

## An update on TB

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## An update on TB

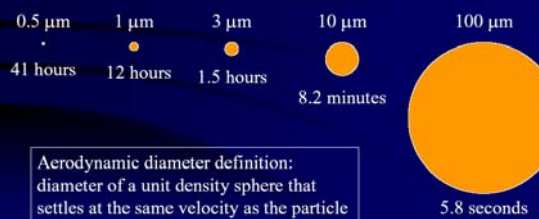
- A brief review of :
  - TB transmission
  - Diagnosis of TB disease and latent TB infection
    - Tuberculin skin testing
    - Chest x-rays
    - Specimen collection
  - Treatment of TB disease and latent TB infection
- An update on TB in Anchorage

## HOW DO WE SPREAD TB?



## Particle Settling in Still Air

Time to settle 5 feet by unit density spheres



## Infectiousness

Patients should be considered infectious if they

- Are coughing
- Are undergoing cough-inducing or aerosol-generating procedures, or
- Have sputum smears positive for acid-fast bacilli and they
- Are not receiving therapy
- Have just started therapy, or
- Have poor clinical response to therapy

## Infectiousness

Patients no longer considered infectious if they meet **all** of these criteria:

- Are on adequate therapy
- Have had a significant clinical response to therapy, and
- Have had 3 consecutive negative sputum smear results

Young children with active TB are not contagious, but there are exceptions:



Curtis A et al. N Engl J Med 1999;341:1491-1495



### Infection Control Measures for TB

• **Administrative controls** to reduce risk of exposure

• **Engineering controls** to prevent spread and reduce concentration of droplet nuclei

• **Personal respiratory protection** in areas where increased risk of exposure



### TB OR NOT TB?

- Medical history
- Physical examination
- Mantoux tuberculin skin test (+ QuantiFERON Gold)
- Chest radiograph
- Bacteriologic or histologic exam

### Conditions That Increase the Risk of Progression to TB Disease

- HIV infection
- Substance abuse
- Recent infection
- Chest radiograph findings suggestive of previous TB
- Diabetes mellitus
- Silicosis
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy
- Cancer of the head and neck
- Hematologic and reticuloendothelial diseases
- End-stage renal disease
- Intestinal bypass or gastrectomy
- Chronic malabsorption syndromes
- Low body weight (10% or more below the ideal)
- **Young age**

### LTBI vs. Pulmonary TB Disease

#### Latent TB Infection

- TST<sup>+</sup> or QFT<sup>+</sup> positive
- Negative chest radiograph
- No symptoms or physical findings suggestive of TB disease

#### Pulmonary TB Disease

- TST or QFT usually positive
- Chest radiograph may be abnormal
- Symptoms *may* include one or more of the following: fever, cough, night sweats, weight loss, fatigue, hemoptysis, decreased appetite
- Respiratory specimens *may* be smear or culture positive

\*tuberculin skin test

†QFT (QuantIFERON-TB and QuantiFERON-Gold) is a blood test to detect *M. tuberculosis* infection.



A decision to test is a decision to treat

## Groups That Should Be Tested for LTBI

### 1. Higher risk for exposure to or infection with TB:

- Close contacts of a person known or suspected to have TB
- Foreign-born persons from areas where TB is common
- Residents and employees of high-risk congregate settings
- Health care workers who serve high-risk clients
- Medically underserved, low-income
- High-risk racial or ethnic minority
- Children exposed to high-risk adults
- Persons who inject illicit drugs

## Groups That Should Be Tested for LTBI

### 2. Higher risk for TB disease once infected:

- Persons with HIV infection
- Persons recently infected with *M. tuberculosis* (PPD converters)
- Persons with certain medical conditions (diabetes, immunosuppressed, CRF, silicosis, malnourished, etc.)
- Persons who inject illicit drugs
- Persons with a history of inadequately treated TB

## Reading the Tuberculin Skin Test

- Measure reaction in 48 to 72 hours
- Measure induration, not erythema
- Record reaction in millimeters, not "negative" or "positive"
- Ensure trained health care professional measures and interprets the TST



## Factors that May Affect the Tuberculin Skin Test Reaction

Type of Reaction	Possible Cause
False positive	Nontuberculosis mycobacteria BCG vaccination
False negative	Recent TB infection Very young age (<6 mo old) Overwhelming TB disease Anergy Vaccination

