



## Tuberculosis: Ancient Disease, Modern Challenges

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## TB in History

- At least 7,000 years old: found in Egyptian mummies
- Scrofula (ancient Greece)
- The Great White Plague (Europe, 18<sup>th</sup>c)
- Consumption
- est. 1 Billion died from TB between 19<sup>th</sup> and early 20<sup>th</sup> centuries (WHO)

## They all had TB...

Nelson Mandela John Keats Emily Bronte Fyodor Dostoevsky Sarah Bernhardt Frederick Chopin William Kingdon Clifford Eleanor Roosevelt Albert Camus Alexander Graham Bell Abel Gance Jay Gould Niels Abel Anne, Charlotte, and Emily Bronte Cheng Man-ching Beulah Annan Tutankhamen Elizabeth Barrett Browning Franz Kafka Robert Lewis Stevenson George Orwell Vivian Leigh Simon Bolivar Henry David Thoreau Maxim Gorky Frédéric Bastiat John Reed Anton Chekhov Edgar Allan Poe Miguel Hernandez Nixau W. C. Fields Wolfgang Amadeus Mozart Anne Porden Lord Byron D. H. Lawrence Okita Saji Louis Braille John Young Ernie Kovacs Doc Holliday Immanuel Kant Frédéric Bartholai John Ruskin Voltaire Aubrey Beardsley Harry Clarke Boris Kustodiev Amedeo Modigliani Alexander Pope Thomas Wolfe Dylan Thomas Marie Bashkirtseff Paganini Eugene O'Neill Robert Burns Paul Gauguin

## Consumption: "Captain of Death"

- Dry, persistent cough, difficulty breathing, coughing blood (hemoptysis)
- Weakness, wasting, periodic fever, night sweats
- Terminal stage: "the emaciation is frightful...the lungs are hollow... the cough, known as graveyard cough, was unmistakable... pain in the joints is constant, diarrhea becomes uncontrollable... All these changes gave a ghostly and cadaverous appearance."
- Variable and unpredictable course of disease

## TB as romance

"It was the fashion to suffer from the lungs; everybody was consumptive, poets especially; it was good form to spit blood after any emotion that was at all sensational, and to die before reaching the age of thirty."  
 -- Alexandre Dumas

"I look pale . . . I should like to die of consumption – because the ladies would say 'Look at poor Byron, how interesting he looks in dying.'"  
 --Lord Byron

## The invalid's responsibility: to seek the cure

- Ocean voyages
- Fresh air, vigorous activity
- Complete rest
- Long journeys on horseback
- Farming
- Geographical cures
  - The West: Albuquerque, Pasadena, El Paso, Tucson
  - The Mountains: Adirondacks, Rockies, the Alps
  - The Seashore

## Dr. Robert Koch

- 1882: discovery of the tubercle bacillus
- 1890: discovery of tuberculin
- Koch's postulates
  1. Organism is regularly found in lesions of the disease in question
  2. Pure cultures can be grown from it
  3. When inoculated into animals, the disease can be reproduced
  4. The organism can be obtained from the infected animal

## 20<sup>th</sup> Century

### Proximity = Contagion

Evolution of TB as a disease of the poor, immigrants living in crowded conditions (tenements)



Jacob Riis, Five Cents Lodging, Bayard St, ca. 1889

### Treatment, prevention and containment

- Anti spitting laws
- Criminalizing of vagrancy
- Attempts to register
- Isolation of TB patients in sanatoriums
- TB attached to moral crusades



### Policing Poverty and Squalor



### Associations with Moral Crusades

#### Too Much Dancing Brings T. B.

**R**ECENT scientific investigations have proved that dancing must bear a part of the responsibility for the increase of tuberculosis among young people. Addiction to the terpsichorean diversion usually results in loss of sleep, which cannot be made up adequately on other nights. Insufficient rest and sleep lowers bodily resistance and gives the tuberculosis germs an easy conquest.

Daylight saving also has a hand in inflicting tuberculosis on young people, since it shortens the time permitted for sleeping. Children especially need all the rest they can get.

