The Epidemiology of Tuberculosis

William Clapp, MD

September 25, 2007
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William Clapp MD
Heartland National TB Center
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TB Take Home Points

• TB is a really bad problem in the world
• TB is the gasoline, the human body is the oxygen, HIV is the match
• TB in the US is beginning to look like the rest of the world
• Modern TB control programs are like fire departments and work really well if given adequate resources
Mycobacterial Isolations in Captive Elephants in the United States

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ABSTRACT: Interest in tuberculosis in elephants has been increasing over the past several years in the United States. Several techniques have been used to diagnose mammalian tuberculosis. Currently, the test considered most reliable for diagnosis of TB in elephants is based on the culture of respiratory secretions obtained by trunk washes.

2002 Ann N.Y. Acad Sci 969: 256-258

Mycobacterium tuberculosis Complex DNA from an Extinct Bison Dated 17,000 Years before the Present

Bruce M. Rothschild,1,2,4 Larry D. Martin,1 Galit Lev,1 Helen Bercovier,1 Gila Kahila Bar-Gal,1 Charles Greenblatt,1 Helen Donoghue,1 Mark Spigelman,1 and David Brittain1

Clin Inf Dis 2001;33: 305-11
Epidemiology of Tuberculosis

Spinal TB Neolithic Man: 3000-7000 B.C.E.

Egyptian art and mummies
• 400 BC: Hippocrates – honey, barley gruel, wine, herbs from the gardens of healing temples

• China – pith balls soaked in the blood of executed criminals

Epidemiology of Tuberculosis

The White Plague

• Medieval Europe: Royal Touching (1056: Edward the Confessor)

• 17th – 18th Century: Louis the XIV
The White Plague

- 17th-19th centuries – swept Europe – the “White Plague” (mortality as high as 1200/100,000)

- Mid 17th century 1/5 of all London deaths due to TB

TB History

- 18th century: John Wesley: advocated fresh human milk

- 19th century Europe: “A living trout was attached to the sufferer’s chest, a fresh catskin was wound round the body, a piece of meat moistened with the sufferer’s urine was fed to a dog”

- 20th century Japan – potassium cyanide plus copper-cyanurate
Sanatorium Movement

1859 - Sanatoria – Fresh Air, Rest, Nutrition

1942 - 97,720 TB sanatorium beds in U.S.

TB History

1822 Collapse Therapy – pneumothorax, pneumoperitoneum, plomage, thoracoplasty
TB History

• March 1882 – Robert Koch demonstrates (in the presence of Rudolph Virchow and Paul Ehrlich) that TB is caused by a microorganism (fulfilled “Koch's Postulates”)
• Developed Tuberculin as TB cure

Selman Wakesman/Albert Schatz 1943
Streptomycin
TB History

Jorgen Lehman: Para-Amino Salaslyc Acid (PAS) 1943

PAS (Para-Amino Salacylic Acid)

Salicylic Acid
(2-hydroxybenzoic acid)

Para-Amino Salicylic Acid
(4-amino-2-hydroxybenzoic acid)
Epidemiology of Tuberculosis

TB History

Gerhard Domagk

- Sulphonamides
- Thiosemicarbazone (Thiacetazone) 1943-44

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Tuberculosis Death Rates 1800-1940

Deaths per 100,000

- Massachusetts
- New York, Boston, Philadelphia
- England and Wales

Years
1800 1820 1840 1860 1880 1900 1920 1940

Deaths per 100,000
Epidemiology of Tuberculosis

Tuberculosis Rates in New York City

Factors Contributing to the Increase in TB Morbidity: 1985-1992

- Deterioration of the TB public health infrastructure
- Immigration from countries where TB is common
- HIV/AIDS epidemic
Deterioration of the TB Control Infrastructure

- 1968 NYC – 21 TB clinics and 1000 beds dedicated to TB
- NYC TB budget cut by 95% between 1968 and 1978
- Case rates began to rise in the 1980s
- NYC 1980-1990: 12,000 excess TB cases with incidence of 50/100,000

Deterioration of the TB Control Infrastructure - NYC

- 1998 Harlem Hospital
- 224 consecutive patients admitted with TB
- 178 discharged while still on treatment
- 89% lost to follow-up and felt not to have completed Rx
- 48 of these re-admitted with active TB, 40 of these discharged and 35 lost again

Deterioration of the TB Public Health Infrastructure

• “…after several years of decreasing federal support, in 1972 categorical federal funding (U.S.) for tuberculosis control was eliminated entirely.”

