



LATENT TUBERCULOSIS

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2009 CDC TB CASE DEFINITION

<http://wwwn.cdc.gov/nndss/conditions/tuberculosis/case-definition/2009/>

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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**.



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

To learn more about TB, visit
www.cdc.gov/tb

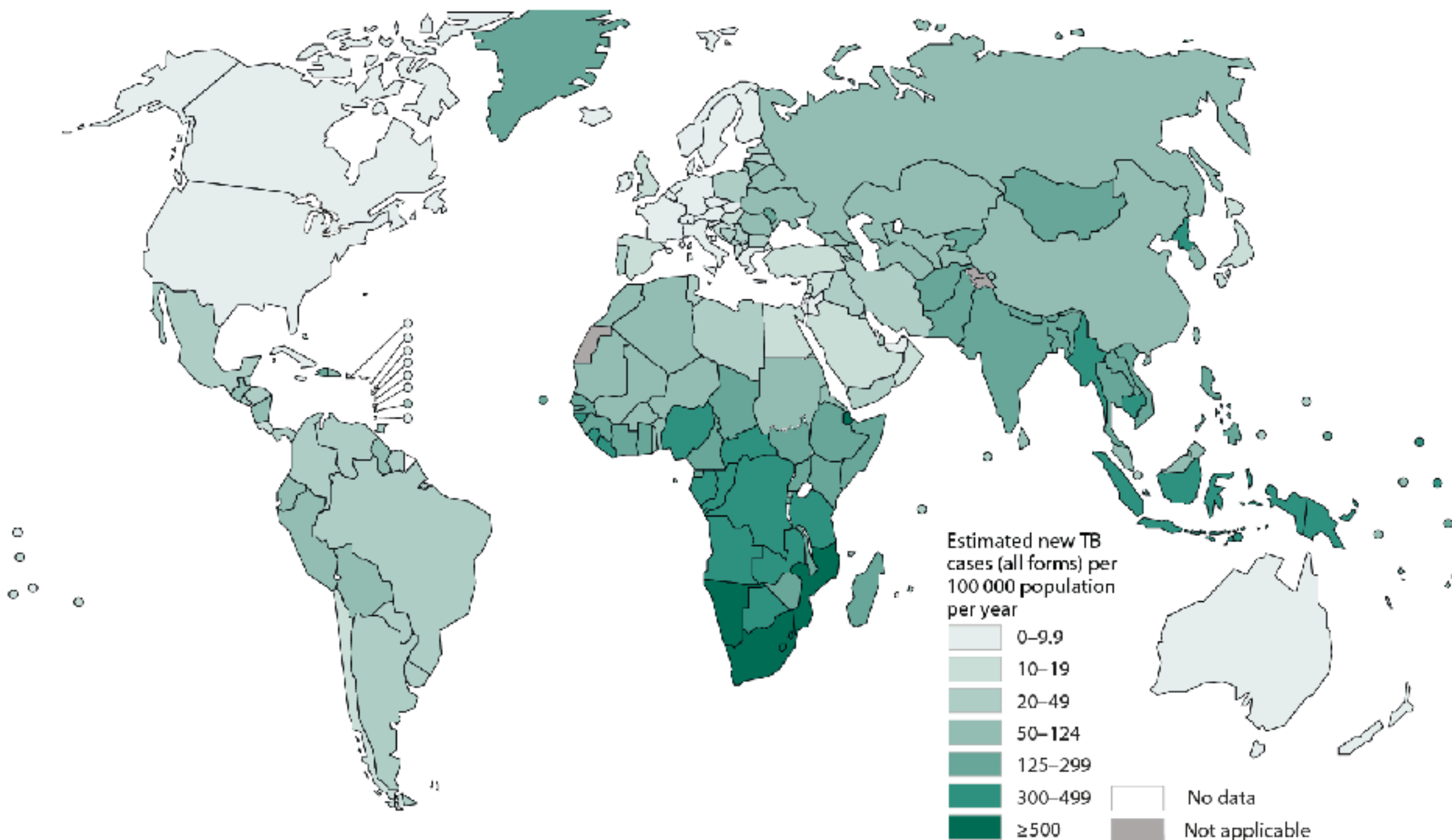
<http://www.cdc.gov/tb/publications/ltbi/intro.htm>



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.

Data Source: *Global Tuberculosis Report 2015*. WHO, 2015.

