TUBERCULOSIS FOR THE INFECTION CONTROL PROFESSIONAL

Alawode Oladele, MD, MPH
One person dies of TB every 20 seconds. TB is preventable and curable.
• One third of the world’s population is infected with TB.

• Nearly 9.6 million people around the world became sick with TB disease.

• Almost 1.5 million TB-related deaths worldwide.

• TB is a leading killer of people who are HIV infected (0.4 million out of 1.2 million HIV deaths).
• TB has been known as Pthisis, King’s Evil, Pott’s disease, consumption, and the White Plague.

• Egyptian mummies from 3500 BCE have the presence of *Mycobacterium tuberculosis*
On March 24, 1882, Dr. Robert Koch announced the discovery of *Mycobacterium tuberculosis*. His discoveries ushered in a ‘golden age’ of scientific discovery and a new era of public health. Koch's studies inspired a generation of scientists. In the span of just 30 years – from 1876 to 1906 –

- Anthrax;
- Tuberculosis;
- Cholera;
The New World

Infected the New World before the Europeans

After more than a century of debate, it is now firmly established that tuberculosis existed in the New World before the arrival of Columbus. What is not yet known is how or when, exactly, the infection reached the Americas.

10% deaths in the 19th century were due to TB
Development of Sanatoriums:

In 1854, Hermann Brehmer proposed the idea that tuberculosis was indeed a curable disease.
Sanatoriums in the United States tried to simulate that environment by providing the following:

- Fresh Air
- Large amounts of food
- Lots of milk
- Sleep
- Exercise
1890: Pneumothorax treatments: Artificial pneumothorax: The infected lung was collapsed and filled with gas or filtered air.

Treatments were daily for 3 to 4 years after the initial treatment.

Discontinued after 1946 because it proved little benefit.
PNEUMOTHORAX
for thinking folks:

TUBERCULOSIS

No two cases of tuberculosis are exactly alike. These diagrams show only in a general way what happens to the sick lung when pneumothorax treatment is applied.

- From 15 to 45 the leading cause of death
- A communicable—NOT an inherited disease
- Every case comes from another
- Caused by germs
- Can be prevented
- Can be cured
- One may have it without knowing it

Diagram showing how pneumothorax apparatus works. Water flows from bottle A to bottle B which dispenses air into rubber tube and then into the chest. Before the air is allowed to flow, pressure is measured at C. There is a three-way valve at C so that air passage can be directed to supporting gauge or needle.

1. Healthy right lung. Tuberculosis of upper part of left lung with a large hole or cavity. Root of hollow Faculty in between the two layers of the pleura.

2. Lung partially collapsed. Cavity not entirely closed.


4. Lung is held flat in chest wall by acting of suction, thus preventing collapse of cavity.

5. Lung has burst and has again expanded. Only a star of the cavity remains.
Other surgical procedures employed included:

• phrenic nerve crush,
• thoracoplasty,
• pneumoperitoneum,
• Monaldi drainage,

• Pneumonolysis - also known as plombage therapy. Plombage is derived from the French word “plombe,” literally meaning lead, but it refers to placing any inert object against the lung to collapse the underlying cavity.
Posteroanterior chest radiograph of a 78-year-old man with a history of benign prostatic hypertrophy and diverticulosis.
Lucite balls for plombage therapy, used until the 1950s, on display at the former Battey State Tuberculosis Hospital in Rome, Georgia.
“How the battle against TB was won ... and almost lost.”
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1944-</td>
<td>Streptomycin first administered to human patient</td>
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<tr>
<td>1947-</td>
<td><em>Mycobacterium tuberculosis</em> shows resistance to streptomycin.</td>
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<tr>
<td>1949-</td>
<td>p-aminosalicylic acid (PAS)</td>
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<tr>
<td>1951-</td>
<td>A new drug, <strong>Isoniazid</strong> (INH) is created.</td>
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<tr>
<td>1954-</td>
<td>Pyrazinamide is created.</td>
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<tr>
<td>1955-</td>
<td>Cycloserine is produced.</td>
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<tr>
<td>1962-</td>
<td>Ethambutol is created.</td>
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<tr>
<td>1963-</td>
<td>Rifampicin</td>
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1960s  Combination treatment
1970s  Near eradication?
1981  HIV
1998  DNA code of Mtb genome
2005  Improved diagnostic test (FDA)
2006  XDR outbreak South Africa
2013  Sirturo, known chemically as bedaquiline
       MDR treatment
Today  1/3 of the world infected
       (>2 billion people)
TB Drug Development Timeline

