LATENT TUBERCULOSIS

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Clinical Description

A chronic bacterial infection caused by Mycobacterium tuberculosis, usually characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved.

Clinical Criteria

A case that meets all the following criteria:
• A positive tuberculin skin test or positive interferon gamma release assay for M. tuberculosis
• Other signs and symptoms compatible with tuberculosis (TB) (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease)
• Treatment with two or more anti-TB medications
• A completed diagnostic evaluation

Laboratory Criteria for Diagnosis

• Isolation of M. tuberculosis from a clinical specimen,* OR
• Demonstration of M. tuberculosis complex from a clinical specimen by nucleic acid amplification test,** OR
• Demonstration of acid-fast bacilli in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated.
Latent TB Infection (LTBI)

LTBI is the presence of *M. tuberculosis* organisms (tubercle bacilli) without signs and symptoms or radiographic or bacteriologic evidence of TB disease.
Tuberculosis (TB) Disease: Only the Tip of the Iceberg

There are two types of TB conditions: TB disease and latent TB infection.

People with **TB disease** are sick from active TB germs. They usually have symptoms and may spread TB germs to others.

People with **latent TB infection** do not feel sick, do not have symptoms, and cannot spread TB germs to others.

But, if their TB germs become active, they can develop **TB disease**.

**Millions** of people in the U.S. have latent TB infection. Without treatment, they are at risk for developing TB disease.

To learn more about TB, visit [www.cdc.gov/tb](http://www.cdc.gov/tb)
Approximately one-third of the world’s population is infected with M. tuberculosis. It is estimated that more than 11 million people in the United States have LTBI, which is about 4% of the total population.

- Centers for Disease Control
Estimated TB incidence rates, 2014

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.


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“For the third year in a row, the Last Frontier has come in first among U.S. states for its rate of new infections. Rates of new infection are highest in rural Alaska, and Alaska Natives are most at risk for contracting the disease. … For 2013, the Yukon-Kuskokwim region recorded a TB infection rate 700 percent higher than the rest of the state.”
Again in 2015 Alaska is the top TB state

<table>
<thead>
<tr>
<th>State or District</th>
<th>Number Cases</th>
<th>Incidence of TB</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>68</td>
<td>9.2</td>
<td>737,625</td>
</tr>
<tr>
<td>Hawaii</td>
<td>127</td>
<td>8.9</td>
<td>1,431,603</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>33</td>
<td>4.9</td>
<td>672,228</td>
</tr>
<tr>
<td>California</td>
<td>2,137</td>
<td>5.5</td>
<td>39,144,818</td>
</tr>
<tr>
<td>Texas</td>
<td>1,334</td>
<td>4.9</td>
<td>27,469,114</td>
</tr>
</tbody>
</table>
Tuberculosis in Alaska

Tuberculosis Rate, Alaska, 1992 - 2015

Cases/100,000


Data for AK and U.S.
Death due to Tuberculosis

Although there are very few, most years in Alaska there are deaths attributable to TB. While individuals with TB may also die from unrelated causes, 21 deaths determined to be related to TB occurred from 2010-2015 in Alaska.

