Diagnosis & Treatment of TB Infection

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Latent Tuberculosis (LTBI)

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Latent TB infection (LTBI) definition:

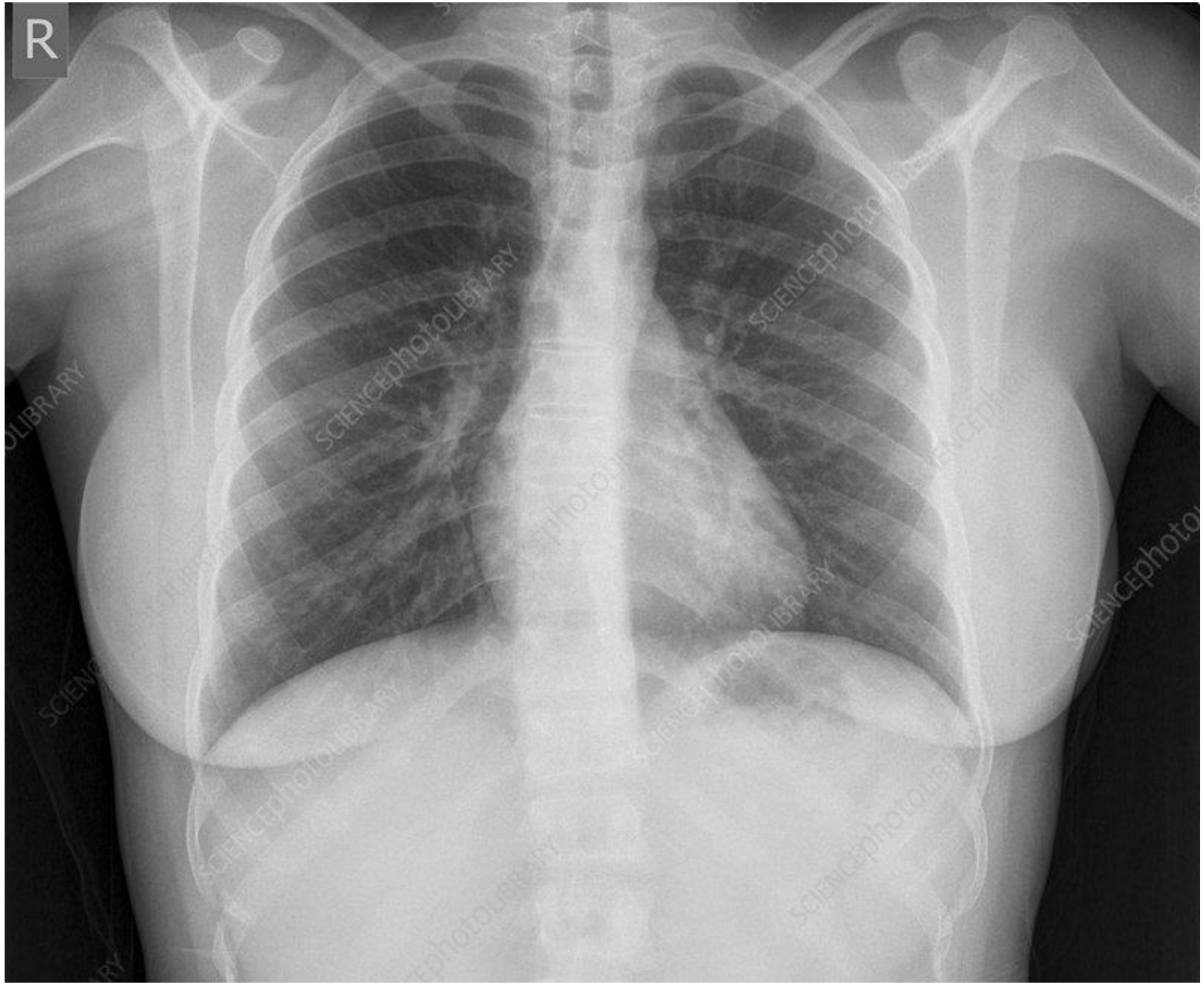
A symptom **free** clinical state diagnosed by a **positive** test result for ***Mycobacterium tuberculosis complex*** infection and an absence of clinical and radiologic findings of **active TB disease.**