• 1989 World Health Organization budget for tuberculosis control was $2.5 million with a staff of only two professionals

Directly Observed Therapy (DOT)

"I cannot so properly say that he died of one disease, for there were many that had consented, and laid their heads together to bring him to his end. He was dropsical, he was consumptive, he was surfeited, was gouty, and, as some say, he had a tang of the Pox in his bowels. Yet the captain of all these men of death that came against him to take him away, was the Consumption, for 'twas that that brought him down to the grave."
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The captain of these men of death

- 2 billion infected (LTBI)
- 1 billion deaths in 19th and 20th centuries (Ryan)
- 8.8 million new active cases 2005 (3.9 million sputum smear+)*
- Case rate planet Earth 2005 ; 136/100,000
- 14, 602,353 people with active TB;* (90% in developing nations)
- 1.6 million deaths 2005 (24/100,000) (75% ages 15 and 45)
- TB is the most common cause of death due to a single infectious agent

*Kaiser Family Foundation 6-06: http://www.globalhealthfacts.org/

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Tuberculosis: Planet Earth

- TB accounts for ¼ of all preventable deaths in the developing world
- Kills 13-50% of people who die with HIV
- “TB is the most pervasive and lethal epidemic in all of human history” (Iseman)

*Kaiser Family Foundation 6-06: http://www.globalhealthfacts.org/
Epidemiology of Tuberculosis

Estimated TB incidence rate, 2005

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Leading Causes of Death: Planet Earth 2002

WHO 2004
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Leading Infectious Causes of Death: Planet Earth 2002

Disability Adjusted Life Years (DALYs) Lost to Infectious Diseases 2002
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TB Cases United States 1997-2006

Rate* of tuberculosis cases, by state – United States, 2006†

*Cases per 100,000.
†Data provisional.
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Rate of TB in the United States, 1993-2006

![Graph showing the rate of TB in the United States from 1993 to 2006. The rate decreased over time, from approximately 8.0 cases per 100,000 population in 1993 to 2.5 cases per 100,000 population in 2006. The graph includes two lines, one for U.S.-born persons and one for foreign-born persons. The declines for both groups are statistically significant.]

Number of TB Cases in U.S.-born vs. Foreign-born Persons
United States, 1993–2006*

![Bar chart showing the number of TB cases in U.S.-born and foreign-born persons from 1994 to 2006. The chart indicates a decrease in the number of cases for both groups over the study period.]

*Updated as of April 6, 2007.
Epidemiology of Tuberculosis

Percentage of TB Cases Among Foreign-born Persons, United States*

<table>
<thead>
<tr>
<th>Year</th>
<th>&gt;=50%</th>
<th>25%-49%</th>
<th>&lt;25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Updated as of April 6, 2007.

Countries of Birth of Foreign-born Persons Reported with TB
United States, 2006

- Mexico (25%)
- Philippines (11%)
- Viet Nam (8%)
- India (7%)
- China (5%)
- Haiti (3%)
- Guatemala (3%)
- Other Countries (38%)
**TB Case Rates* by Age Group**

*United States, 1993–2006*

- <15 yrs: 20 cases per 100,000
- 15–24 yrs: 15 cases per 100,000
- 25–44 yrs: 10 cases per 100,000
- 45–64 yrs: 5 cases per 100,000
- >65 yrs: 2 cases per 100,000

*Updated as of April 6, 2007.

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**Reported TB Cases by Age Group, United States, 2006**

- <15 yrs: 6% (19 cases)
- 15–24 yrs: 11% (34 cases)
- 25–44 yrs: 34% (22 cases)
- 45–64 yrs: 29% (20 cases)
- >65 yrs: 19% (6 cases)
TB Case Rates by Age Group and Sex, United States, 2006

Epidemiology of Tuberculosis

TB Case Rates by Race/Ethnicity* United States: 1993–2006**

*All races are non-Hispanic. In 2003, Asian/Pacific Islander category includes persons who reported race as Asian only and/or Native Hawaiian or Other Pacific Islander only.

