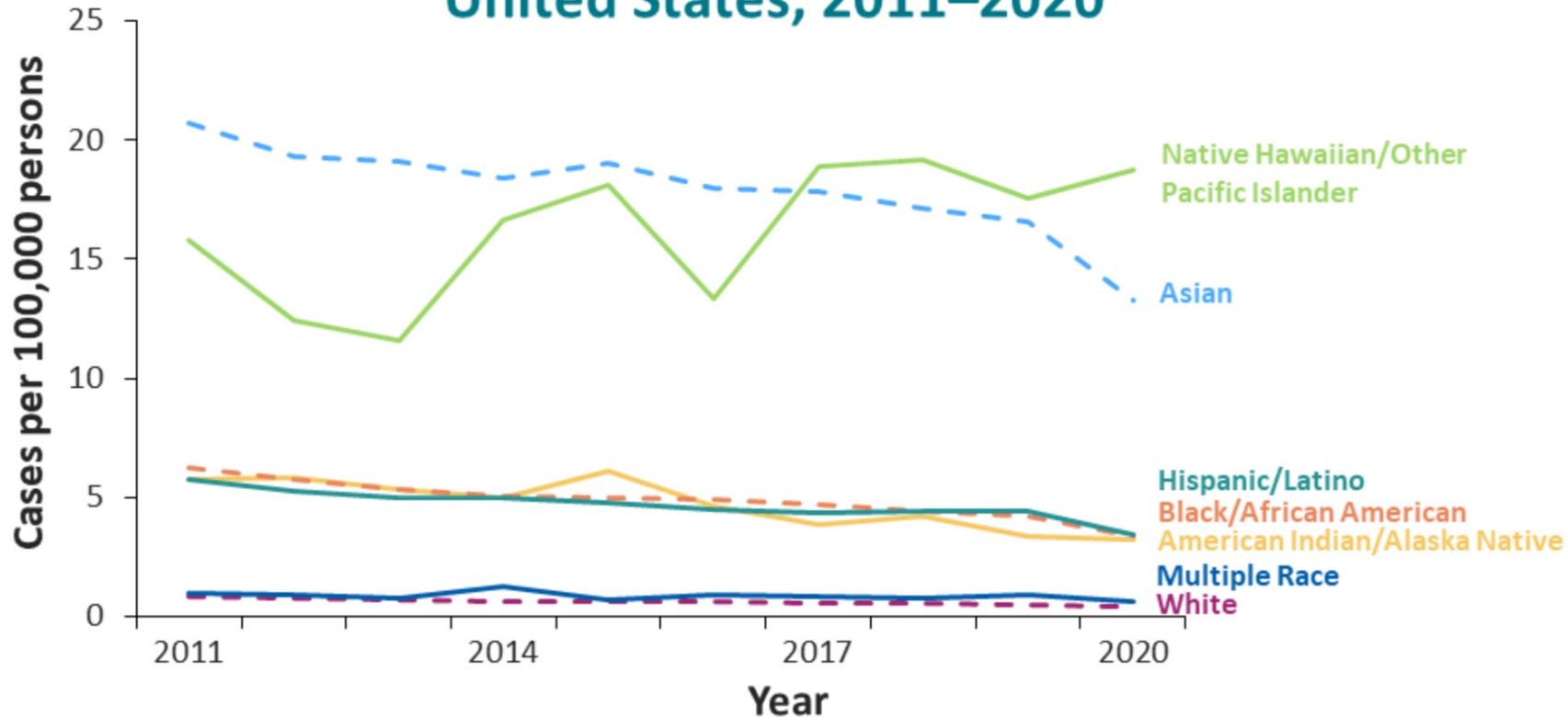


•Low body weight

TB Disparities



TB Incidence Rates by Race/Ethnicity,* United States, 2011–2020



All races are non-Hispanic; multiple race indicates two or more races reported for a person but does not include persons of Hispanic or Latino origin.