TB background:

- **Bacteria**: **mycobacterium tuberculosis**; identified in 1882, Robert Koch
- **Active** TB vs **Inactive** TB **(LTBI)**
- Person with **active** TB **disease** of the **lungs/throat** can spread TB germs **through the air** to another person thru **cough/speaking/singing**
- TB germs can **stay in the air** for several hours depending on the environment
- TB germs are more likely to spread in **indoor** areas with **poor** air circulation vs **outdoor** areas
- People with **active** TB **disease** can spread TB germs to people they **spend time with every day**

CDC 2025

Normal CXR

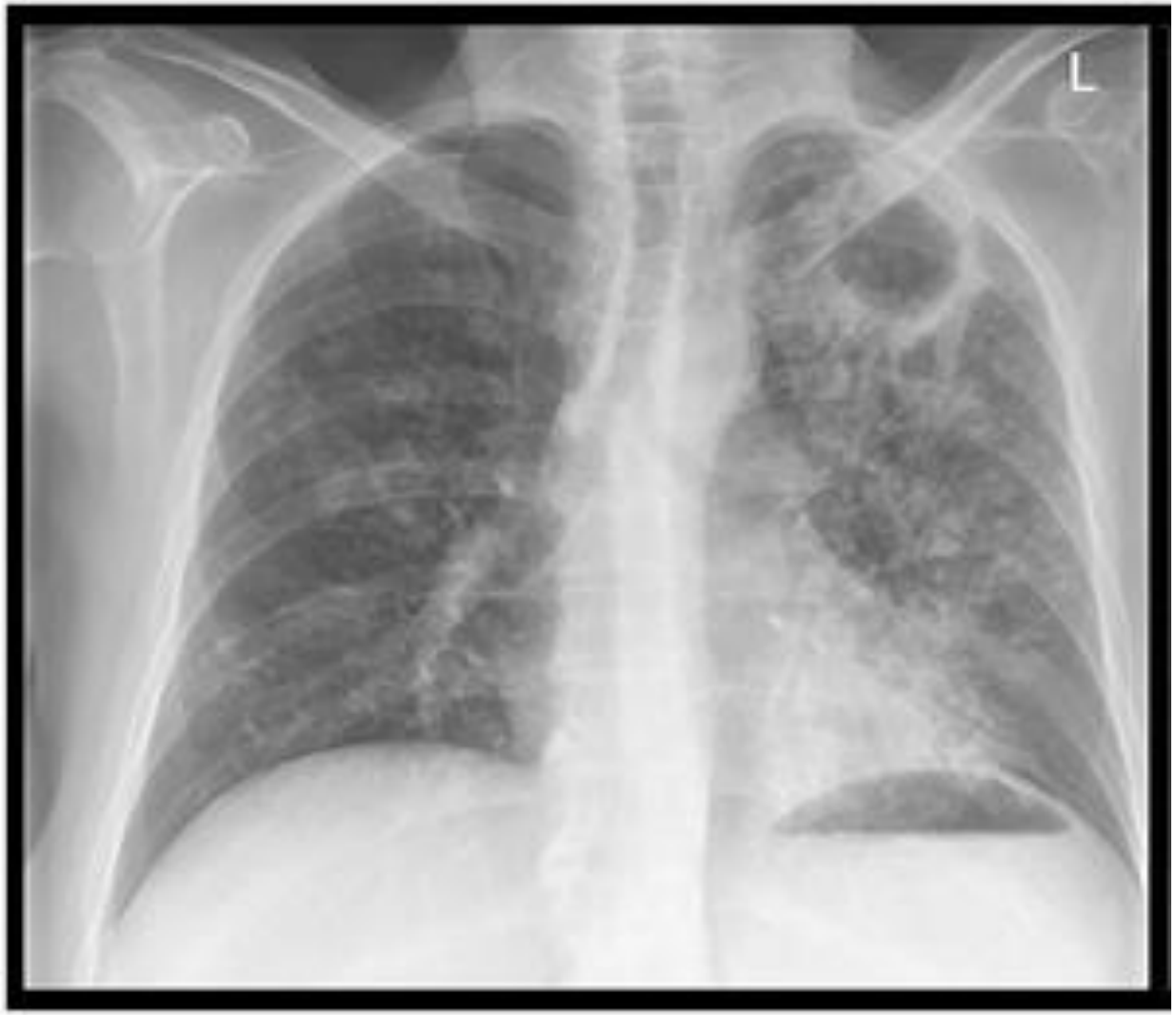


Science Photo Library

CXR Active TB

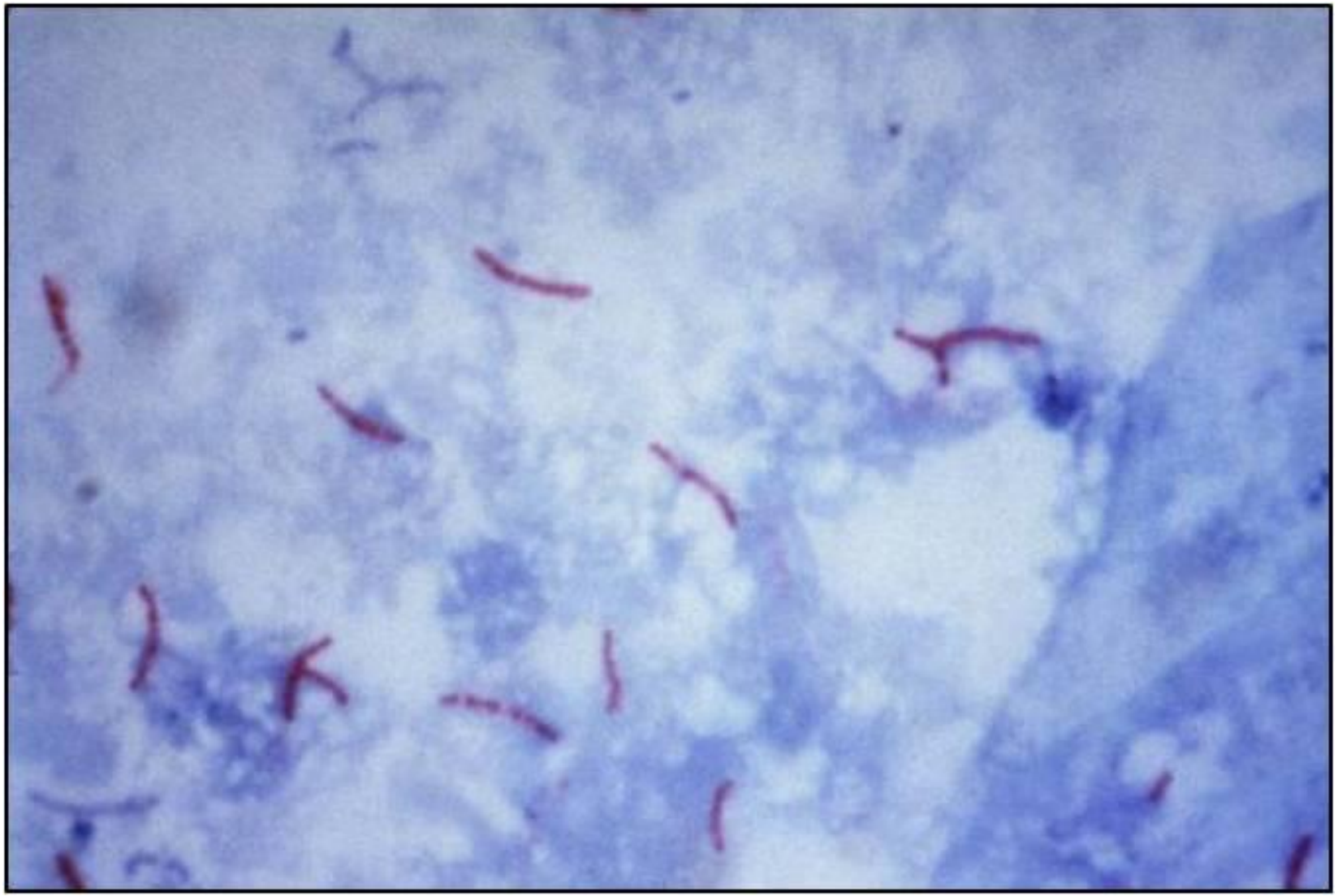
Radiopaedia, 2025

CXR of cavitary TB



PLOS, 2025

Sputum: +AFB smear



CDC 2025

CXR of COPD/smoker

Asuquo Otu et al, 2023

Symptoms of TB disease:

- Cough
- Coughing up blood or sputum
- Chest pain
- Fever
- Night sweats
- Chills
- Loss of appetite
- Weakness or fatigue
- Weight loss

HHS, 2025

Latent TB infection (LTBI) definition:

A symptom **free** clinical state diagnosed by a **positive** test result for ***Mycobacterium tuberculosis complex*** infection and an absence of clinical and radiologic findings of **active TB disease.**