**Updated as of April 6, 2007.
Reported TB Cases by Race/Ethnicity*
United States, 2006

- American Indian or Alaska Native (1%)
- White (17%)
- Asian (24%)
- Black or African-American (27%)
- Native Hawaiian or Other Pacific Islander (<1%)
- Hispanic or Latino (30%)

*All races are non-Hispanic. Persons reporting two or more races accounted for less than 1% of all cases.
Heartland National TB Center 2006

<table>
<thead>
<tr>
<th>State</th>
<th>Cases</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Texas</td>
<td>1585</td>
<td>6.7</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>144</td>
<td>4.0</td>
</tr>
<tr>
<td>Arizona</td>
<td>311</td>
<td>5.0</td>
</tr>
<tr>
<td>Illinois</td>
<td>569</td>
<td>4.4</td>
</tr>
<tr>
<td>Minnesota</td>
<td>217</td>
<td>4.2</td>
</tr>
<tr>
<td>Kansas</td>
<td>81</td>
<td>2.9</td>
</tr>
<tr>
<td>Missouri</td>
<td>104</td>
<td>1.8</td>
</tr>
<tr>
<td>Nebraska</td>
<td>25</td>
<td>1.4</td>
</tr>
<tr>
<td>New Mexico</td>
<td>48</td>
<td>2.5</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>75</td>
<td>1.3</td>
</tr>
<tr>
<td>Iowa</td>
<td>40</td>
<td>1.3</td>
</tr>
<tr>
<td>South Dakota</td>
<td>14</td>
<td>1.8</td>
</tr>
<tr>
<td>North Dakota</td>
<td>9</td>
<td>1.4</td>
</tr>
</tbody>
</table>

TB Cases
Illinois, 1980-2004

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>1653</td>
<td>1270</td>
<td>596</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Epidemiology of Tuberculosis


- Born USA
- Foreign Born

TB Cases by Race/Ethnicity
Chicago, 1993-2006

- Black Only
- White Only
- Hispanic
- Asian/PI
- Native American Only
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Reported TB Cases by Origin and Race/Ethnicity, Chicago, 2006

U.S.-born*  
(N = 160)

- Asian: 4%
- NH/PI: 0%
- Multiple Race: 0%
- White: 11%
- Black: 72%

Foreign-born**  
(N = 132)

- Asian: 35%
- NH/PI: 0%
- Multiple Race: 0%
- White: 9%
- Black: 12%
- Hispanic: 44%

Selected Risk Factors Associated with Tuberculosis, Chicago, 2006

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No. of Cases</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injecting Drug Use</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Non-Injecting Drug Use</td>
<td>35</td>
<td>12</td>
</tr>
<tr>
<td>Excess Alcohol Use</td>
<td>54</td>
<td>18</td>
</tr>
<tr>
<td>Any Substance Abuse</td>
<td>74</td>
<td>25</td>
</tr>
<tr>
<td>Homeless</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Correctional Facility at Diagnosis</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Long-Term Care at Diagnosis</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>
Global TB/HIV

- TB kills up to half of all AIDS patients worldwide
- HIV is the greatest risk factor for progression from latent to active TB (50% without proper treatment)
- Approximately 90% of those living with HIV die within months of developing active TB.
- The majority of people who are co-infected with both diseases live in sub-Saharan Africa.

[http://www.who.int/tb/hiv/faq/en/]
38.6 million people [range: 33.4-46.0 million] living with HIV in 2005

TB incidence closely correlated with HIV prevalence in Africa

HIV prevalence, adults 15-49y

Estimated TB incidence (per 100,000 population)
Fifteen Countries with Highest TB Incidence with Corresponding HIV Co-Infection Rates 2005

Geographical Distribution of HIV-Positive TB Cases 2005
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Estimated HIV Prevalence: Newly Diagnosed TB Cases 2005


Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group.