- 1.1% of all US TB patients were American Indian/Alaskan Natives (AI/AN)
- AI/AN TB Incidence was 5.9 per 100,000 population
 - 5 x greater than non-Hispanic white persons

TB Disparities: Mortality



- **TB Death rates for AI/AN significantly higher compared with Whites**
 - 1990-1998: **3.3 vs 0.3 deaths per 100,000 per year (RR 11.37)**
 - 1999-2009 **1.5 vs 0.1 deaths per 100,000 per year (RR 11.5)**

- Death rate for persons > 85 in 1990-1998 for AI vs White: **RR 14.7**

Reilley B, Bloss E, Byrd K, Iralu J, Neel L, Cheek J. Death Rates from HIV and TB Among American Indian/Alaska Native in the United States, 1990-2009. Am J Pub Health, Supplement 3, 2014(104)S253-S459.



US Army and
the long
walk...

...to
Fort Sumner



001_002_3.21

Photograph. The Museum of New Mexico.



Navajo History and Tuberculosis

- Yellow Fever and Cholera plagued the Navajo at Ft Sumner
- Upon return to Dinetah, the first US government physician noted “consumption” among the Navajo
- By 1912, 10% of the Diné had TB
- TB was responsible for 50% of all illness seen on Navajo
- In 1925 25% of reservation deaths due to TB
- TB Hospital opened at Ft Defiance 1938: 343 TB patients of whom 230 died

| | Navajo | US all races |
|-----------------------------------|-----------------------|-----------------------|
| TB Incidence rate 1953 | 1042/100,000 per year | 11.2/100,000 per year |
| TB Mortality rate 1950 | 1.9/ 1000 per year | 0.2/ 1000 per year |



AI/AN History and Tuberculosis: TB Sanitoriums



Students at the Tuberculosis Sanitorium, Phoenix Indian School, ca. 1890-1910. American policies of forced indoctrination, such as boarding schools, often coincided with poor health conditions at home and at school.



Navajo History and Tuberculosis: Annie Wauneka

- **Background**
 - Only woman on tribal council in 1951
 - Studied TB for 4 months at Fort Defiance
 - Did home visits to teach people about “the bugs that eat the body”
- **Impact**
 - Navajo patients with TB AMA discharges dropped dramatically
 - Traditional Medicine Practitioners learned about TB
 - Let to Navajo Nation and Navajo Area IHS Collaboration
 - *BILINGUAL TB Community Health Workers*
 - Screen for TB in the field with PPD
 - Administer DOT
 - Home visits, patient support
 - Contact investigations in **Dine bizaad and English**





AI/AN History and Tuberculosis: TB Research

- **Background**
 - In the 1950's Alaskan Natives experienced some of the highest rates of TB
- **Study**
 - In the mid-1950's a cluster-randomized trial with Isoniazid Prophylaxis Treatment (IPT) showed a 69% reduction in TB incidence and protection that lasted over 5 years
- Additional studies on BCG, TST and latent TB rates and treatment were conducted from the 1940s through the 1980s in multiple AI/AN settings.
 - Some of these were of pure scientific interest
 - Some had potential benefit to the local community
 - **Many do not meet current standards for informed consent, and expectations about community participation in research**

The first step in the survey of tuberculosis among school children was a skin test of each child for tuberculous infection. The test was given to all Indian children without asking for consent of the parents. With white children, consent of the parents had to be obtained. (Crouch 1932, 1911)

- **In the last several decades AI/AN have taken a more proactive approach to regulating research within their communities.**
 - **For example, the Navajo took over IRBs to ensure ethical research practices, culturally sensitive and community-collaborative research approaches in their population.**



Secret to Success in Reaching the Marginalized TB Patient

100% DOT for TB Disease and Latent TB Infection

Bilingual care and contact investigations

Traditional **AI/AN** approach including **traditional medicine**

Compassion and patience: treat patients like family members

Train HIS primary care providers to become local TB experts



Case Presentation

- CHW/PH teams identify 12 household members as close contacts
- Patient's son reports a slowly growing left neck mass, chills at night. No cough, fever, weight loss.
- What is the differential, and what should we do next?