## Classifying the Tuberculin Reaction

5 mm is classified as positive in

- HIV-positive persons
- Recent contacts of TB case
- Persons with fibrotic changes on chest radiograph consistent with old healed TB
- Patients with organ transplants and other immunosuppressed patients

## Classifying the Tuberculin Reaction (cont.)

10 mm is classified as positive in

- Recent arrivals from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children <4 years of age, or children and adolescents exposed to adults in high-risk categories

## Classifying the Tuberculin Reaction (cont.)

15 mm is classified as positive in

- Persons with no known risk factors for TB
- Targeted skin testing programs should only be conducted among high-risk groups

## BCG and the tuberculin skin test

**Table 1** Distribution of TST induration among 783 children 3 to 60 months of age, Botswana, July–August 1996

TST induration (mm)	n = 783 n (%)
0	617 (79)
1–4	49 (6)
5–9	59 (8)
10–14	43 (5)
≥15	15 (2)

Lockman S et al. Tuberculin reactivity in a pediatric population with high BCG vaccination coverage. *Int J Tuberc Lung Dis.* 1999 Jan 3(1):23-30.

## BCG and the tuberculin skin test

AAP Red Book 2006:

"Tuberculosis disease should be suspected strongly in any symptomatic person with a positive TST result regardless of history of BCG immunization.

When evaluating an asymptomatic child who has a positive TST result and who possibly received BCG, the result should not be attributed to BCG vaccine."

**CDC/ATS Guideline: "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection"**

"BCG-vaccinated persons. A history of BCG vaccination, with or without a BCG scar, should not influence the decision regarding whether to treat LTBI."

City and County of San Francisco  
Department of Public Health  
Tuberculosis Control Section

**QuantIFERON-TB Gold® Blood Test for TB Infection**  
Provider Information and Guidelines for Interpretation

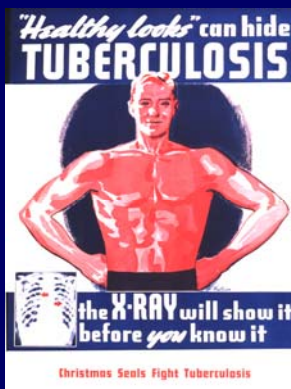
**What is it?**  
The QuantIFERON-Gold test (QFT) is a whole blood test for screening for active tuberculosis (TB) or latent tuberculosis (LTBI).  
If not detected and treated, LTBI may later develop into TB disease. The QFT measures the patient's immune response to all tuberculosis, the bacterium that causes TB. This test was approved by the U.S. Food and Drug Administration (FDA) in 2004.  
QuantIFERON-GOLD represents a significant advance over the first-generation QuantiFERON-TB previously used by SPCoH TB Control.

**How does it work?**  
Blood samples are mixed with antigens and incubated for 16 to 24 hours. The antigens include ESAT-6 and CFP-10, proteins specific to all tuberculosis complex. These antigens are not found in BCG strains or *M. avium*.  
If the patient is infected with all tuberculosis, the patient's lymphocytes will recognize the antigens and release interferon-gamma (IFN-γ) in response. The QFT results are based on the amount of IFN-γ that is released. Additional tests (such as chest radiograph) are needed to exclude TB disease and confirm the diagnosis of LTBI.

**What are the advantages?**  
• Higher sensitivity and specificity than the tuberculin skin test (TST).  
• More likely to be positive with active TB disease than the TST (more sensitive).  
• Less likely to be false-positive in patients with past exposure to BCG or atypical mycobacteria (more specific).  
• Only needs a single patient visit - does not require return visit to determine results.  
• Does not cause the booster phenomenon, which can happen with repeat tuberculin skin tests (TST).  
• Less subject to reader bias and error when compared to the TST.  
• Results are not affected by past TST.