*Updated as of April 6, 2007.
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Estimated HIV Coinfection in Persons Reported with TB, Chicago, 1993-2006

No. of Total Cases → % HIV Infected

Year

1993 1995 1997 1999 2001 2003 2005

% of HIV Infected

0.0% 5.0% 10.0% 15.0% 20.0% 25.0%

No. of Cases

0 100 200 300 400 500 600 700 800 900

Global Burden of TB Resistant to INH and Rifamycins (MDR TB)

<table>
<thead>
<tr>
<th>Region</th>
<th>TB cases</th>
<th>MDR</th>
<th>%</th>
<th>No of cases with prior rx</th>
<th>% total cases with prior rx</th>
<th>MDR (pror rx)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Europe</td>
<td>51,709</td>
<td>1,462</td>
<td>2.8</td>
<td>8,059</td>
<td>15.6</td>
<td>679</td>
<td>8.4</td>
</tr>
<tr>
<td>Established Market Economies (Western Europe)</td>
<td>113,010</td>
<td>1,681</td>
<td>1.5</td>
<td>5,764</td>
<td>5.1</td>
<td>636</td>
<td>11.0</td>
</tr>
<tr>
<td>Latin America</td>
<td>396,158</td>
<td>11,301</td>
<td>2.9</td>
<td>38,944</td>
<td>10.1</td>
<td>4,770</td>
<td>12.2</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>428,662</td>
<td>65,853</td>
<td>15.4</td>
<td>78,190</td>
<td>18.2</td>
<td>31,208</td>
<td>30.9</td>
</tr>
<tr>
<td>Africa, Low HIV Prevalence (North Africa)</td>
<td>519,306</td>
<td>10,449</td>
<td>2.0</td>
<td>29,999</td>
<td>5.8</td>
<td>2,910</td>
<td>9.7</td>
</tr>
<tr>
<td>Eastern Mediterranean Region (Middle East)</td>
<td>555,284</td>
<td>18,330</td>
<td>3.3</td>
<td>27,242</td>
<td>4.9</td>
<td>8,017</td>
<td>29.4</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>2,169,855</td>
<td>152,018</td>
<td>7.0</td>
<td>285,618</td>
<td>13.2</td>
<td>72,697</td>
<td>25.5</td>
</tr>
<tr>
<td>Africa, High HIV Prevalence (Sub-Saharan Africa)</td>
<td>2,356,175</td>
<td>48,141</td>
<td>2.0</td>
<td>175,928</td>
<td>7.5</td>
<td>11,019</td>
<td>6.3</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>3,300,224</td>
<td>114,967</td>
<td>3.5</td>
<td>332,896</td>
<td>10.1</td>
<td>49,473</td>
<td>14.9</td>
</tr>
<tr>
<td>All Countries (n = 184)</td>
<td>9,880,383</td>
<td>424,202</td>
<td>4.3</td>
<td>982,640</td>
<td>9.9</td>
<td>181,409</td>
<td>18.5</td>
</tr>
</tbody>
</table>

Zignol, 2006. JID 194:479-85
Distribution of Multidrug-Resistant Tuberculosis Rates Among New Cases

Distribution of Multidrug-Resistant Tuberculosis Rates Among Previously Treated Cases

*Updated as of April 6, 2007.

Note: Based on initial isolates from persons with no prior history of TB.

Primary MDR TB
United States, 1993–2005*

*Updated as of March 29, 2006.

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
### Epidemiology of Tuberculosis

#### MDR TB*: 2004-2005 United States

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2005†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=11,132)</td>
<td>(n=10,662)</td>
</tr>
<tr>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>MDR Cases</td>
<td>129 (1.2)</td>
<td>124 (1.2)</td>
</tr>
<tr>
<td>US born</td>
<td>31 (24.0)</td>
<td>22 (17.7)</td>
</tr>
<tr>
<td>Foreign born</td>
<td>98 (76.0)</td>
<td>101 (81.5)</td>
</tr>
</tbody>
</table>

* Denominators based on culture confirmed cases with ISUS to INH and RIF
† Missing origin of birth for one MDR case in 2005
§ 2005 is the latest year with complete drug susceptibility test results

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### Epidemiology of Tuberculosis

