Epidemiology of Tuberculosis
Denver TB Course

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Disclosure

- No financial disclosures
- Slides adapted from Dr Randall Reves
Global TB

10.4 million new TB
~ 1 million children

1.8 million deaths

Estimated number of deaths from HIV/AIDS and TB in 2015. Deaths from TB among HIV-positive people are shown in grey.\textsuperscript{a,b}
**FIG. 3.5**

Global trends in the estimated number of incident TB cases and the number of TB deaths (in millions), 2000–2015. Shaded areas represent uncertainty intervals.
Main methods used to estimate TB incidence

- Case notifications, expert opinion
- Prevalence survey
- Case notifications, standard adjustment
- Capture-recapture
- No data
- Not applicable

WHO Global TB Report 2016
Epidemiology of Tuberculosis

- TB epidemiology - a complex, 2-stage process
  - transmission and infection
  - progression from latent TB infection (LTBI) to disease
  - risk factors differ for each stage

- Other risk factors associated with case-fatality rates
  - Differences in population TB mortality rates reflect the first two stages plus differences in case-fatality rates.

Risk Factors for TB Infection ("PPD Positive")

The risk of TB infection in a population related to

- Number of infectious TB cases
- Duration of infectiousness
- Each smear + case infects an mean of 10 people/yr
- Early TB screening studies found 9 prevalent active cases for each annual TB death

Comstock GW Public Health Rep 1980;95:444
Risk factors for TB infection ("PPD positive")

Effective TB control decreased infection rates in Eskimo children age 7-8 years: combination of effective treatment of TB & LTBI

- 92% PPD+ in 1949-51
- 2% PPD+ in 1969-70

Risk factors for TB infection ("PPD positive")

Estimating annual rates of TB infection (ARI or ARTI): untreated pop.

- Calculation from repeated annual TST surveys, or
- Estimated using the “Styblo rule” with assumptions that:
  - Mortality is 50% for individuals with incident smear+ TB cases
  - Prevalent cases are 2X the incidence (duration 2 years)
- The estimate: 1% ARI associated with 50-60 sm+ cases per $10^5$ per yr
- Range for 22 high-burden countries, est. 2011: TB rates/$10^5$ and ARI with Styblo rule

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence</th>
<th>Prevalence (Sm+)</th>
<th>ARI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>42</td>
<td>46 (56%, 23)</td>
<td>0.5%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>424</td>
<td>817 (41%, 335)</td>
<td>7.0%</td>
</tr>
</tbody>
</table>

Risk Factors for Infection: Major Contributors

- Exposure
  - close contacts of new cases - 28% infected

- US LTBI prevalence ‘71-2 & ‘99-00 (age 25-74 yrs):
  - Overall 14.4% → 5.6% - 61% decrease
    - US-born: 12.6 → 2.5% - 80% decrease
    - Foreign-born: 35.9% → 21.3% - 41% decrease
  - Prevalence 1.9- and 2.0-fold higher in males
  - Increase prevalence with age

Prevalence of LTBI (TST ≥ 10 mm) among household contacts & community controls, Uganda, 1995–2004

Prevalence of Abnormal Chest Radiograph (10.4%) & TB (1%) in Adults Immigrant Applicants Cho Ray Hospital, HCMC, Vietnam, 12/08-1/10

Prevalence of Positive TST & QFT by Age for 132 Culture-confirmed TB Cases & Applicant Population

TST & QFT done on 996 with abnormal & 479 with normal X-rays
Risk Factors for Infection:
Other Potential Contributors

- **Immunity**
  - re-infection increases with community TB morbidity
  - BCG protective - some studies (vaccines?)
- **Inherited variation in resistance**
  - Various genetic polymorphisms associated with risk
  - Contribution to morbidity appear small to date (risk ratios & prevalence of specific mutations)
- **Variation in virulence of TB strains**?
Prediction of TB re-infection proportion from the local incidence

Figure 2. Linear regression line for the reinfection proportion (%) and log Incidence (cases/100,000 people/year of tuberculosis). Values in parentheses are the reinfection proportions. US, United States.

Risk for Progression to TB if Infected: Major Contributors

- Age - peaks risk under 5 yrs. and around 19 yrs.; risk increases at 75 years
- Intensity of exposure - 3.5-fold higher for smear - positive than smear - negative
- Time since infection - 50% of cases occur within 2 years
- Size of reaction & exposure history - test specificity/prevalence?