The rise of a public health workforce,  
and system



Public Health Nurse traversing New  
York rooftops, early 20C



Edward Livingston Trudeau  
and Saranac Lake



Cure cottage



Saranac's Rules for Healthy Conduct

Before going to bed open the windows top and bottom, except in the severest weather, and even then have one window open at least a foot. Better still is sleeping in the open.

Avoid exposure to a careless consumptive. Do not live in the same house, sleep in the same bed with someone known to be suffering with tuberculosis, or permit him to cough in your face.

No Spitting

Sleep at least eight hours each night.

The common towel must go. It is a disease spreader and in most cases against the law.

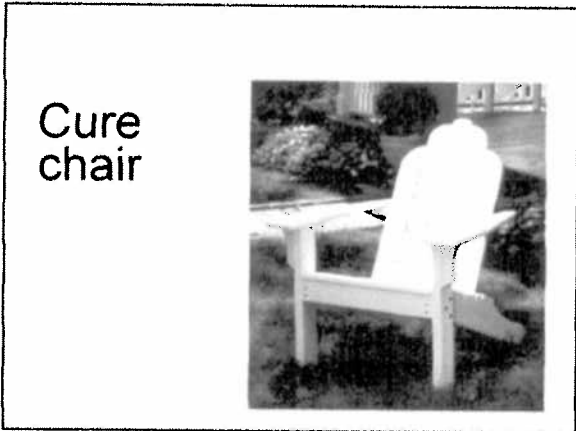
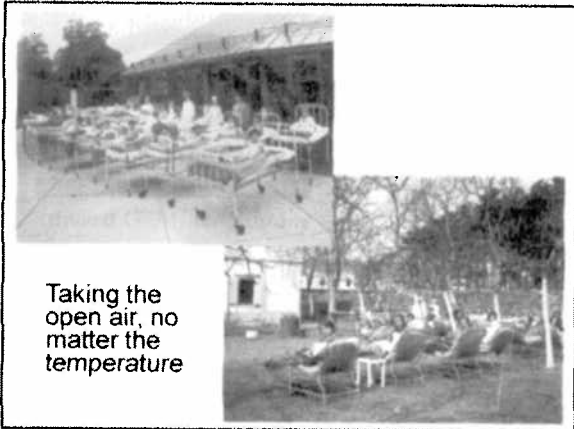
Brain workers need more exercise than those physically engaged.

I must

- keep my skin clean
- wear clean clothes
- breathe pure air,
- and live in the sunlight.

467 Onondaga Sanatorium, Hopper's Glen, Syracuse, N. Y.





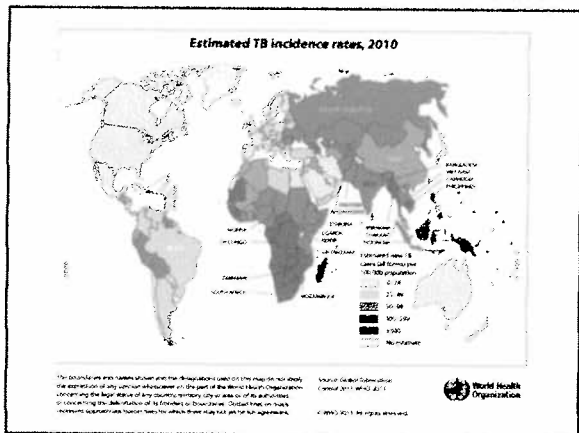
In much of the world, little has changed...