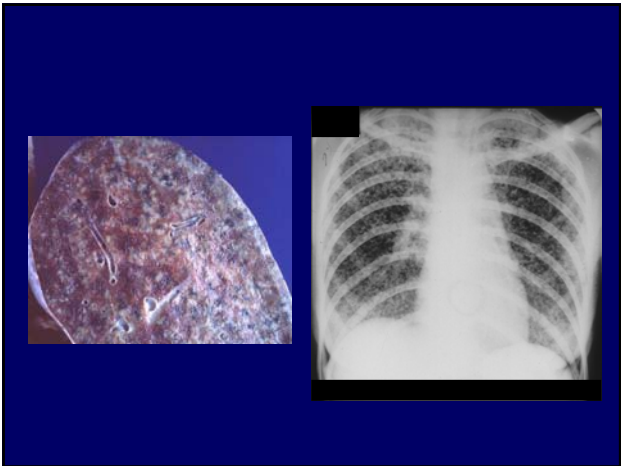
**What are the disadvantages?**  
• As with the TST, additional tests are needed to exclude TB disease and confirm LTBI.  
• Blood samples must be processed within 12 hours of blood draw.  
• Test is currently available Monday through Thursday at select Community Health/Tubercle clinics.

Quantiferon Gold - Interpretation - 1/15/08/08/08



## Chest radiographs

Characteristic:	Adults	Children
Location:	Apical	Anywhere (25% multilobar)
Adenopathy:	Rare (except HIV)	Usual (30-90%)
Cavitation:	Common	Rare (except adolescents)
Signs and symptoms:	Consistent	Relative paucity





## Specimen Collection

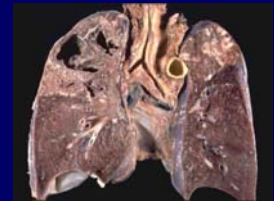
- Obtain 3 sputum specimens for smear examination and culture
- Persons unable to cough up sputum, induce sputum, bronchoscopy or gastric aspiration
- Follow infection control precautions during specimen collection
- Gastric aspirates:
  - Nearly 100% yield for <3 month olds
  - Overall ~ 40% yield for 3 gastric aspirates
  - Smear rarely positive after 3 months

## Basic Principles of TB Treatment

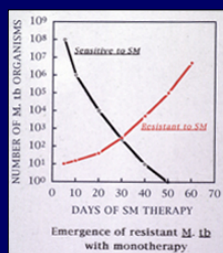
- Provide safest, most effective therapy in shortest time
- Multiple drugs to which the organisms are susceptible
- Never add single drug to failing regimen
- **Directly Observed Therapy (DOT)** to assure adherence to treatment

## Why Multiple Drugs in Active TB

- A cavity can have  $10^9$  to  $10^{11}$  organisms
- Spontaneous mutants resistant to a single drug can arise at a rate of 1 in  $10^8$  -  $10^9$  organisms.
- Cavitory lesions may have hundreds of organisms resistant to a single antimicrobial agent prior to the institution of therapy.



## WHY MULTIPLE DRUGS?



## When to Consider Treatment Initiation

- Positive AFB smear
- Treatment should not be delayed because of negative AFB smears if high clinical suspicion:
  - History of cough and weight loss
  - Characteristic findings on chest x-ray
  - Immigration from a high-incidence country

## Antituberculosis Drugs

### First-Line Drugs

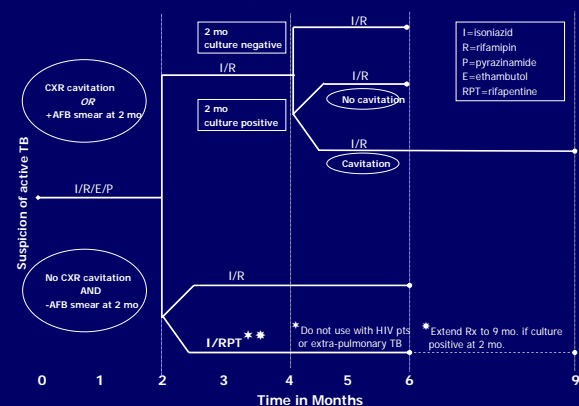
- Isoniazid
- Rifampin
- Pyrazinamide
- Ethambutol
- Rifabutin\*
- Rifapentine

### Second-Line Drugs

- Streptomycin
- Cycloserine
- p-Aminosalicylic acid
- Ethionamide
- Amikacin or kanamycin\*
- Capreomycin
- Levofloxacin\*
- Moxifloxacin\*
- Gatifloxacin\*

\* Not approved by the U.S. Food and Drug Administration for use in the treatment of TB

## CDC Treatment Algorithm for Culture-Positive TB



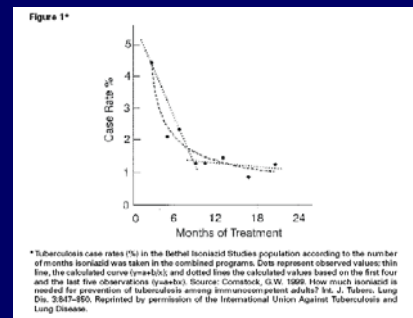
## WHY DO WE TREAT LATENT TB INFECTION?