People with **Latent** TB Infection (LTBI):

- Have a **small** number of TB bacteria in their body that are **alive** but are **in**active
- Can**not** spread TB bacteria to others; are **not** infectious
- Do **not** feel sick, but may become sick if the bacteria in their bodies become **active**
- Usually have a **positive** TB blood test or TB skin test result
- Have typically **normal** chest radiographs
- Have **negative** sputum smears and cultures
- Should consider **treatment** for latent TB to **prevent** TB **disease**
- Do **not** require respiratory isolation

CDC 2025

Who is at risk for getting TB?

- Persons who have **contact** with someone who has **infectious** TB **disease**
- Persons who were **born** or who frequently **travel** to some countries, such as in: **Asia, Africa and Latin America**
- **Health care workers** and **others** who work or live in places at high**er** risk for TB transmission, such as homeless shelters, jails, nursing homes and TB Clinics

HHS 2025

People at higher risk for exposure to TB bacteria:

- **Contacts** of people known/presumed to have **infectious** TB **disease**
- People born in and/or frequently **travel** to countries where TB is **endemic**
- People who live or used to live in **large group** settings
- **Employees** of high-risk **congregate** settings
- **Health care workers** who serve pts with TB **disease**
- Populations with increased incidence of latent TB infection
- **Infants, children** and **adolescents** exposed to adults with **infectious** TB **disease**

CDC 2025

People at higher risk of developing TB **disease once infected** with TB bacteria:

- Living with HIV
- Younger than 5 yrs of age
- History of untreated or inadequately treated TB disease
- Immunosuppressive therapy
- Silicosis, chronic renal failure, leukemia, cancer: head/neck/lung
- Diabetes
- S/p gastrectomy or jejunoileal bypass
- Low body weight
- Substance abuse
- Medically underserved

CDC 2025

Testing for **Latent** TB

- TB **blood** tests (Interferon Gamma Release Assay, IGRA)
  - QuantiFERON-TB Gold Plus (QFT-Plus)
  - T-Spot TB test (T-Spot)
- TB **skin** tests (Mantoux tuberculin skin test, TST)
- Who do you **test**?
  - People at high**er** risk of **exposure** to TB bacteria
  - People at high**er** risk of developing TB **disease** once infected with TB bacteria