**MARCH 24 IS WORLD TUBERCULOSIS DAY. TO MARK THE OCCASION 5,000 PEOPLE ARE GOING TO DIE.**

WORLD TUBERCULOSIS DAY. This marks a century since the first description of tuberculosis, a deadly disease that has caused untold suffering. In the past 100 years, tuberculosis has become a global health crisis. It is the leading cause of death and disability in many developing countries. In 2004, an estimated 8.8 million people were living with tuberculosis, and 2.5 million died from the disease. In 2005, an estimated 9.1 million people were living with tuberculosis, and 2.6 million died from the disease. In 2006, an estimated 9.4 million people were living with tuberculosis, and 2.7 million died from the disease. In 2007, an estimated 9.7 million people were living with tuberculosis, and 2.8 million died from the disease. In 2008, an estimated 10 million people were living with tuberculosis, and 2.9 million died from the disease. In 2009, an estimated 10.3 million people were living with tuberculosis, and 3 million died from the disease. In 2010, an estimated 10.6 million people were living with tuberculosis, and 3.1 million died from the disease. In 2011, an estimated 10.9 million people were living with tuberculosis, and 3.2 million died from the disease. In 2012, an estimated 11.2 million people were living with tuberculosis, and 3.3 million died from the disease. In 2013, an estimated 11.5 million people were living with tuberculosis, and 3.4 million died from the disease. In 2014, an estimated 11.8 million people were living with tuberculosis, and 3.5 million died from the disease. In 2015, an estimated 12.1 million people were living with tuberculosis, and 3.6 million died from the disease. In 2016, an estimated 12.4 million people were living with tuberculosis, and 3.7 million died from the disease. In 2017, an estimated 12.7 million people were living with tuberculosis, and 3.8 million died from the disease. In 2018, an estimated 13 million people were living with tuberculosis, and 3.9 million died from the disease. In 2019, an estimated 13.3 million people were living with tuberculosis, and 4 million died from the disease. In 2020, an estimated 13.6 million people were living with tuberculosis, and 4.1 million died from the disease. In 2021, an estimated 13.9 million people were living with tuberculosis, and 4.2 million died from the disease. In 2022, an estimated 14.2 million people were living with tuberculosis, and 4.3 million died from the disease. In 2023, an estimated 14.5 million people were living with tuberculosis, and 4.4 million died from the disease. In 2024, an estimated 14.8 million people were living with tuberculosis, and 4.5 million died from the disease. In 2025, an estimated 15.1 million people were living with tuberculosis, and 4.6 million died from the disease. In 2026, an estimated 15.4 million people were living with tuberculosis, and 4.7 million died from the disease. In 2027, an estimated 15.7 million people were living with tuberculosis, and 4.8 million died from the disease. In 2028, an estimated 16 million people were living with tuberculosis, and 4.9 million died from the disease. In 2029, an estimated 16.3 million people were living with tuberculosis, and 5 million died from the disease. In 2030, an estimated 16.6 million people were living with tuberculosis, and 5.1 million died from the disease.