Lymphadenopathy: Differential Diagnosis

- Pyogenic adenitis (Staph and Gp A Strep)
- Cat Scratch Disease (Bartonella henselae)
- Tularemia
- Plague
- Tuberculosis
- Atypical mycobacteria
- Cocci, Histo, Blasto
- Secondary Syphilis
- LGV
- Toxoplasmosis
- Lymphoma
- Kawasaki Syndrome
- Kikuchi-Fujimoto Syndrome

Tuberculous adenitis (Scrofula)

Clinical

- Common form of Extra-Pulmonary TB
- Unilateral cervical disease in over 60%
- Posterior and anterior involvement equal
- Mass is present on average 2-6 months
- Always painless
- Draining sinus is present in < 5% of cases

Diagnosis

- Fine needle aspirate is the test of choice
- Smear positive in 14-33% of aspirates
- Culture positive in 56-93% of aspirates
- Send for TB PCR if possible – fast!
- Incisional biopsy should be avoided!

Treatment

- 6 months with standard ATS/CDC regimen
- The role of surgery is limited

Extra-Pulmonary Tuberculosis

Need higher index of suspicion in patients with HIV, immunosuppressed, recent known exposure, risk factors

Sites

- Lymph Nodes
- Pleura → Pleurisy
- Bones, especially spine
- Joints
- Genitourinary system
 - Consider with “sterile pyuria”
- CNS – TB meningitis
- Abdominal (liver, spleen)
- “Cold abscess” in soft tissue

Diagnosis

- Try to sample fluid, CSF, Tissue if possible and send for AFB smear, AFB culture and TB PCR if possible
- Diagnosis can be challenging, role for starting empiric treatment in some cases if high suspicion

Treatment

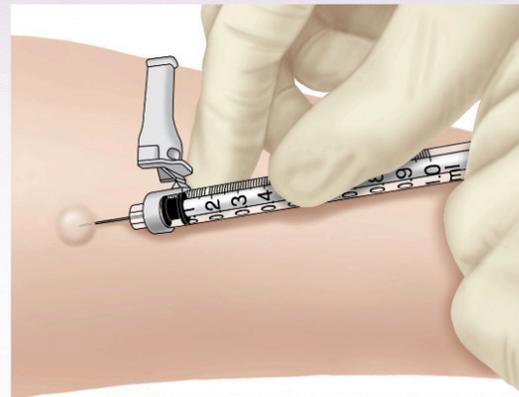
- 6 months with standard ATS/CDC regimen as baseline but sometimes longer if CNS, bone, joint is involved

Case Presentation

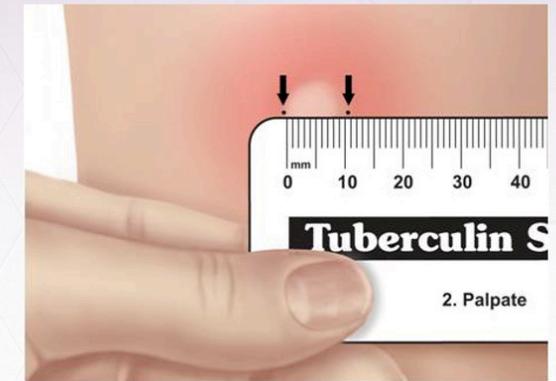
- 65yo daughter lives with and is the primary care provider for her mother (who has pulm TB)
- The daughter's TST/PPD is positive at 15mm
- No cough, fevers, night sweats, weight loss
- HIV and Hep C negative, CBC and CMP WNL, no other notable PMH
- **What next? Should we treat her for latent TB?**

The TB skin test, also called the Mantoux tuberculin skin test (TST) or PPD, requires two visits with a health care provider

On the **first visit**, a test is **placed**



On the **second visit**, the test is **read**



The Role of Chest Radiograph in TB Screening

Background

- Historically TB screening just involved symptom screening; cough, fever, night sweats, weight loss, hemoptysis etc
- Recent data from prevalence studies show that symptom TB screen alone misses ~20-40% of patients with true pulmonary TB
- **Of all patients with pulmonary TB ~95% will have an abnormal CXR**

Question

- What is role of CXR in screening for TB?