CDC 2025

Bacille Calmette-Guerin (BCG) vaccine:

- **Infants and small children** in other countries where TB is more **common**
- **Not** widely used in the **US**
- **Not** part of routine childhood vaccination schedule in **US**
- Goal: **protect** infants/small children from getting **severe** forms of TB
- **Positive** TB **skin** test
- TB blood tests **not** affected by prior BCG vaccine

HHS 2025

Testing for **Latent** TB

- **Annual** TB testing of **health care personnel** is **not recommended** unless there is a **known exposure** or **ongoing transmission.**

HHS 2025

Interpreting TST:

- A TST reaction of ≥ to **5 millimeters (mm)** of **induration** is considered **positive** for:
  - People living with **HIV**
  - Recent **contacts** of people with **infectious TB**
  - People with **cxr** findings suggestive of **previous** TB **disease**
  - Organ **transplant** recipients
  - Other immuno**suppressed** pts (prednisone, biologics)

HHS/CDC 2025

Interpreting TST:

- A TST reaction of ≥ **10 mm** of **induration** is considered **positive** for:
  - People born in countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, Guatemala, etc.
  - Use of illicit drugs
  - Mycobacteriology laboratory workers
  - People who work in high-risk congregate settings
  - People with certain medical conditions that place them at risk for TB
  - People with low body weight
  - Children younger than 5 years of age
  - Infants, children and adolescents exposed to adults in high-risk categories

HHS/CDC 2020

Interpreting TST:

- A TST reaction ≥ of **15 mm** of **induration** is considered **positive** for:
  - People with no risk factors for TB

HHS/CDC 2020

A false <u>positive</u> TST may result from:

- Infection with non- tuberculous mycobacteria
- Prior BCG vaccination
- Incorrect administration technique
- Incorrect measurement or interpretation of the reaction

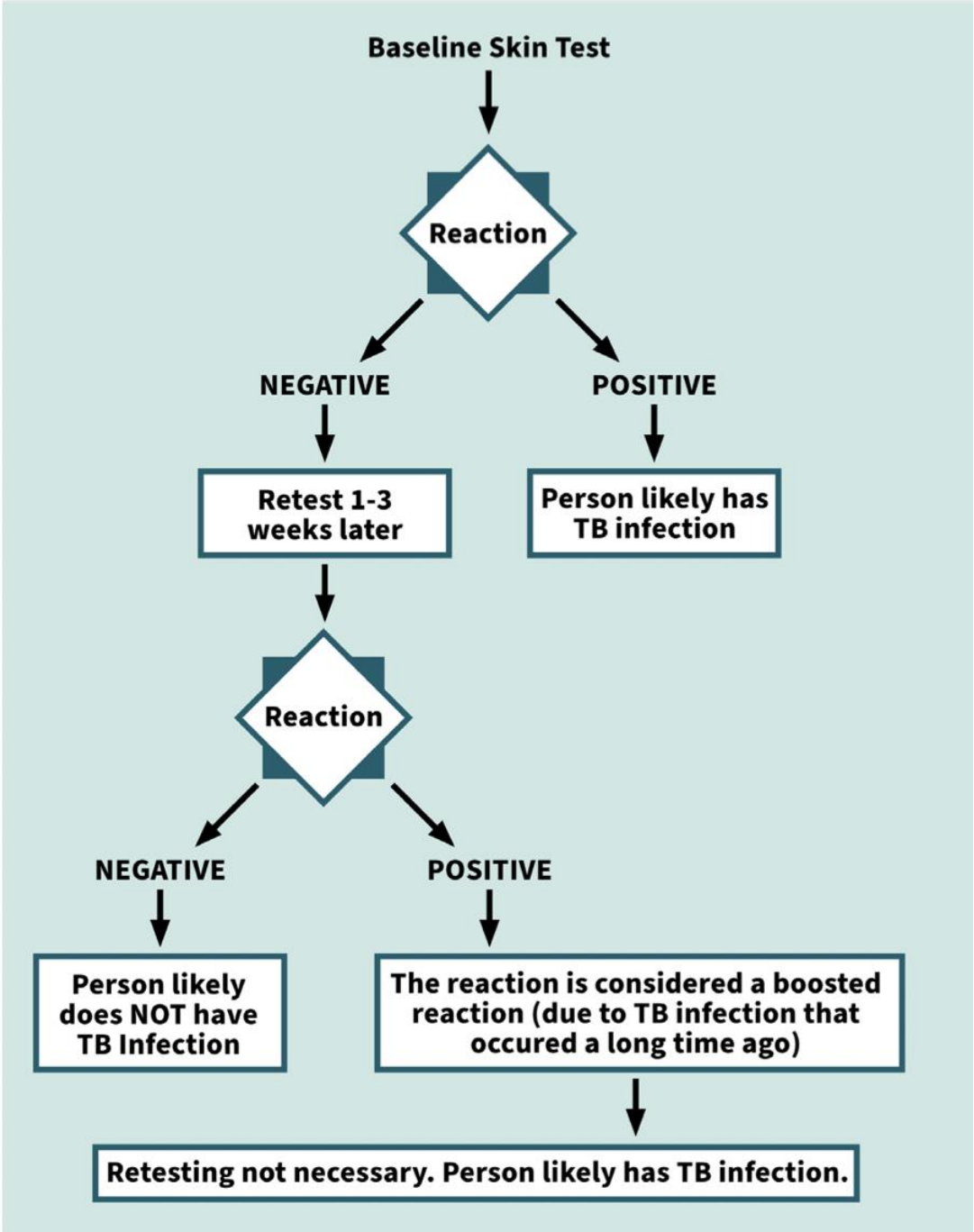
A false <u>negative</u> TST may result from:

