PASSPORT TO PREVENTION
TB OR NOT TB?
COLLABORATION WITH PUBLIC HEALTH
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Objectives

At the conclusion of this presentation, participants will be able to:

- Discuss at least two populations impacted by TB
- Discuss the core treatment regimen for active TB
- Discuss two molecular laboratory tests that can aid in the diagnosis of TB
- Discuss at least two treatment regimen for Latent TB Infection

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Epidemiology

- In US, continue to see TB reported in every state
- Approximately 10-15 million Americans are infected with *M. tuberculosis*
- Without intervention, approximately 10% will progress to active TB

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Epidemiology (Cont.)

- Drug resistant cases reported in almost every state
- World-wide, billions are infected
- World-wide, In 2017, 1.6 million died from the disease (including 0.3 million among people with HIV).
- California reported 2,091 cases in 2018

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TB Cases and Rates in the US, 1982-2017

TB Rates in the United States, 1982-2017

In 2017, preliminary data indicate a rate of 2.8 per 100,000 population. This is the lowest rate on record, representing a 2.5% decrease in from 2016 to 2017. However, the TB rate remains at levels 28 times higher than the TB elimination target rate.

Reported TB Cases in the United States, 1982-2017

In 2017, preliminary data indicate that 9,093 new TB cases were reported in the United States, representing a decrease in case count of 1.8% from 2016 to 2017. This is the lowest case count and rate on record.

Source: CDC website

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TB Cases by Race/Ethnicity in the US, 2017

Minority populations continue to disproportionately bear the burden of TB disease.

Race/Ethnicity	Incidence Rate of TB Cases per 100,000 – 2017	Percentage of Reported TB Cases in the United States – 2017
American Indians or Alaska Natives	3.9	1%
Asians	17.7	35.7%
Blacks or African Americans	4.7	21%
Native Hawaiians and other Pacific Islanders	19.1	1.2%
Hispanics or Latinos	4.4	28.2%
Whites	0.5	11.8%

Note: for this report, persons identified as white, black, Asian, American Indian/Alaska Native, native Hawaiian or other Pacific Islander, or of multiple races are all non-Hispanic. Persons identified as Hispanic may be of any race.

Source: CDC website

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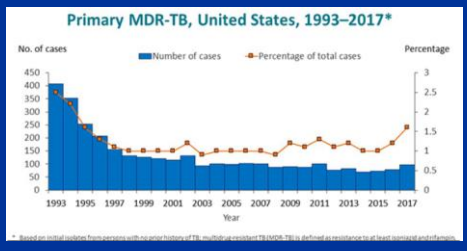
Tuberculosis Cases with Primary (MDR): United States 1993-2017



Source: CDC website

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PROFILE OF TB CASES CALIFORNIA

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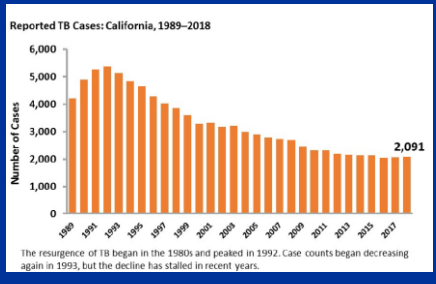
Number of Tuberculosis Cases: California, 1989-2018



Source: CDPH website

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TB Cases by National Origin California 2018

Source: CDPH website

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Tuberculosis Cases with Multidrug Resistance (MDR) on Initial or Final Drug Susceptibility Testing: California, 2008-2017

Source: CDPH website

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Etiology of TB

- TB is caused by *Mycobacterium tuberculosis*
- Can cause infection in almost any organ of the body (secondary infections)
- Spread by droplet nuclei from infected person
- Can cause either LTBI or active TB

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Clinical Presentation

- Pulmonary TB symptoms include:
  - Productive, prolonged cough (greater than 3 weeks duration)
  - Chest pain
  - Hemoptysis

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Clinical Presentation (Cont.)

- Symptoms of systemic TB include:
  - Fever
  - Chills
  - Night sweats
  - Appetite loss
  - Weight loss
  - Fatigue

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Diagnosis

- Evaluation for TB includes:
  - Medical history and physical exam
  - Mantoux tuberculin skin test
  - Quantiferon or other blood assay test
  - Chest radiograph
  - Bacteriologic exam

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Mantoux Tuberculin Skin Test

- Tuberculin skin test useful for:
  - Detecting LTBI
  - Large group examinations
  - Examining individuals with S/S of TB
- Preferred method of testing in children ≤ 5 years of age

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Mantoux Tuberculin Skin Test (Cont.)