Recommendation

- **Consider CXR as part of screening package for TB to identify asymptomatic patients with active TB disease, Get a CXR for all patients prior to tx LTBI**
- **Internationally in 2021 WHO formally endorsed CXR/CAD for TB screening**

AI-powered computer aided detection (CAD) software provides new opportunities and challenges in public health

Chest-X-ray (CXR) is an important tool for TB screening and may contribute to finding the missing millions globally

- CXR is sensitive tool (~95%) for screening for active TB
- CXR can pick up asymptomatic patients with TB
- CXR can improve efficiency of Xpert MTB/RIF use

Use and access to CXR is hampered by

- Sufficient trained radiologists
- Intra- & inter-reader variability

CAD systems have potential as a screening or triaging tool for TB

- Automatically 'read' CXR, or can help radiologists with their workflow, reduce missed findings
- Generate a standardized interpretation of CXR in the form of a heatmap/bouncing box combined with an abnormality score



Case Presentation

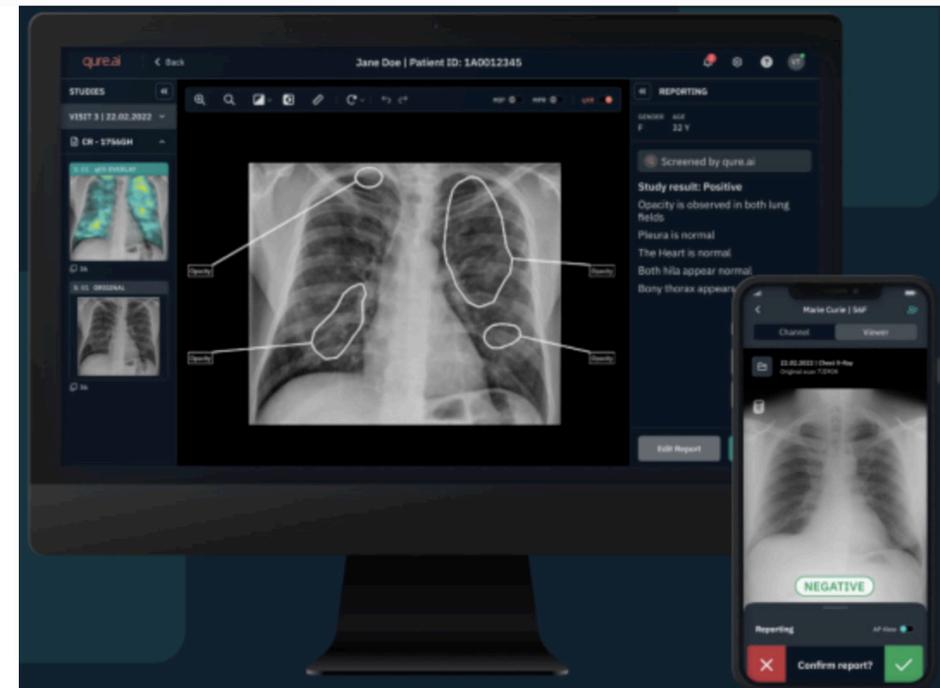
- 65 daughter gets a CXR with a LUL moderate sized opacity, possible cavity
- Her provider tests her for pulmonary TB with 3 sputums
- All 3 initial AFB smear and TB PCRs are negative
- **But.... at 6 weeks one AFB culture turns positive and is confirmed to be MTB**
- She starts treatment for TB disease



NEWS | ARTIFICIAL INTELLIGENCE | JANUARY 08, 2024

Qure.ai's AI-Driven Chest X-ray Solution Receives FDA Clearance for Enhanced Lung Nodule Detection

This reinforces Qure.ai's position as a pioneer in the field of AI-powered advancements for plain film radiography and medical imaging