Deaths Related to Tuberculosis, Alaska, 2010-2015

- 2010: 4
- 2011: 5
- 2012: 3
- 2013: 1
- 2014: 4
- 2015: 4
TUBERCULOSIS IN ALASKA BY REGION

Incidence of TB in Alaska by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>2010 (cases/100,000)</th>
<th>2011 (cases/100,000)</th>
<th>2012 (cases/100,000)</th>
<th>2013 (cases/100,000)</th>
<th>2014 (cases/100,000)</th>
<th>2015 (cases/100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anch/Mat-Su</td>
<td>18 (4.8)</td>
<td>29 (7.5)</td>
<td>10 (2.5)</td>
<td>25 (6.3)</td>
<td>22 (5.5)</td>
<td>18 (4.5)</td>
</tr>
<tr>
<td>Gulf Coast</td>
<td>0 (0.0)</td>
<td>5 (6.2)</td>
<td>3 (3.7)</td>
<td>4 (5.0)</td>
<td>0 (0.0)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Interior</td>
<td>11 (10.1)</td>
<td>4 (3.6)</td>
<td>4 (3.5)</td>
<td>1 (0.9)</td>
<td>4 (3.6)</td>
<td>6 (5.3)</td>
</tr>
<tr>
<td>Northern</td>
<td>11 (46.5)</td>
<td>8 (29.7)</td>
<td>16 (58.6)</td>
<td>10 (36.3)</td>
<td>17 (61.7)</td>
<td>7 (25.2)</td>
</tr>
<tr>
<td>Southeast</td>
<td>2 (2.9)</td>
<td>1 (1.4)</td>
<td>5 (6.7)</td>
<td>1 (1.3)</td>
<td>2 (2.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Southwest</td>
<td>15 (38.2)</td>
<td>20 (48.1)</td>
<td>28 (66.6)</td>
<td>30 (70.5)</td>
<td>17 (39.9)</td>
<td>35 (82.5)</td>
</tr>
<tr>
<td><strong>STATE TOTAL</strong></td>
<td><strong>57 (8.0)</strong></td>
<td><strong>67 (9.3)</strong></td>
<td><strong>66 (9.0)</strong></td>
<td><strong>71 (9.6)</strong></td>
<td><strong>62 (8.4)</strong></td>
<td><strong>68 (9.2)</strong></td>
</tr>
</tbody>
</table>
INH
Bethel district Alaska

- RTC in 1957-1959
  - 1 year INH versus placebo
  - 69% reduction in TB
- Community-wide prophylaxis began in 1963
- 12-months INH recommended for LTBI treatment in 1970
RISK FACTORS FOR TUBERCULOSIS (CDC)

- Recent close or prolonged contact with infectious TB disease
- Foreign born person from or recent traveler to high prevalence area
- Chest x-ray suggesting inactive or past TB
- HIV infection
- Organ transplant recipient
- Immunosuppression secondary to use of prednisone (> 15 mg/day for > 1 month) or other immunosuppressants
- Intravenous drug abuser
- Resident or employee of “high risk congregate setting” (e.g. prison, long term care facility, hospital, homeless shelter)
- Signs and symptoms of TB disease
TB OR NOT TB

Tests of Immune Response

delayed hypersensitivity reaction is detectable 2-8 weeks after infection

➤ Tuberculin Skin Test (TST), also known as Mantoux or purified protein derivative (PPD)

➤ Interferon-Gamma Release Assays (IGRAs)
  ➤ QuantiFERON Gold-in-Tube test (QFT-GIT)
  ➤ T-SPOT
THE TUBERCULIN SKIN TEST (TST)

➤ Do not perform on a person with previous positive TST or history of treatment for TB disease

➤ Read in 48 to 72 hours

➤ Result is induration, not erythema

➤ Result must be recorded in millimeters, not “positive” or “negative”

➤ “Interpretation of the TST results is the same for persons who have had the BCG vaccination because most BCG cross-reactivity wanes with time.” (CDC)
> 5 mm is positive in …

➤ HIV infected persons

➤ recent contacts of a person with infectious TB disease

➤ persons with fibrotic changes on chest x-ray consistent with prior TB

➤ Patients with organ transplants and other immunosuppressed patients (including patients taking > 15 mg/day of prednisone for > 1 month or those taking TNF-alpha antagonists)
INTERPRETING THE TUBERCULIN SKIN TEST (TST)

> 10 mm is positive in ...