TB today

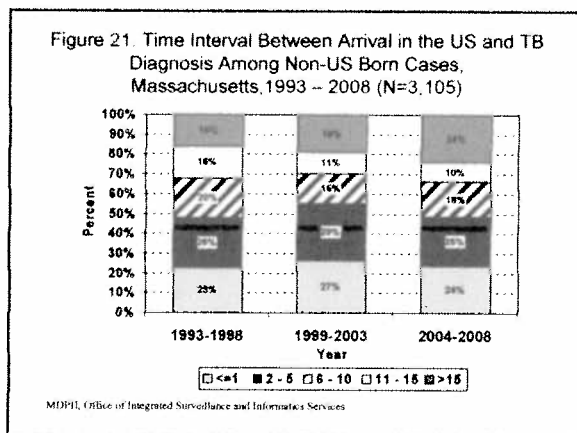
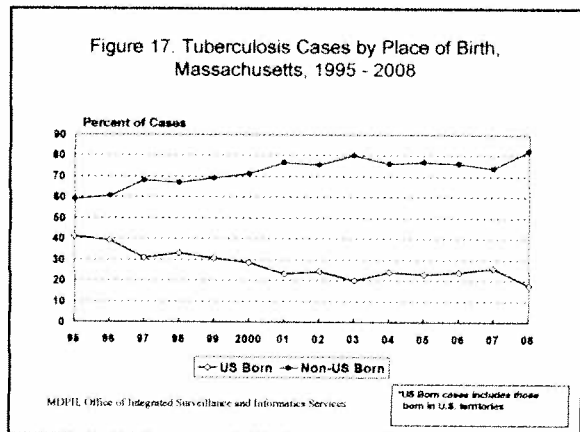
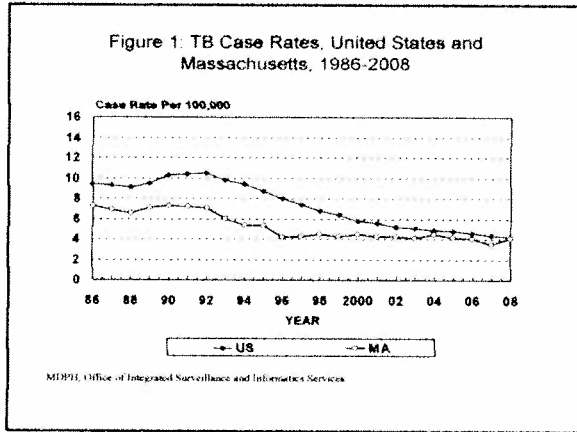
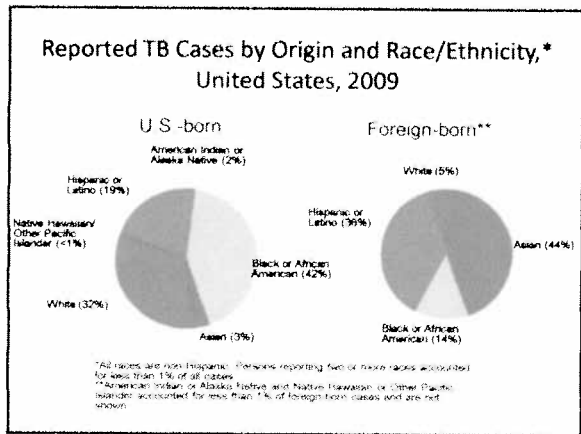
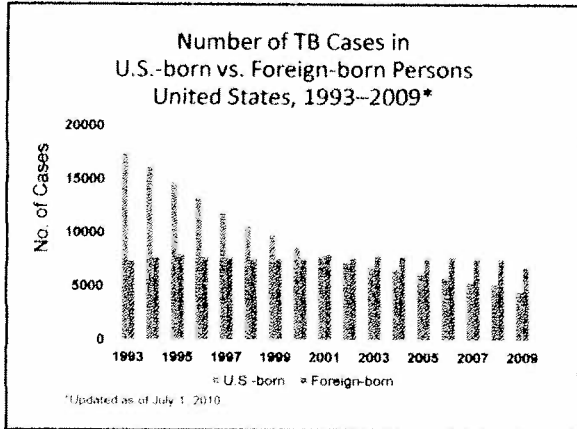
- One third of the world's population is infected with the TB bacillus
- 9M ~~new~~ new cases annually, 2M deaths
- Intersecting epidemics of poverty, war, displacement:
  - HIV, malnutrition, other infectious diseases
- Development of resistant strains *that are transmissible*
- XDR-TB among 53 HIV-infected individuals, KwaZulu-Natal, South Africa
  - 98% mortality, average 25 days from diagnosis



Have germs, will travel...  
Migrating populations in the 1990s

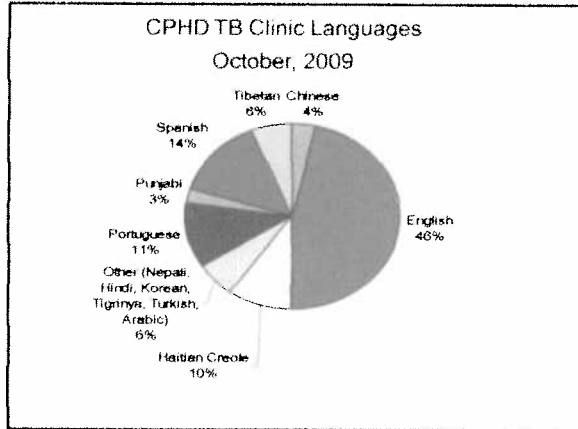
Compared to 1960-75, four-fold increase in migration

Source: Population Action International 1994



### TB Clinic population at The Cambridge Hospital

- Many new arrivals, many languages
- Half have no health insurance coverage
- Tripled from '03 - '05