Sensitivity of AFB smear, AFB Culture, and TB PCR for pulmonary TB



For 100 patients with pulmonary TB Disease:

- 99-100% will have a positive AFB culture for TB in at least 1 of 3 sputum samples
 - This is considered the “Gold Standard”
 - Requires a level 3 Biohazard lab, results of AFB culture take 6-8 weeks
- 90-95% will be TB PCR positive
 - Results in 90 minutes, also tests for resistance to rifampin
- 60-70% will be AFB smear positive
 - Lower rates in patients with HIV, immunosuppressed, lower bacillary burden
 - Newer LED microscopy with fluorescent stain is more sensitive than traditional Ziehl-Neelsen stain

Case Presentation

- 20yo grandson also lives in the household
- Saw PCP and IGRA/Quantiferon Gold resulted **positive**
- No cough, fevers, night sweats, weight loss
- HIV and Hep C negative, CBC and CMP WNL, no other notable PMH, CXR is normal
- **What next? Should we treat him for latent TB? With what regimen?**



Comparison of Tests for Latent TB



| Tuberculin Skin Test | T-SPOT.TB IGRA | QuantIFERON-TB Gold Plus IGRA |
|--|---|--|
| <p>Intradermal inoculation of PPD into volar aspect of forearm</p> <p>Wait 48–72 hr.</p> <p>Measure and record diameter of induration.</p> | <p>Phlebotomy</p> <p>Whole blood</p> <p>Centrifugation</p> <p>PBMCs</p> <p>Plate 250,000 cells into each of four wells per patient.</p> <p>Add nil control, <i>M. tuberculosis</i> antigens (x2), and mitogen positive control. Incubate for 16–20 hr.</p> <p>Interferon-γ antibodies capture interferon-γ as it is released from cells. A secondary enzyme-labeled antibody is added and binds to captured interferon-γ. A detection reagent is added, resulting in spots that are a footprint of the location where the interferon-γ was released by a cell. Spots are counted.</p> | <p>Phlebotomy</p> <p>Whole blood</p> <p>Add blood to tubes pre-coated with nil control, <i>M. tuberculosis</i> antigens (tubes TB1 and TB2), and mitogen positive control.</p> <p>Incubate 16–24 hr. Add aliquot of stimulated plasma to wells of ELISA plate that contains interferon-γ antibodies.</p> <p>A secondary enzyme-linked antibody is added and binds to interferon-γ. A detection reagent is added, and absorbance at 450 nm is measured. Concentration of interferon-γ is calculated on the basis of a standard curve.</p> |
| In vivo assay | In vitro enzyme-linked immunosorbent spot assay | In vitro ELISA |
| No instrumentation | Laboratory instrumentation required; assay results can be affected by manufacturing, preanalytic, and analytic factors ¹¹ | |
| Two patient encounters required to obtain result | One patient encounter sufficient to obtain result | |
| Interpretation subjective; positivity thresholds are risk-stratified | Interpretation less subjective to not subjective; positivity thresholds fixed | Interpretation not subjective; positivity thresholds fixed |
| Cross-reacts with BCG (PPD consists of many components) | Does not cross-react with BCG on the basis of selection of stimulation antigens | |
| A previous tuberculin skin test can boost a subsequent such test or IGRA | A previous IGRA does not boost a subsequent tuberculin skin test or IGRA | |

- Either IGRA or TST can be used to test for latent TB
- IGRA offers advantage in specificity and convenience, particularly in patients vaccinated with BCG
- CHWs/PHNs trained to do TST/PPD in the field as part of contact tracing
 - Requires two visits
- Neither test is perfect and can have false negative results, or false positive results
 - If the result is surprising, consider asking a specialist to review the case

Risk Calculators for LTBI and Progression to TB Disease



California TB Risk assessment: Who to test?

- Predicts who is at high risk for TB exposure or progression to TB disease
- Focuses on birth/travel/residence, immunosuppression and contact
- <https://www.currytbcenter.ucsf.edu/sites/default/files/tbcb-ca-tb-risk-assessment-and-fact-sheet.pdf>

McGill online TST/IGRA interpreter: Who to treat?