- **1880s**: Mycobacterium tuberculosis discovered by Robert Koch as cause of consumption
- **1920s**: Large-scale BCG immunization
- **1940s**: The first human trials of the vaccine Bacille Calmette Guérin (BCG), an attenuated version of *Mycobacterium bovis* (bovine TB)
- **1950s**: Introduction of TB drug regimens
- **1960s**: First outbreak of drug-resistant TB in US
- **1970s**: WHO declares TB a global emergency
- **1980s**: MDR
- **1990s**: DOTS
- **2000s**: XDR
- **2010s**: Beyond

Key Drugs and Inhibitors:
- Kanamycin
- Cycloserine
- Ethionamide
- Ethambutol
- Capreomycin
- Rifampin
- Rifamycin
- Moxifloxacin
- Gatifloxacin
- SQ109
- Linezolid
- AZD5847
- Nitroimidazoles
- New-generation diarylquinolines
- Mycobacterial gyrase inhibitors
- Bi-functional molecules
- InhA inhibitors
- MTB protein kinase inhibitors
- DNA metabolism
- MTB vaccine
## Evolution of new TB technologies in the last five years

<table>
<thead>
<tr>
<th>Year</th>
<th>Technology</th>
<th>Turnaround time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 2007</td>
<td>Solid Culture DST (Phenotyping) (1st &amp; 2nd line)</td>
<td>30-60 days</td>
</tr>
<tr>
<td>2007</td>
<td>Liquid Culture DST (Phenotyping) (1st / 2nd line)</td>
<td>15-30 days</td>
</tr>
<tr>
<td>2008</td>
<td>Line Probe Assay (Genotyping) (1st line, Rif &amp; INH)</td>
<td>2 days</td>
</tr>
<tr>
<td>2010</td>
<td>Genotyping second generation (1st line, Rif &amp; INH)</td>
<td>90 minutes</td>
</tr>
</tbody>
</table>
Reported Tuberculosis (TB Disease) Cases
United States, 1982–2015
Reported Tuberculosis (TB Disease) Cases
United States, 1982–2015

9,563 TB cases in 2015
(Rate 3.0/100,000)
Increase in number of TB cases in 2015

For the first time since 1992, the annual number of reported TB cases in the US increased from the previous year.

Twenty-nine states and the District of Columbia (DC) reported an increase in TB cases in 2015.

Overall TB rate has remained at 3.0 cases per 100,000 persons for 2013, 2014, and 2015.

Leveling of TB might represent the limits of what is achievable at present, or it might represent the beginning of another national TB resurgence.
What makes a plateau?

During the past 3 years, no substantial decline occurred in the number of TB cases in the US.

For the first time since 1992, the number of TB cases in the U.S. increased from the previous year.

Two thirds of the total U.S. TB burden is associated with foreign birth -- most likely representing reactivation of LTBI that was acquired outside of U.S.

Among the U.S.-born, ongoing TB transmission continues to be a problem.

Possibly this is the lowest level of TB in the U.S. that can be achieved at present.
Rate of TB Cases*, By State – United States, 2014

*Cases per 100,000.
Number and rate* of newly diagnosed tuberculosis (TB) cases among U.S.-born and foreign-born persons, by year reported — United States, 2000–2014†

• * Per 100,000 population.
• † Data updated as of February 13, 2015. Data for 2014 are provisional.
TB Cases and Case Rates Georgia, 1984-2014

*63% drop in number of cases between 1991 and 2014!

**322 in 2015
Figure 2. TB Case Rates
Georgia and U.S., 1984-2014
Number of TB Cases by Health Districts
Georgia, 2014

Number of TB Cases:
- Low incidence: 1-10
- Medium incidence: 11-20
- High incidence: >20 (25-76)
TB Case Rates by Health Districts
Georgia, 2014

Case rates/100,000 population:
- <= 3.3 (State Average)
- > 3.3 (State Average)
High TB Incidence Counties
Georgia - 2015

Number of TB Cases:
- >= 15 cases: Cobb (34), Gwinnett (57), DeKalb (64)
- < 15 cases: Fulton (26)
Together We Can!