**Table 4. Efficacy of various durations of isoniazid preventive therapy for persons with fibrotic lesions, by length of treatment—International Union Against Tuberculosis (IUAT) Trial, 1969–1977**

Group	5-yr Tuberculosis incidence* (% reduction)			
	Placebo	12 wk	24 wk	52 wk
All participants (n = 27,830) <sup>1</sup>	14.3	11.3 (21)	5.0 (65)	3.6 (75)
Adherent participants <sup>2</sup> (n = 21,835) <sup>1</sup>	15	9.4 (31)	4.7 (69)	1.1 (93)
Fibrotic lesions <2 cm <sup>2</sup> (n = 18,663) <sup>1</sup>	11.6	9.2 (20)	4.0 (66)	4.2 (64) <sup>4</sup>
Fibrotic lesions >2 cm <sup>2</sup> (n = 9,428) <sup>1</sup>	21.3	16.2 (24)	7.0 (67)	2.4 (89)

\* Per 1000 person-years.  
<sup>1</sup> Comparing placebo to 24 and 52 wk, p < 0.05; differences between placebo and 12 wk and between 24 and 52 wk not significant.  
<sup>2</sup> Collected pill calendars for "almost all" of the months assigned for their regimen and had taken at least 80% of the pills from the calendar by the time of the next monthly visit.  
<sup>3</sup> For all interregimen comparisons (p < 0.05).  
<sup>4</sup> Persons who developed tuberculosis on 52-wk regimen and had small fibrotic lesions were less likely to have collected pill calendars (47% than all other groups (58%)) (p < 0.001).  
 Source: International Union Against Tuberculosis Committee on Prophylaxis. Efficacy of various durations of isoniazid therapy for tuberculosis: five years of follow-up in the IUAT trial. *Bull. WHO* 1982;66:555-64.

## WHY 9 MONTHS OF ISONIAZID FOR LATENT TB INFECTION?



\* Tuberculosis case rates (%) in the Bethel Isoniazid Studies population according to the number of months isoniazid was taken in the combined programs. Dots represent observed values; this line, the calculated curve (y=ab<sup>x</sup>), and dotted lines the calculated values based on the first four and the last five observations (y=ab<sup>x</sup>). Source: Conrath, G.W. 1980. How much isoniazid is needed for prevention of tuberculosis among immunocompetent adults? *Int. J. Tuberc. Lung Dis.* 3:587-590. Reprinted by permission of the International Union Against Tuberculosis and Lung Disease.

## Treatment of latent TB infection

Regimen	Adults	Children
Isoniazid	9 months	9 months
Isoniazid	6 months	
Rifampin	4 months	6 months
Rifampin/ pyrazinamide	Not recommended	Not recommended

## Window prophylaxis

- For high risk individuals, especially young children
  - with negative TST
  - no evidence of active TB
  - exposed to a likely contagious case of TB
  - with INH (unless source case resistant)
- Repeat TST 3 months after source case non-contagious
- Stop prophylaxis if TST negative and no other source case!



Report Suspected Cases to Alaska Section of Epidemiology: 269-8000, 1-800-478-0084