- Assesses individual risk for TB disease
- Stress INH monotherapy drug hepatitis risk only, not 3HP or 4R
- <https://www.tstin3d.com/en/calc.html>

Treatment for Latent Tuberculosis Infection (LTBI)

Also called TB Preventive Therapy (TPT)



Preferred

- **3HP = Isoniazid plus rifapentine once weekly for 12 weeks (plus pyridoxine)**
 - Similar efficacy, lower hepatotoxicity, higher completion rates vs Isoniazid
- 4R = Rifampin once daily for 4 months
 - Similar efficacy, lower hepatotoxicity, higher completion rates vs Isoniazid
 - Check for drug interactions
- 3 months daily isoniazid and rifampin (effective, but rarely used, plus pyridoxine)

Alternative

- 6 or 9H = Isoniazid daily for six or nine months (plus pyridoxine)
 - Original regimen, but higher hepatotoxicity and lower completion
- ***3HP is preferred but use whatever regimen makes sense for the patient. The key is to COMPLETE tx for LTBI, which reduces risk of developing TB disease by 90%**



Details of LTBI Regimens from NEJM

Latent Tuberculosis Infection. N Engl J Med. December 8, 2021.

Table 2. Dose, Frequency, and Prescribing Information for Recommended Regimens for Treatment of LTBI.*

| Priority and Regimen† | Dose for Adults and Children ≥12 Yr of Age ^{37,38} | Additional Prescribing Information‡ |
|---|--|---|
| Preferred | | |
| Isoniazid plus rifapentine once weekly for 3 mo (12 doses)§ | Isoniazid: 15 mg/kg/dose rounded up to nearest 50 or 100 mg; maximum dose, 900 mg Rifapentine: 750 mg per dose if weight is 32.1–49.9 kg; 900 mg per dose if weight is ≥50 kg; maximum dose, 900 mg | Administration: taking with high-fat foods increases rifapentine absorption and is recommended. Avoid concomitant aluminum-containing antacids and foods with high monoamine content. Adverse reactions: possible hypersensitivity reaction (3.8%), rash (0.8%), hepatotoxic effects (0.4%). ²⁶ Hypersensitivity reactions can include hypotension, bronchospasm, angioedema, conjunctivitis, and urticaria. Drug–drug interactions: rifapentine causes reductions in plasma concentrations of certain drugs, including warfarin, apixaban, rivaroxaban, dabigatran, hormonal contraceptives, levothyroxine, methadone, and many HIV antiretroviral drugs. The effect of once-weekly rifapentine appears to be less than that of daily rifampin, but data are limited. For interactions with isoniazid, see below. |
| Rifampin once daily for 4 mo | 10 mg/kg/day; maximum daily dose, 600 mg | Administration: taking on an empty stomach is preferable, if side effects are acceptable. Adverse reactions: hepatotoxic effects (0.3%), rash or other allergy (0.2%), hematologic toxic effects (0.2%), unacceptable GI adverse events (0.1%). ³¹ Drug–drug interactions: as for rifapentine, above. |
| Isoniazid plus rifampin once daily for 3 mo | Isoniazid: 5 mg/kg/day; maximum daily dose, 300 mg Rifampin: 10 mg/kg/day; maximum daily dose, 600 mg | Administration: taking on an empty stomach is preferable, if side effects are acceptable. Avoid concomitant aluminum-containing antacids and foods with high monoamine content. Adverse reactions: limited published data; hepatotoxic effects (1–6%), rash (1–8%), unacceptable GI adverse events (0–6%). ³⁵ Isoniazid can cause peripheral neuropathy that can be mitigated by pyridoxine (25–50 mg/day).¶ Drug–drug interactions: as for rifapentine (above) and isoniazid (below). |
| Alternative | | |
| Isoniazid once daily for 6 mo ** | 5 mg/kg/day; maximum daily dose, 300 mg | Administration: taking on an empty stomach is preferable, if side effects are acceptable. Avoid concomitant aluminum-containing antacids and foods with high monoamine content. Adverse reactions: hepatotoxic effects (2–3%), rash (0.6%), possible hypersensitivity (0.5%). ^{26,31,36} Isoniazid can cause peripheral neuropathy that can be mitigated by pyridoxine (25–50 mg/day).¶ Drug–drug interactions: Isoniazid can increase the serum concentrations of carbamazepine, phenytoin, warfarin, disulfiram, and others. Isoniazid can decrease the serum concentrations of itraconazole and ketoconazole. |
| Isoniazid once daily for 9 mo †† | Same as above | Same as above |