#### Tuberculosis Cases by Drug Susceptibility Patterns and Place of Birth: Chicago, 2006

<table>
<thead>
<tr>
<th>Place of Birth</th>
<th>Cases with Susceptibility Results¹</th>
<th>Any Drug Resistance (No. (%)²)</th>
<th>INH – Resistant No. (%)³</th>
<th>MDR – TB No. (%)⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign-Born Cases</td>
<td>89</td>
<td>13 (15%)</td>
<td>10 (11%)</td>
<td>0</td>
</tr>
<tr>
<td>U.S.-Born Cases</td>
<td>123</td>
<td>9 (7%)</td>
<td>8 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>212</td>
<td>22 (10%)</td>
<td>18 (9%)</td>
<td>0</td>
</tr>
</tbody>
</table>

¹Culture-confirmed cases with drug susceptibility results available
²Resistance to one first-line anti-TB drug (i.e., INH, PZA, or SM)
³INH mono-resistant cases, including high (N=8, 4%) and low-level (N=10, 5%) resistance
⁴Multi-drug resistant TB cases, with resistant to at least INH and rifampin
Global WHO/IUATLD/CDC Survey

- Convenience sample (17,690 isolates) submitted to participating international SRL network, 2000-2004
  - 3520 (20%) of isolates MDR TB
  - 347 (2%) of isolates XDR TB

- XDR TB in all regions, more common in FSU and Asia (Republic of Korea)

- Denominator information unavailable
Church of Scotland Hospital, Tugela Ferry, 
KwaZulu-Natal Province, South Africa

- 53 of 544 patients defined as XDR-TB cases
- 52 of the 53 patients died on average within 25 days, including those on antiretroviral therapy
- Further investigations being carried out
- XDR-TB likely in bordering African countries

Given the underlying HIV epidemic in Africa, drug-resistant TB could have a major impact on mortality and requires urgent action on care and prevention

Epidemiology of Tuberculosis

Survival after sputum collection in patients with XDR tuberculosis with confirmed dates of death (n=42)

Lancet 2006; 368: 1575-80
Epidemiology of Tuberculosis

XDR TB in the United States 1993-2006

- 49 XDR TB cases from 9 states
- 19 cases from NYC, 11 cases from CA
- 16/29 (55%) HIV (+)
  - 1993-1999: 14/19 (74%) HIV (+)
  - 2000-2006: 2/10 (20%) HIV (+)
- Foreign born
  - 1993-1999: 12/32 (39%)
  - 2000-2006: 13/17 (76%)

MMWR 2007;56:250-53
XDR TB Cases Reported to CDC (N=47)
United States, 1993–2005*

*Updated as of November 28, 2006.

Epidemiology of Tuberculosis

XDR TB in the United States
1993-2006: Outcomes

- 41 with known outcomes
- 12 (29%) died, 10 HIV (+), 2 HIV status unknown
- 17 completed treatment
- 8 outcome not yet reported

MMWR 2007;56:250-53

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**Epidemiology of Tuberculosis**

**XDR TB in the United States**

- Probably relatively little acquired MDR and XDR TB in the U.S.
- Major source of MDR and XDR TB patients foreign-born patients (33% Hispanic)
- Suspicion of drug resistance paramount
- May be difficult to devise initial empiric regimens

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**TB Celebrity Quiz**
Epidemiology of Tuberculosis

Amadeo Modigliani 1884-1920

Epidemiology of Tuberculosis

Carlos Santana  July 20, 1947 -
Epidemiology of Tuberculosis

Bud Powell  1924-1966

Judy Collins  May 1, 1939 -
Epidemiology of Tuberculosis

Eleanor Roosevelt October 11, 1884 – November 7, 1962

Nelson Mandela 1936-
“We cannot win the battle against AIDS if we do not also fight TB. TB is too often a death sentence for people with AIDS. It does not have to be this way. We have known how to cure TB for more than fifty years. What we have lacked is the will and the resources to quickly diagnose people with TB and get them the treatment they need. The world has made the defeat of AIDS its top priority. This is a blessing, but TB remains ignored. Today, we are calling on the world to recognise that we can't fight AIDS unless we do much more to fight TB as well.”

Nelson Mandela, Bangkok 2004
**Mycobacterium tuberculosis Complex**

- *Mycobacterium bovis*
- *Mycobacterium microti*
- *Mycobacterium africanum*
- *Mycobacterium tuberculosis*