- Underlying immunosuppression
- Very recent TB infection (within the last 8-10 weeks)
- Incorrect administration
- Live virus vaccination within the last 4 weeks

Pediatrics 2021

Two-Step TST Testing

HHS/CDC 2020



IGRA

TST

- Antigens are chosen to optimize specificity
- Laboratory instruments are required
- One patient encounter is sufficient
- Little subjectivity
- Does not cross-react with BCG or most NTM
- Previous IGRA does not boost future IGRA
- Results can be available within 24hrs
- Generally more expensive
- Blood must be processed within 8 – 32 hours after collection

- Less specific antigens
- No lab instruments are required
- Requires two visits to complete test
- Interpretation is subjective and risk-stratified
- Cross-reacts with BCG and some NTM
- Can boost subsequent TST or IGRA
- Results available in 48-72 hrs
- Generally lower cost
- No blood draw or specimen collection required, only intradermal injection

Tx for **Latent TB (LTBI)**:

- CDC and National TB Controllers Association:
  - 3 mths of once-weekly: isoniazid + rifapentine (3HP)
  - 4 mths of daily rifampin (4R)
  - 3 mths of daily isoniazid + rifampin (3HR)

- Alternative:
  - 6 to 9 mths of isoniazid + vit B6

HHS 2025

LTBI Tx

HHS/CDC 2020

Drug(s)	Duration	Dose and Age Group	Frequency	Total Doses
Isoniazid (INH)* and Rifapentine (RPT)†	3 months	**Adults and children aged >12 years** INH: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT: 10.0–14.0 kg, 300 mg 14.1–25.0 kg, 450 mg 25.1–32.0 kg, 600 mg 32.1–49.9 kg, 750 mg ≥50.0 kg, 900 mg maximum **Children aged 2–11 years:** INH*: 25 mg/kg; 900 mg maximum RPT†: as above	Once weekly	12
Rifampin (RIF)¶	4 months	**Adults:** 10 mg/kg **Children:** 15-20 mg/kg** Maximum dose: 600 mg	Daily	120
Isoniazid (INH)* and Rifampin (RIF)¶	3 months	**Adults** INH*: 5 mg/kg; 300 mg maximum RIF¶: 10 mg/kg; 600 mg maximum **Children** INH*: 10-20 mg/kg††; 300 mg maximum RIF¶: 15-20 mg/kg; 600 mg maximum	Daily	90
Isoniazid (INH)*	6 months	**Adults:** 5 mg/kg **Children:** 10-20 mg/kg†† Maximum dose: 300 mg	Daily	180
		Adults: 15 mg/kg **Children:** 20-40 mg/kg†† Maximum dose: 900 mg	Twice weekly§	52
Isoniazid (INH)*	9 months	**Adults:** 5 mg/kg **Children:** 10-20 mg/kg†† Maximum dose: 300 mg	Daily	270
		Adults: 15 mg/kg **Children:** 20-40 mg†† Maximum dose: 900 mg	Twice weekly§	76

Contacts to infectious TB case:

- Pulmonary or laryngeal TB case with a positive sputum smear
- If initial TST/TB blood test negative, then retest
- Retest at 8-10 weeks after end of TB exposure
- Retest/2nd test is needed to determine if infection occurred but was too recent to be detected at the time of the first test