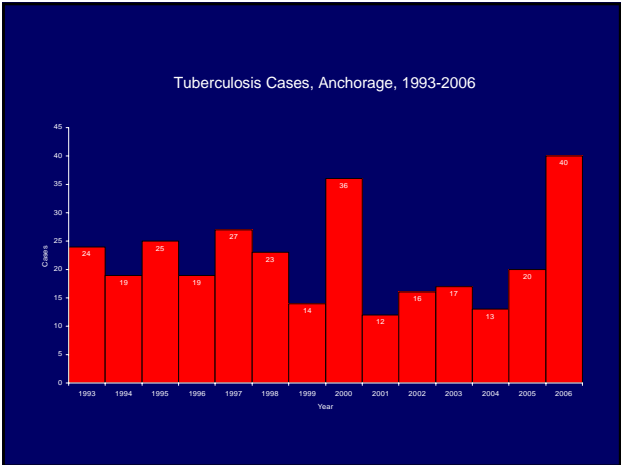
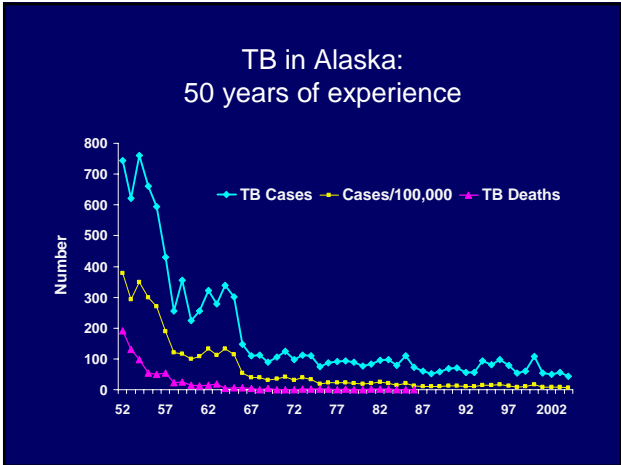
Expert consultants:

National Jewish Mycobacterial Diseases Consult Line 1-800-423-8891 ext 1353

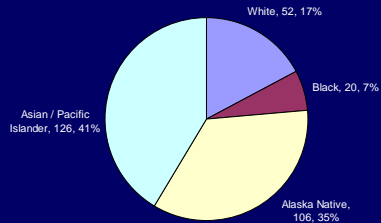
Francis Curry National TB Center Warmline 1-877-390-6682; 415-502-4700

Dr. Beth Funk, Alaska TB Control Officer, Alaska Section of Epidemiology 907-269-8000

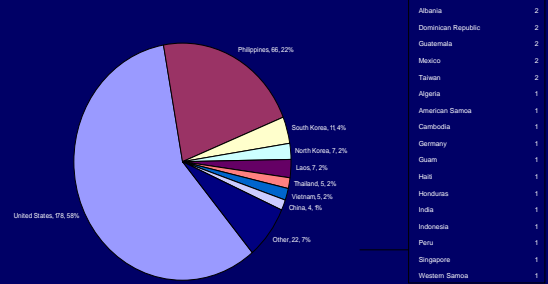
The Anchorage Update



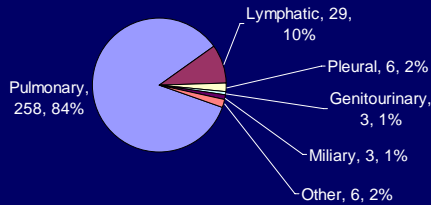
Racial distribution of Anchorage TB cases, 1993-2006



Birth Country of Anchorage TB Cases, 1993-2006

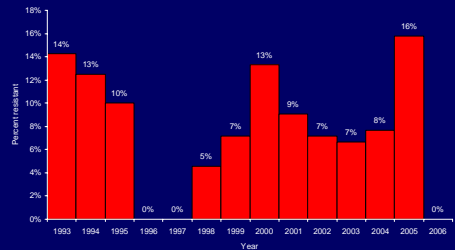


Site of disease in Anchorage TB cases, 1993-2006 (n=305)



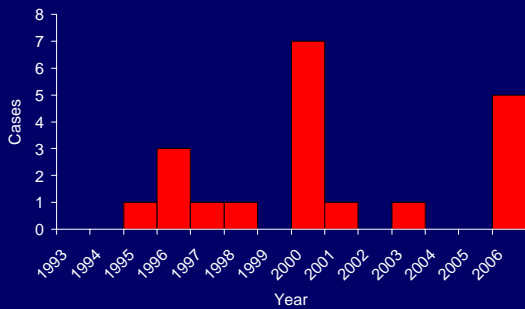
Antibiotic Resistant TB in Anchorage, 1993-2006

- Isoniazid resistance: 7.5%
- Multi-drug (isoniazid and rifampin) resistance: 0.7%