- Negative test does not exclude possibility of LTBI or active TB
  - Especially in those who are immuno-compromised
  - Severe TB disease
- BCG is not a contraindication for administering a TST
- Booster Phenomenon

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Interferon Gamma Release Assays (IGRA)

- Whole blood tests that can be done as part of a TB work-up does not differentiate latent TB infection from TB disease
- Two tests are approved by FDA for use in the US
  - QuantiFERON TB Gold in tube test (QFT-GIT)
  - SPOT TB Test (T-SPOT)
  - Lab must be validated to process QFT blood
  - Does not cross react with BCG

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Chest Radiograph

- Findings usually in apical and posterior segments of the upper lobe
- May also be seen in superior segments of lower lobe
- May cause cavitary lesion
- May also have different CXR findings, especially in patients with HIV
- Only adds to diagnostic probability, does not confirm TB

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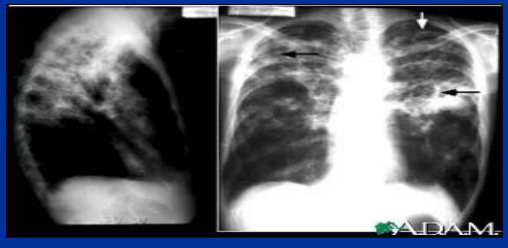
Chest X-Ray



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MYCOBACTERIAL NOMENCLATURE

Legitimate Name	Runyon Group	Acceptable Common Name	Suggested Report Based on Use of Minimal Differential Test
M. tuberculosis		Human tubercle bacillus	M. tuberculosis
M. bovis		Bovine tubercle bacillus	M. bovis
M. avium	III	Avian tubercle bacillus	M. intracellulare M. avium complex
M. kansasii	I		M. kansasii (high) catalase (low) variety
M. marinum	I		M. marinum
M. scrofulaceum	II	Scrofula scotochromogen	M. scrofulaceum
M. gordonae**	II	Tap water scotochromogen	M. gordonae
M. szulgai	II		M. szulgai
M. flavescens	II		M. flavescens
M. intracellulare	III	Battey bacillus	M. intracellulare M. avium complex
M. xenopi	III		M. xenopi
M. simiae (M. habana)	III		M. simiae or M. simiae M. habana complex
M. nonchromogenicum M. terrae	III III	Radish bacillus	M. terrae complex
M. triviale	III		M. triviale
M. gastri	III		M. gastri
M. fortuitum	IV		M. fortuitum or M. fortuitum complex
M. chelonei*** (N+) M. chelonei, subsp. M. abscessus	IV	(M. borstelense) (M. abscessus)	M. fortuitum complex
M. phlei M. smegmatis	IV IV		Group IV, not M. fortuitum
M. ulcerans			M. ulcerans
Rhodochrous group			Rhodochrous group

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Cultures

- Confirmatory test for TB
- Should culture all specimens, even if smear negative
- May have dual infection (e.g., TB & MAC)

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Bacteriologic Exam

- Smear examination
  - Rapid turn around, usually less than 24 hours
  - Smears containing AFB are strongly indicative of TB
  - Gives rough idea of burden and infectivity of *M. tuberculosis*
  - Negative AFB smear does not rule out TB or communicability

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Acid Fast Bacilli (AFB)

Tuberculosis diagnosis: TB Culture
Distinctive clusters of colorless *Mycobacterium tuberculosis* form in this culture.

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GeneXpert

- The Xpert MTB/RIF detects DNA sequences specific for *Mycobacterium tuberculosis* and rifampicin resistance by polymerase chain reaction
- It is based on the Cepheid GeneXpert system, a platform for rapid and simple-to-use nucleic acid amplification tests (NAAT). The Xpert® MTB/RIF purifies and concentrates *Mycobacterium tuberculosis* bacilli from sputum samples, isolates genomic material from the captured bacteria by sonication and subsequently amplifies the genomic DNA by PCR
- Results can be obtained from unprocessed sputum samples on 90 minutes

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TB Molecular Epidemiology: Targeting Recent Transmission

- TB molecular epidemiology targets recent transmission with the goal of reducing the burden of TB by identifying where transmission is currently occurring and interrupting it
- The challenge is to distinguish TB cases that are due to recent transmission from cases that were infected long ago and are just now developing active disease

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TB Molecular Epidemiology: Targeting Recent Transmission (Cont.)

- This is done by combining molecular, clinical, and epidemiologic data to detect, investigate and monitor recent transmission
- Whole-genome sequencing (or WGS) can provide added resolution for examining genetic relatedness of isolates by expanding coverage of the genome to about 90%, compared to the 1% that is covered by GENTyping

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Treatment of TB Disease

- Goal is to provide safest, effective treatment in shortest period of time
- Use multi-drug regimens
- Never add single drug to failing regimen
- Ensure adherence (DOT recommended, can be provided by Public Health)

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Treatment of TB Disease (Cont.)