* GI denotes gastrointestinal.

† With respect to priority, “preferred” indicates excellent side-effect profile and efficacy, shorter treatment duration, and higher completion rates than longer regimens and therefore higher effectiveness; “alternative” indicates good efficacy but lower completion rates than shorter regimens and therefore lower effectiveness. The guidelines for regimens do not apply in circumstances in which there is evidence that the infecting strain of *M. tuberculosis* is resistant to both isoniazid and rifampin.

‡ An online resources for up-to-date information about drug–drug interactions is the Medscape Drug Interaction Checker: <https://reference.medscape.com/drug-interactionchecker>. Information about possible interactions between tuberculosis drugs and HIV drugs is available at <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv>.

§ A regimen of once-weekly isoniazid plus rifapentine is not recommended for use in pregnant persons or those who anticipate becoming pregnant during the treatment period because its safety in these populations has not been adequately studied.

¶ Pyridoxine is recommended for persons with preexisting neuropathy or neuropathy risk factors such as diabetes or HIV infection.

|| Isoniazid may also be administered twice weekly by directly observed therapy for 6 or 9 months, at a dose of 15 mg per kilogram per dose for adults.

** Once-daily isoniazid is strongly recommended for HIV-negative adults who are unable to take a preferred regimen. For persons living with HIV infection, either 6 or 9 months of isoniazid can be used.

†† The recommendation for a 9-month regimen emerged after a reanalysis of data showed that increased protection was obtained with 9 to 10 months of treatment; clinical-trial data are lacking that directly compare 9 months of isoniazid with other durations.^{39,40}

3HP is the IHS Preferred Regimen to Treat LTBI



Regimen

- 900mg PO INH (3 pills) plus 900 mg PO Rifapentine (6 pills) weekly plus pyridoxine

Details

- Approved for ages two and up
- Can be self administered, but Directly Observed Therapy (DOT) is preferred
 - Belknap et al: DOT 87% effective vs 74% effective for self administered
- 3HP is fine for patients with:
 - ESRD and on Dialysis
 - HIV (if on the correct antiretrovirals)



Hot Topics in TB



TB and HIV

- Test all patients with HIV for latent TB
- Watch for TB IRIS after starting ARV in a newly diagnosed patient with HIV
- Watch medication interactions when treating HIV and TB – consult a specialist

Drug Resistant TB (DR-TB)

- Huge issue globally, thankfully it is relatively uncommon in the USA
- Please ensure appropriate drug-resistance testing is ordered for all patients with TB disease. If resistance is detected, please consult a specialist
- There are a number of new DR-TB medications and shorter regimens that are transforming treatment

Vaccines and Better Diagnostics

- An active area of study with only modest progress

Together We Can Work Towards TB Elimination in the IHS and the United States

TB elimination threshold is <1 case per 1,000,000 population, which is approximately 335 cases per year for the current U.S. population.