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Alaska Dispatch News

Alaska again leads nation in TB infection rates

Sean Doogan | May 25, 2014

“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.”

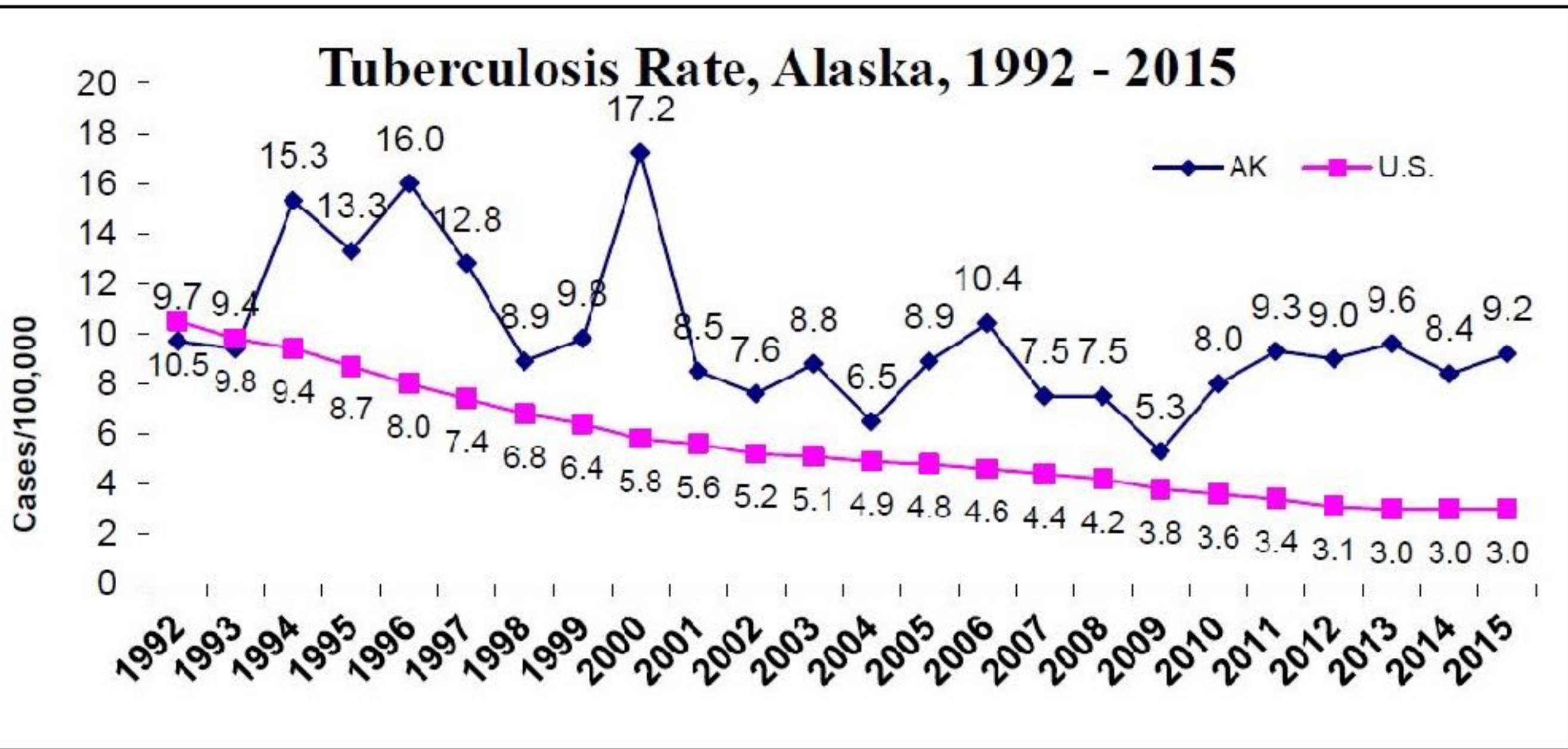
AGAIN IN 2015 ALASKA IS THE TOP TB STATE

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States and district with the highest incidence of tuberculosis, 2015