- Usually start with 4-drug regimen and adjust as necessary:
  - Isoniazid (INH)
  - Rifampin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)
- MDR – TB requires treatment for 18-24 months
- XDR – TB requires treatment for 18-24 months

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HIV Testing of TB Patients

- Important to assess individuals with TB for HIV infection
- Co-infection with TB and HIV requires expert care and coordination of treatment for both diseases

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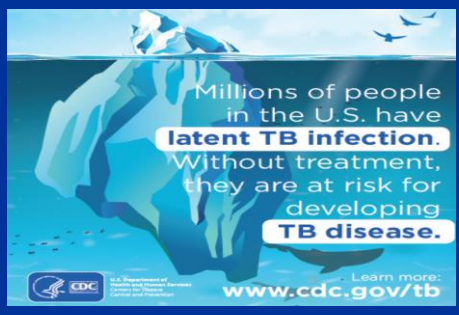
Tip of the Iceberg



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Risk Factors For Progression From Latent TB Infection (LTBI) To Active TB

- Recent contact with a person with active pulmonary TB disease
- Recent (within 2 years) TST (or QFT) conversion from negative to positive (active disease may occur in up to 5-10% of recently infected persons)
- HIV infection

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Risk Factors For Progression From LTBI To Active TB (Cont.)

- Injection drug use
- Diabetes mellitus (esp. insulin dependent)
- Chronic immunosuppression
  (e.g. transplant recipients, prolonged corticosteroid treatment)

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Risk Factors For Progression From LTBI To Active TB (Cont.)

- Hematologic or reticuloendothelial diseases (e.g., leukemia and Hodgkin's disease)
- Malnutrition and clinical situations associated with rapid weight loss (e.g., cancers of the head and neck, intestinal bypass or gastrectomy)
- Immunosuppressive drugs (e.g., ≥ 15 mg prednisone QD > 3 weeks or treatment with TNF – antagonists [e.g., Humira, Enbrel])

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Treatment of LTBI

- Consider treatment with skin test result greater than 5 mm (or positive IGRA) in:
  - HIV positive
  - Recent contacts of TB case
  - Fibrotic changes on CXR consistent with old granulomatous disease

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Treatment of LTBI (Cont.)

- Consider treatment with skin test result greater than 10 mm (or positive IGRA) for < 35 and those over 35 with high risk factors:
  - IV drug users
  - Residents of high risk congregate settings
  - Certain high risk HCW
  - Recent arrivals from endemic countries
  - Persons with high risk clinical conditions

Note: 15 mm cut off is not used in California

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Treatment Of LTBI (Cont.)

- Treatment for Latent TB Infection
  - INH: 6-9 months
  - INH - Rifapentine: once per week for 12 weeks*
  - Rifampin: 4 months

* Requires Directly Observed Therapy

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CASE STUDY

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Case Study (Cont.)

- A 72 year old male was hospitalized June 2, 2015, due to bilateral pneumonia
- CXR from June 5, 2015, showed the right and left lower lobe infiltrates and small bilateral pleural effusions compared to the August 24, 2014, radiologists impression – bilateral lower lobe pneumonia

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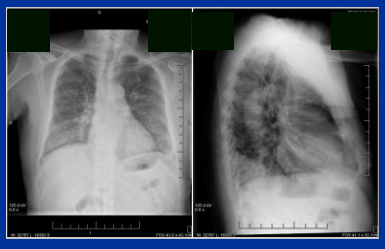
Case Study (Cont.)

- CXR August 24, 2014



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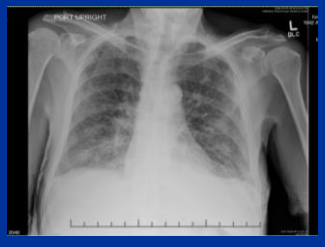
Case Study(Cont.)

- CXR June 5, 2015



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Case Study (Cont.)

- AFB smears were negative x 3
- Patient had a history of being treated for *Mycobacterium avium* in 2012
- Patient was discharged to a skilled nursing facility (SNF) on June 10, 2015 without Public Health approval

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Case Study (Cont.)

- Patient was discharged from SNF to home on June 16, 2015
- Post Hospital Course:
  - AFB culture reported out positive for MTB – pan sensitive on August 15, 2015
  - Started on anti-TB medications by DOPH on August 22, 2015 (INH, RFB, EMB, PZA – B6)
  - Patient received 9 months of TB meds by Directly Observed Therapy (DOT)
  - AFB Culture was still positive after 2 months of RIPE

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Case Study (Cont.)

- TB exposures:
  - PMD office – 10 contacts
  - Hospital – 100 contacts
  - Skilled nursing facility – 15 contacts

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Summary

- Although progress is being made, TB continues to be a significant Public Health concern
- The Pathway to preventing TB and moving us towards TB elimination must include treatment of individuals with latent TB infection
- Collaboration between public health, hospitals, and healthcare providers is essential for the protection of the community

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QUESTIONS?

TB free
CALIFORNIA

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THANK YOU!

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