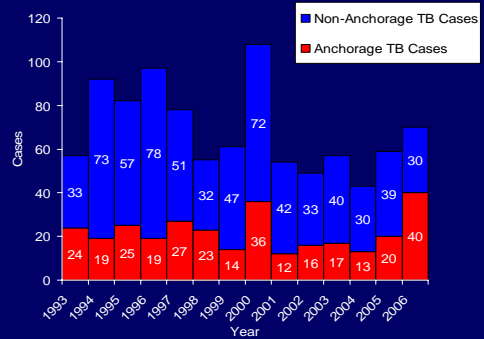


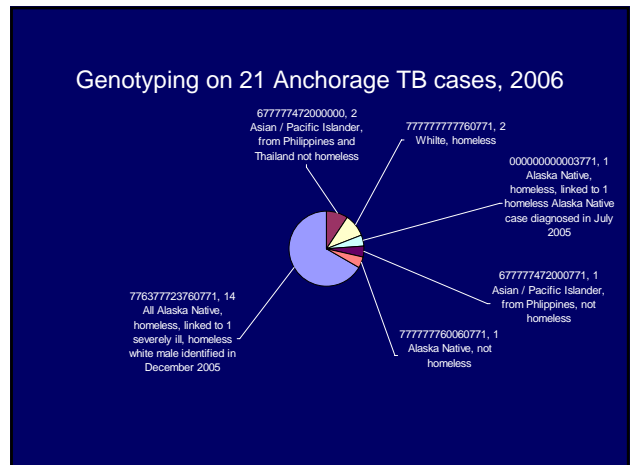
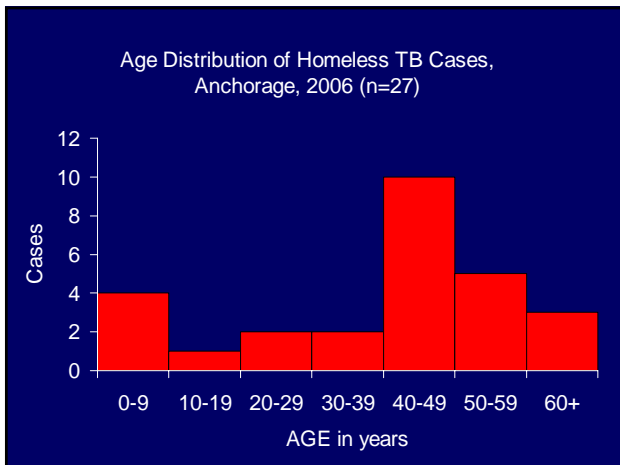
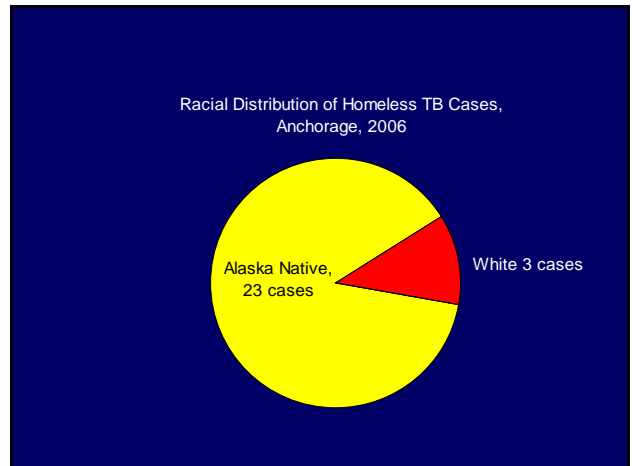
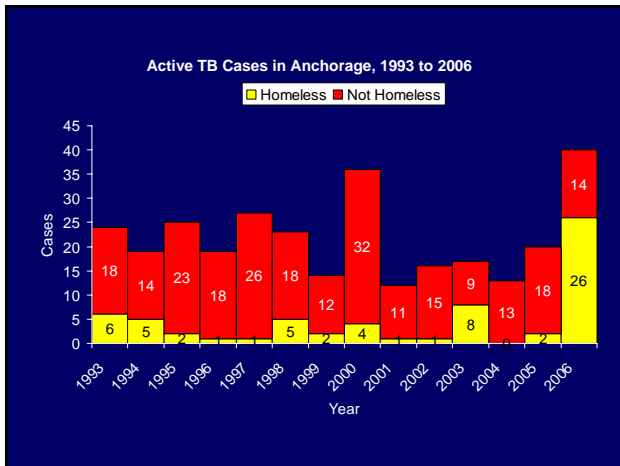
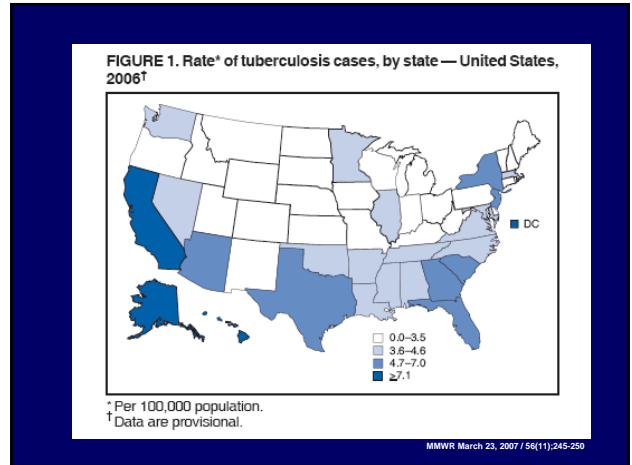
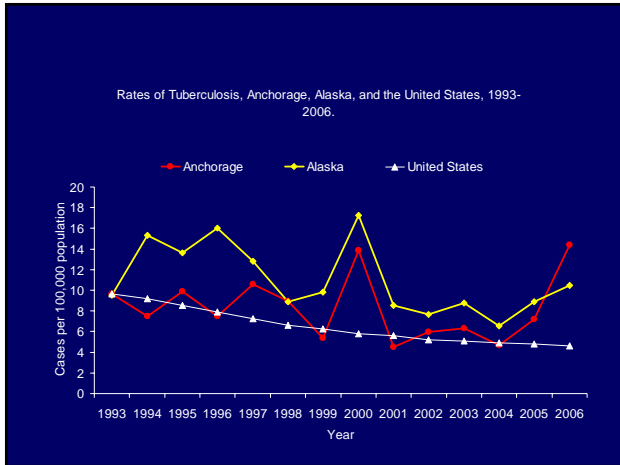
Percentage of TB Isolates Resistant to Isoniazid, Anchorage, 1993-2006