- Usually takes 2-8 weeks after being infected with MTB for the body's immune system to mount a response detectable by the tests

HHS/CDC 2020

Contacts to infectious TB case:

- Children younger than 5 yrs of age, with negative TST/TB blood test gets cxr
- Immunosuppressed contacts (e.g., person living with HIV), with negative TST/TB blood test gets cxr
- If cxr normal, treatment for LTBI is started
- Contact is retested 8-10 weeks with same type of test after last exposure to infectious TB case
- If repeat test is positive, treatment for LTBI is continued
- If repeat test is negative, can consider discontinuation of LTBI treatment

HHS/CDC 2020

Window prophylaxis:

- Children younger than 5 yrs of age, who have been exposed to TB, and active TB has been ruled out, should receive LTBI tx, even with initial negative TB testing.

- Children should be retested 8-10 weeks after they were last exposed to TB.

- Window prophylaxis can be stopped only if:
  - Child is not older than 6 mths
  - Repeat TST is negative
  - Repeat TST was collected at least 8 weeks after last contact with the infectious TB case

HHS/CDC 2020

Medical Conditions that Weaken the Immune System:

- HIV
- Substance Use
- Specialized tx for rheumatoid arthritis or Crohn’s disease
- Organ transplants
- Severe kidney disease
- Head and neck cancer
- Diabetes
- Medical treatments such as corticosteroids
- Silicosis
- Low body weight

HHS 2025

TB and HIV:

- **Worldwide**, TB is the **leading** cause of **death** among people living with HIV.
- The risk of progression from LTBI to TB disease is **7-10% each year** for those with **both** LTBI and **un**treated HIV.
- The risk is substantially reduced with effective ART for HIV, but the risk to progression to TB disease, is **still higher** than it is for HIV negative people with LTBI

HHS 2020

Tx for LTBI in Children:

- Recommended regimens:
  - 3 mths once weekly regimen of INH and RPT (3HP)
  - 4 mths of daily RIF
  - 3 mths of daily regimen of RIF and INH
  - 6 or 9 mths daily regimen of INH
- 3HP is recommended for children **older** than 2 yrs of age, via **DOT**
- Risk of INH-related hepatitis in infants, children and adolescents is **minimal**

HHS 2020

Tx of LTBI in Pregnancy:

- TST or TB blood test
- +TST or +TB blood test, cxr with proper shielding
- LTBI tx can be **delayed** 2-3 mths post-partum to avoid administering medication during pregnancy
- LTBI tx should be started, even in the lst trimester, if **contact** to **infectious** TB **disease** case
- LTBI tx:
  - 4 mths of RIF, daily
  - 3 mths of INH and RIF (+ vit B6), daily
  - 6 or 9 mths of INH (+vit B6), daily
- 3HP **not** recommended for pregnant women because safety during pregnancy **not** studied
- Can breastfeed, taking RIF and INH