## What is Tuberculosis ?

A communicable disease caused by *Mycobacterium Tuberculosis*

## Transmission of *M. tuberculosis*

- Spread by droplet nuclei
- Expelled when person with infectious TB coughs, sneezes, speaks, or sings
- Close contacts at highest risk of becoming infected
- Transmission occurs from person with infectious TB disease (not latent TB infection)

## Probability TB will be transmitted

- Infectiousness of the person with TB
- Environment in which exposure occurred
- Duration of exposure

## Pathogenesis

- Droplet nuclei inhaled, settle in alveoli where infection begins
- Spreads via bloodstream, lymph system
- The tubercle bacilli may reach any part of the body, including areas where TB disease may develop
  - Brain, larynx, lymph nodes, lungs, spine bone, kidney

## Pathogenesis

- Infection – after 2-10 weeks, immunologic response prevents further bacterial multiplication and results in a positive skin test
  - Exception - Immunocompromised people
- Most infections do not progress to clinical illness / active disease

### Pathogenesis

- Most infections do not lead to clinical illness
  - Dependent on age and Immunologic status
  - 5% will develop active disease - TB - within first 2 years
  - 5% will develop TB later in life
  - 90% will never develop active disease

### Latent TB Infection (LTBI)

- NOT INFECTIOUS
- Not considered a "Case"
- Positive skin test (PPD)
- Usually a negative chest x-ray
- No clinical symptoms of TB
- *Tubercle bacilli* controlled, remain viable, capable of producing active disease

### TB Disease

- Positive skin test (PPD) or blood test
- May have abnormal chest x-ray
- Is considered a case
- May be symptomatic
- May be capable of transmitting infection

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

- HIV Infection
- Substance Abuse
- Recent Infection
- Chest x-ray findings suggestive of previous TB
- Diabetes mellitus
- Silicosis
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy

### Conditions that Increase the Risk of Progression to TB Disease (cont.)

- Cancer of the head and neck
- Hematologic and reticuloendothelial diseases
- End-stage renal disease
- Intestinal by-pass or gastrectomy
- Chronic malabsorption syndromes
- Low body weight (>10% below ideal)

### TB Skin Testing (PPD)

TB testing is for high-risk persons rather than the general public

## Skin testing

- *purified protein derivative* (ppd) of the tubercle bacillus inserted under the skin
- Reaction means antibodies are present for TB = infection, not disease
- Size of reaction important in diagnosis, depending on risk status
- An imperfect test

## High-risk categories:

- Close contacts of a person with active TB
- People with HIV or at risk for HIV
- Foreign-born persons from areas where TB is common
- People with certain chronic medical conditions
- Medically underserved, low income populations
- IDU's and alcoholics
- Residents and employees in *congregate* settings such as homeless shelters, detoxes, etc
- Health care workers who serve high risk clients
- Children exposed to adults in high risk categories (above)

## BCG vaccine (Bacille Calmette-Guerin)

- Common in countries with high prevalence of TB
- Reported protection is 0 – 80%
- Protection wanes over time
- Not always given at birth
- Vaccine and host variability result in lack of uniform response to BCG vaccine
- PPD testing not contraindicated for people who have had BCG vaccine
- May confer a positive PPD result, but with a limited size

## Blood testing for TB

### Interferon-Gamma Release Assays (IGRAs)

- Currently in use in some areas
  - FDA approved in 2005
- The wave of the future
  - May replace skin testing
  - May become a useful tool in treatment decisions
- May be able to quantify TB infection

## TB Treatment



## 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



## Newer Drugs

Used when first-line drugs not tolerated, or when strains are resistant

- Rifabutin
- Rifapentine
- Fluoroquinolones
  - Levofloxacin
  - Moxifloxacin
  - Gatifloxacin

## Basic Principles of Treatment

- Provide safest, most effective therapy in shortest time
- Multiple drugs to which the organisms are susceptible
- Never add just one drug to a failing regimen
- Ensure adherence!