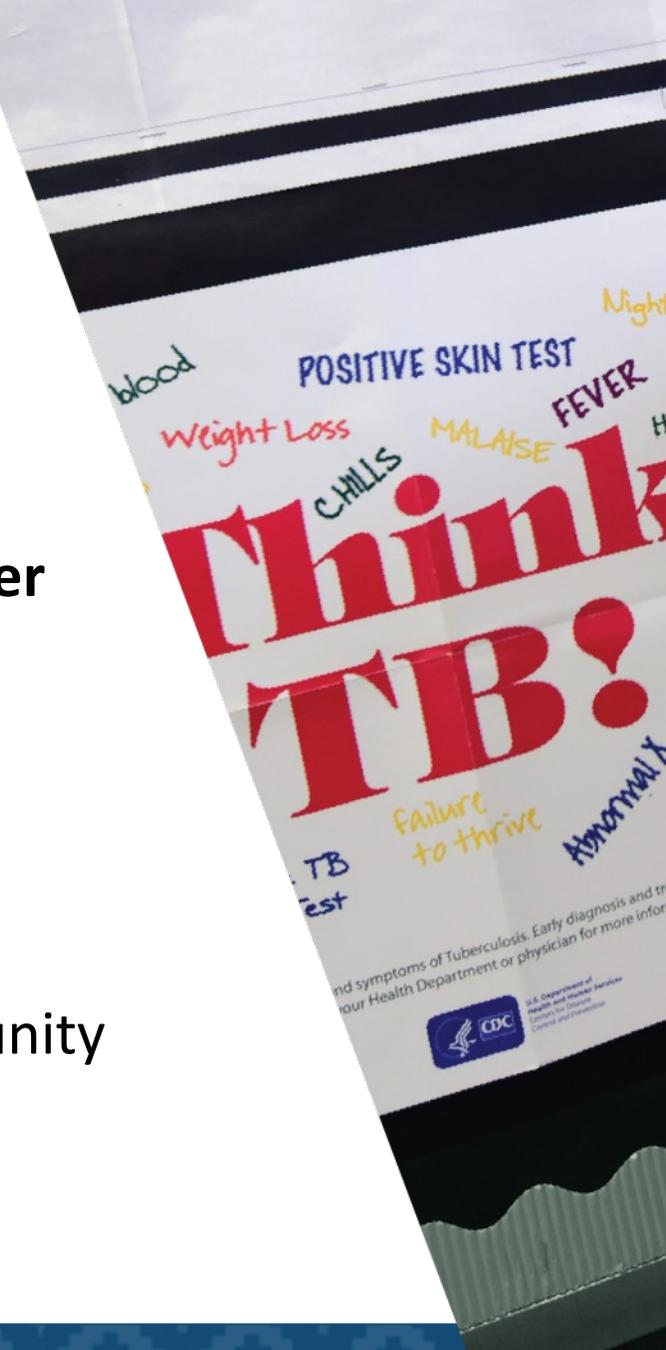


Conclusion: IHS Providers and Communities need to “Think TB!”

Avoid delays in TB diagnosis, or even overlooking TB cases

Protect the health and well-being of community members at higher risk for TB:

- Know who is most at risk for TB
- Recognize the signs and symptoms of TB
- Test and treat patients who are at high risk for TB
- Be aware of latest TB research and shortest treatment options
- Encourage conversations about TB and how it affects the community to reduce stigma



Resources



CDC TB website:
www.cdc.gov/tb/



State & Local TB Control Offices:
<https://www.cdc.gov/tb/php/tb-programs/index.html>



Find TB Resources:
<https://findtbresources.cdc.gov>



TB Centers of Excellence:
<https://www.cdc.gov/tb-programs/php/about/tb-coe.html>



Facebook:
www.facebook.com/CDCTB/



X (formerly Twitter):
www.twitter.com/cdc_tb

Acknowledgements and References



- Dr. Jon Iralu – slides
- Dr. Leslie Stewart – slides
- CDC “Introduction to Tuberculosis” slides and images
- WHO TB Guidelines and Annual TB Report

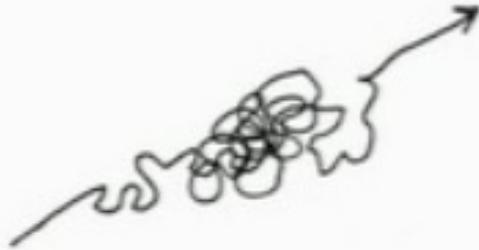
Questions

Success



what people think
it looks like

Success



what it really
looks like