➢ Recent arrivals to the United States (within the past 5 years) from high prevalence areas

➢ Intravenous drug abusers

➢ Residents or employees in high-risk congregate settings (e.g. correctional facilities, long-term care facilities, hospitals, & homeless shelters)

➢ Mycobacteriology lab personnel

➢ Persons with clinical conditions increasing the risk of progression to TB disease

➢ Children younger than 5

➢ Children exposed to adults in high risk categories
> 15 mm is positive in …

➤ Persons with no known risk factors for TB
Factors That May Cause False-Positive TST Reactions

- **Nontuberculous mycobacteria**
  - Reactions caused by nontuberculous mycobacteria are usually ≤10 mm of induration

- **BCG vaccination**
  - Reactivity in BCG vaccine recipients generally wanes over time; positive TST result is likely due to TB infection if risk factors are present
Factors That May Cause False-Negative TST Reactions

- **Anergy**
  - Inability to react to a TST because of a weakened immune system
  - Usefulness of anergy testing in TST-negative persons who are HIV infected has not been demonstrated
Factors That May Cause False-Negative TST Reactions - 2

- **Recent TB Infection**
  - Defined as less than 10 weeks after exposure

- **Very young age**
  - Newborns (< 6 months)
Factors That May Cause False-Negative TST Reactions - 3

- **Live virus vaccination**
  - For example, measles or smallpox
  - Can temporarily suppress TST reactivity

- **Overwhelming TB Disease**

- **Poor TST administration technique**
  - For example, TST injection too shallow or too deep, or wheal is too small
IGRAs (INTERFERON-GAMMA RELEASE ASSAYS)

“Tuberculosis is no longer skin deep!”

➤ QuantiFERON Gold-in-Tube test (QFT-GIT)
➤ T-SPOT

➤ Measures the immune response to TB proteins in whole blood, by assaying interferon-gamma released by white blood cells
➤ Requires a single patient visit to conduct the test
➤ Does not cause a booster phenomenon
➤ Results available within 24 hours
➤ Unaffected by BCG
➤ Limited data on children under 5 years of age, and so not recommended for this age group
Interferon-Gamma Release Assays (IGRAs)

- Whole-blood test used to detect *M. tuberculosis* infection
- Two U.S. Food and Drug Administration (FDA) approved IGRAs are commercially available in the U.S.:
  - QuantiFERON®-TB Gold-in-tube test (QFT-GIT)
  - T.SPOT®.TB test (T-Spot)
QuantiFERON Gold @ YK

➤ Costs $55 per test
➤ Can’t be collected on Fridays
➤ Must be sent out to LabCorp
The serum is inexpensive, but the true cost must include the labor involved to place & read.

CVS Pharmacy, in the lower 48, charges $35 to place the test and $29 to read it, for a total charge of $64. [http://www.cvs.com/minuteclinic/services/price-lists](http://www.cvs.com/minuteclinic/services/price-lists)

Walgreens charges $28 to place the test and $25 to read it, for a total charge of $53. [https://www.walgreens.com/topic/healthcare-clinic/price-menu.jsp](https://www.walgreens.com/topic/healthcare-clinic/price-menu.jsp)
In the YK Delta, all LTBI’s get a sputum test, even if there’s no cough.
LATENT TUBERCULOSIS INFECTION (LTBI) TREATMENTS

- Isoniazid (isonicotinylhydrazide or “INH”) 5 mg/kg or maximum dose of 300 mg by mouth daily for 6-9 months

- **Directly Observed Therapy (DOT):** isoniazid 15 mg/kg or maximum dose of 900 mg AND rifapentine 900 mg (if over 50 kg) by mouth weekly for 12 weeks

- Pyridoxine (vitamin B6) 25-50 mg by mouth daily to prevent isoniazid-associated neuropathy

- Rifampin 10 mg/kg or maximum dose of 600 mg by mouth once daily for 4 months
WHEN TO STOP ISONIAZID

Asymptomatic elevations of liver enzymes occur in 10-20% of patients, and they usually return to normal even when treatment is continued.

➤ STOP if transaminase level greater than 3 times the upper limit of normal with symptoms (nausea or vomiting)

➤ STOP if transaminase level greater than 5 times the upper limit of normal in the asymptomatic patient
"Dad always thought laughter was the best medicine, which I guess is why several of us died of tuberculosis.

- Jack Handey
HELP

➤ Dr. Jacob Gray (ANMC ID) - cell: 907-231-5881
➤ Alaska Section of Epidemiology - 907-269-8000
➤ Curry Center Warmline - 877-390-6682
AN APP FOR THAT

CDC LTBI

a FREE download for your iPhone or Android device