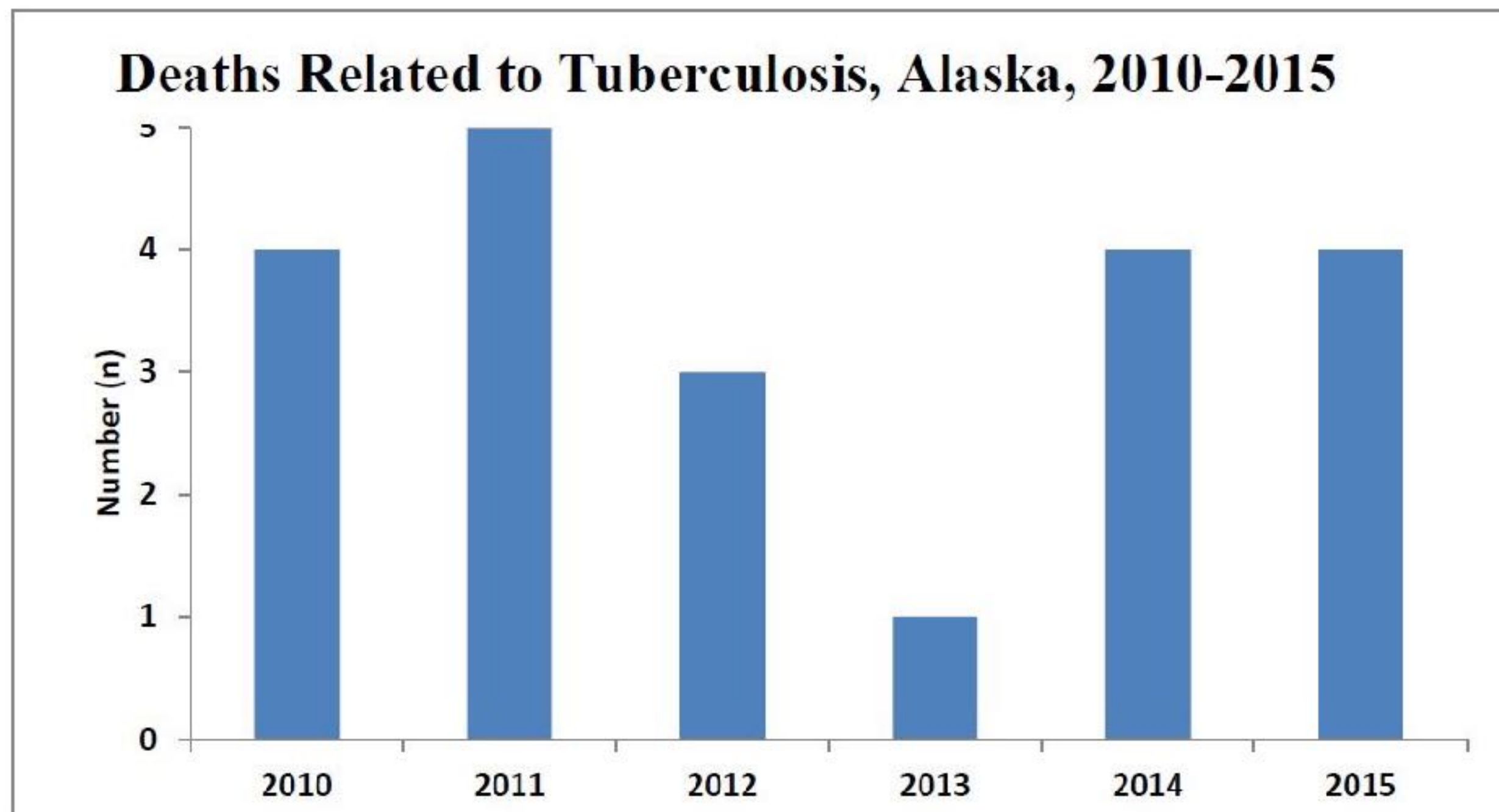
State or District	Number Cases	Incidence of TB	Population
Alaska	68	9.2	737,625
Hawaii	127	8.9	1,431,603
District of Columbia	33	4.9	672,228
California	2,137	5.5	39,144,818
Texas	1,334	4.9	27,469,114