Pediatric TB Cases (<10 years), Anchorage, AK 1993-2006 (N= 20)



Active TB Cases, Alaska, 1993-2006





## Current Status of Anchorage 2006 TB Cases

### Homeless cases

- 17 finished treatment
- 4 remain on treatment, two are missing frequent doses
- 2 died of hypothermia
- 2 moved to home village
- 1 missing since November

### Non homeless cases

- 8 finished treatment
- 3 remain on treatment, one is missing some doses
- 1 moved to home village
- 2 died before diagnosis of TB established.

## Cases Who Died Before TB Diagnosis Was Established, Anchorage, 2006

- Case 1. 71-year-old male with heart failure and end-stage renal disease, died one day after admission for fever and pneumonia 71-year-old male with heart failure and end-stage renal disease, died one day after admission for fever and pneumonia. Pleural fluid collected on the day of admission grew *Mycobacterium tuberculosis* (*M.Tb.*).
- Case 2. 85-year-old female in hospice care for terminal lymphoma; she also had cardiomyopathy, congestive heart failure, pulmonary emboli, and anemia. Pleural fluid collected during hospitalization 3 weeks prior to death was smear negative for acid fast bacilli but subsequently grew *M. Tb* on culture.

## TB 2006

- Temporary housing for homeless TB patients: \$100,000+
- TB Incentives: \$23,736 -food, bus tokens
- TB home visits: 4,539 (34% more than 2004)
- TB clinic visits: 6,844 (13% more than 2004)

## As of 3/21:

- 25 cases on directly observed therapy
  - 17 have culture-confirmed TB
  - 3 are AFB smear positive, cultures are pending.
  - 5 are on treatment for culture negative/inactive TB.
- 2 are in jail
- 13 are homeless
- 13 have been identified in 2007, 6 are homeless
- 2 are new culture-confirmed cases identified at the screening at Bean's Café in February.

**TB ANYWHERE IS EVERYWHERE**

**TB is preventable and curable.**