HHS 2020

Monitoring while on LTBI treatment:

For healthy adults *without* underlying risk factors for hepatotoxicity, check in monthly to ask about

- adherence
- signs and symptoms of TB disease
- signs and symptoms of adverse medication reactions

For adults *with* risk factors for hepatotoxicity

- check a baseline AST, ALT, total bilirubin, alk phos, albumin; If starting a rifamycin also check CBC
- check in monthly for adherence and new signs and symptoms
- consider rechecking labs periodically if baseline was abnormal or new signs or symptoms appear

Potential adverse events of drugs used for latent tuberculosis infection (LTBI) treatment

Drug	Potential adverse effects	Comments
Isoniazid	Elevation of aminotransferases Symptomatic hepatitis Peripheral neuropathy	Close follow-up and caution in patients with baseline liver disease
Rifamycins (includes rifampin,rifapentine, and rifabutin)	Cutaneous rash Hematologic abnormalities Flu-like illness Elevation of aminotransferases Symptomatic hepatitis Orange discoloration of body fluids	Consider multiple potential drug-drug interactions (i.e., warfarin, anticonvulsants, opioids, antiretrovirals) Isoniazid-rifapentine not recommended in pregnant women or women expecting to be pregnant during treatment Isoniazid-rifapentine not recommended for children < 2 years of age

Clin Chest Med 2019

DOT for LTBI treatment:

- Required for LTBI treatment if using an intermittent INH regimen
- Initially required for 12 dose INH + rifapentine weekly regimen, but now this is considered optional in the guidance depending on the setting and resources available
- Recommended in any situation where the risk of progression to TB disease is very high if the preventive treatment is not taken (for example in children and adolescents).
- May also be considered if there is special concern for non-adherence to treatment

CDC 2020

Refusing tx for LTBI:

- Reinforce that pts can come back to TB Clinic
- Reinforce signs/symptoms of active TB disease
- Document discussion with pt
- Have pt sign: refusal of medication form

After completion of LTBI tx:

- Make sure the person is given documentation of their positive TB test and completion of treatment for LTBI.

- Educate them that they would be expected to have a positive TB test in the future. It does not mean that their treatment did not work.

TB Concepts:

- **Latent** TB/**In**active TB vs TB **Disease**
- **Latent** TB: are infected with **live** TB bacteria
- **Latent** TB: if the live TB bacteria become active/multiply, **latent** TB develops into TB **disease**
- Treating people for latent TB infection **reduces** the risk for latent TB infection to **progress** to TB disease
- **Latent** TB cases: **5-10%** of infected persons will develop TB **disease**
- **Progression** from **un**treated **latent** TB **infection** to TB **disease** accounts for approximately **80%** of **US** TB cases
- **Children less than age 5,** have a higher risk of developing TB **disease** once infected and at higher risk for **life threatening** forms of TB **disease**
- Estimated that up to **13 million** people in the **US** have **latent** TB

CDC 2025

DCHHS TB Clinic LTBI Experience in 2024:

- 514 cases
- 3 cases: greater than/equal to 85 yrs old
- 29 homeless; 485 not homeless
- 54 contact; 460 no known contact
- 318 completed tx; 114 refused tx; 44 lost; 20 blank; 8 other; 9 moved; 1 atypical

Age Range	# of TB Cases
0-4 yrs old	5 cases
5-9 yrs old	15 cases
10-14 yrs old	35 cases
15-17 yrs old	33 cases
18-24 yrs old	45 cases
25-34 yrs old	95 cases
35-44 yrs old	93 cases
45-54 yrs old	90 cases
55-64 yrs old	66 cases
65-74 yrs old	24 cases
75-84 yrs old	10 cases