## Treatment for latent TB (LTBI)

- Three options:
  - Good: Rifampin alone for four months
  - Better: INH daily for six months
  - Optimal: INH daily, or twice weekly, for nine months
- Treatment determined by
  - Age
  - Tolerance
  - Other health conditions
  - Liver toxicity, interactions with other drugs

## Latent TB Infection (LTBI):

### Who should be treated???

- Close contacts of known active cases
- Foreign-born persons from high prevalence countries
- Abnormal chest x-ray
- Clinical conditions associated with progression to active TB (HIV, lung disease, diabetes, >15% underweight)
- Injection drug users
- Immunocompromised individuals

## LTBI Considerations



- Nine months is a long time!
  - Nine months treatment is the optimal therapy
  - If nonadherent, patient may have to repeat again and again
  - Nonadherence may lead to resistance of the TB organism
- Nursing assessment and patient education
  - LTBI treatment is an **option**, not a requirement

## Treatment of Active TB

### Initial Phase

2 months - INH, RIF, PZA, EMB daily (56 doses, within 8 weeks)

### Continuation Phase

#### Options:

- 1) 4 months - INH, RIF daily (126 doses, within 18 weeks)
- 2) 4 months - INH, RIF twice / week (36 doses, within 18 weeks)
- 3) 7 months - INH, RIF daily (217 doses, within 31 weeks)\*
- 4) 7 months - INH, RIF twice / week (62 doses, within 31 weeks)\*

\* Continuation phase increased to 7 months if initial chest x-ray shows cavitation and specimen collected at end of initial phase (2 months) is culture positive

## Drug Resistance

- Drug-resistant TB is transmitted the same way as drug-susceptible TB
- Two types of drug resistance:
  - Primary resistance develops in persons initially infected with resistant organisms
  - Secondary resistance (acquired resistance) develops during TB therapy often due to nonadherence

## Multidrug Resistant TB (MDR-TB)

- Resistant to first line drugs INH and rifampin
- Presents difficult treatment challenges
- Treatment must be individualized
- Requires expert consultation, multiple second-line drugs

## Global Drug-Resistant TB

- 2004 MDR TB estimates: 424,203 (4.3%)
- 2000 MDR TB estimates: 272,906 (1.1%)
- Estimated 43% of global MDR TB cases have had prior treatment
- China, India, and Russian Federation account for 62% of the MDR burden

*Prevalence of XDR TB not known*

## Extensively-Drug Resistant TB (XDR-TB)

Resistant to

- INH and rifampin
- AND
- Any fluoroquinolone
- AND
- At least one of three injectable second line drugs (amikacin, kanamycin, or capreomycin)

## Massachusetts Department of Public Health Division of TB Prevention and Control

- Active TB must be reported within 24 hours
- Positive skin tests are reportable
- Public Health laws
- Tuberculosis Treatment Unit (TTU) at Shattuck Hospital

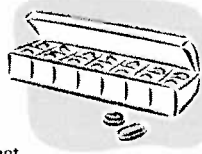
## Public Health Nurses...



- Case finding
- Clinical assessment
- Case management
- Directly observed therapy

## Case management: Active TB

- Coordinate Directly Observed Therapy with local PHNs
- Home visits
- Monthly TB clinic visits for
  - Education and health teaching
  - Medication evaluation and dosing
  - Symptom evaluation and management
  - Lab testing
- Coordinate care for other health concerns (HIV, diabetes, etc)



## Directly Observed Therapy (DOT)

- Health care worker watches patient swallow each dose of medication
- DOT is the standard of care for all active cases
- DOT can lead to reductions in relapse and acquired drug resistance
- Use DOT with other measures to promote adherence



## If a case refuses treatment...



- “Menace” law
  - Mass General Laws Chapter 111, sec. 94B – 94F
  - Allows for forcible hospitalization
- Shattuck Hospital Tuberculosis Treatment Unit

## Isolation and Quarantine

### Isolation:

The voluntary or involuntary confinement of a person with a contagious disease, so that others don't get it.

### Quarantine:

The voluntary or involuntary confinement of a person who has been exposed to a contagious disease, for the period of time that they may come down with it and may be infectious themselves.

## In conclusion...

- TB prevention and containment is well understood
- TB Medications work
  - TB treatment, when followed, is effective in eliminating TB
  - TB treatment is free to anyone
- Why is TB still with us?