Tuberculosis in Alaska



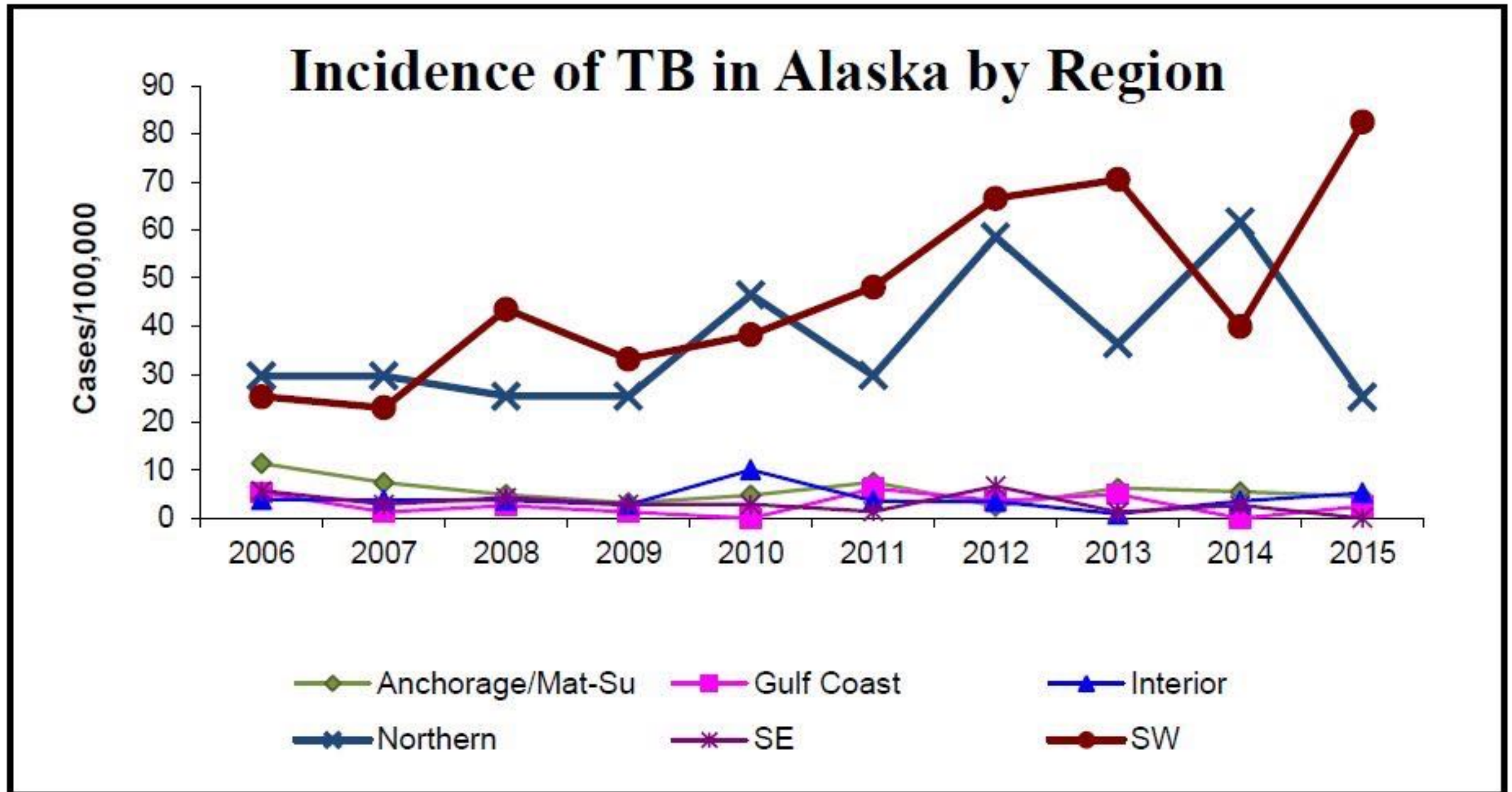
Death due to Tuberculosis

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.





TUBERCULOSIS IN ALASKA BY REGION



http://dhss.alaska.gov/dph/Epi/id/SiteAssets/Pages/TB/TB_Report_2015.pdf

Number and incidence of TB cases by region, Alaska, 2010-2015

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

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

TST positivity in children



Cornstock GW. Am Rev Respir Dis 86:810-822, 1962

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)

INTERPRETING THE TUBERCULIN SKIN TEST (TST)

> 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

INTERPRETING THE TUBERCULIN SKIN TEST (TST)

> 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 -1

□ **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

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- Costs \$55 per test
- Can't be collected on Fridays
- Must be sent out to LabCorp

COST OF TB SKIN TEST

- 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>
- 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>



WE DO IT DIFFERENTLY IN THE DELTA

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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

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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

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CDC LTBI



a FREE download for your
iPhone or Android device

<http://www.cdc.gov/tb/publications/mobileltbiapp/default.html>