Comstock GW. Am Rev Respir Dis 1982
Cohort study of TB risk for TST: Puerto Rico BCG trial, 1949-51 (19 yr follow-up)

- Enrolled 191,827 children 1-18 yrs old
  - 82,269 ≥ 6 mm with 1 or 10 TU – excluded
  - 1,400 TB cases - 90 per 10^5 / yr
  - 109,558 < 6 mm
    - Vaccine: 186 TB in 50,634, - 19.7 per 10^5/yr
    - Control: 141 TB in 27,338 - 27.6 per 10^5/yr
    - 28.7% reduction by BCG

Age and Progression of LTBI to TB: Puerto Rico BCG Trial, 1949-1951

- 82,269 children age 1-19 yrs with $\geq 6$ mm PPD

- 1,400 TB cases in 19 yrs: 90 per $10^5$/year
  - $\geq 16$ mm: 160 per $10^5$/year
  - 11-15 mm: 98 per $10^5$/year
  - 6-10 mm: 46 per $10^5$/year per year
  - < 6 mm: 28 per $10^5$/year (controls)

- Those $> 15$ mm PPD: 5% active TB in 19 yrs.

- Peak rates ages < 4 yr. and 19 yrs

TB Rate by Age in PPD+ Puerto Rican Children

Figure 1. Incidence of tuberculosis among initial reactors to tuberculin, by age when tuberculosis was first diagnosed.
Risk for Progression to TB if Infected: Major Contributors (Cont.)

- Parenchymal fibrotic lung lesion - extent of scar (less for granulomas)
- HIV infection
- Certain malignancies, disorders of immunity
- Immunosuppressive therapies
- Silicosis

Rieder HL. Epidemologic Rev 1989;11:79
47 Year-old Ukranian Immigrant

10/96 visa applicant in Moscow

- RUL fibrosis, Cl. B2
- Treated 5 yrs ago for pneumonia
- 9/97 immigrated to Denver
47-Year-old Ukranian Immigrant Brought to TB Clinic by Family

- Wt. loss of 10 lb, fatigue, cough
- 33 yr smoking history
- Sputum AFB smears positive
Risk for Progression to TB If Infected: Other Contributors

- Gender - 18% higher risk for young women
- Ethnicity - Asian (Filipino) U.S. Navy recruits at greater risk
- Others - hemodialysis, diabetes, gastrectomy, low weight, heavy smoking, injection drug use

Rieder HL. Epidemiologic Rev 1989;11:79
Cohort study of US Navy recruits 1958-69

- 1.2 million, 5 TU TST at entry
- 63,824 (5.25%) TST \(\geq 10\) mm induration
- 604 TB cases during 4 yrs follow-up
- Overall rates declined 21.4 to 3.7 cases /10^5 per yr from 1958-69
- Elevated TB rates during follow-up for
  - \(> 10\) mm
  - \(> 5\) mm with history of household TB exposure
  - Asians – mostly Filipinos

Hazard function curves of active TB for different body mass index categories in the overall Cox model: 42,116 persons > 65 ys in Hong Kong.

Risk for Death With TB
(Case: Notification Ratios)

- Without treatment: extremes of age & comorbidities
- HIV/AIDS especially without ART
  - US ‘93-95 vs ‘99-’02 (median CD4 86-90): 39 vs 15% 1 yr mortality (Burman 2006)
  - Africa: smear+ vs negative: mortality 20 vs 50% (Harries 2001)
- Timely and adequate therapy
- DOT associated with survival in HIV-infected cases
- Older age and black race are current risk factors - the latter likely due to socioeconomic status, access to care
<table>
<thead>
<tr>
<th>Age</th>
<th>1880</th>
<th>1890</th>
<th>1900</th>
<th>1910</th>
<th>1920</th>
<th>1930</th>
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<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
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<td>0–4</td>
<td>760</td>
<td>578</td>
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<td>209</td>
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<tr>
<td>5–9</td>
<td>43</td>
<td>49</td>
<td>31</td>
<td>21</td>
<td>24</td>
<td>11</td>
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<td>10–19</td>
<td>126</td>
<td>115</td>
<td>90</td>
<td>63</td>
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<td>20–29</td>
<td>444</td>
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<td>30–39</td>
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<td>368</td>
<td>296</td>
<td>253</td>
<td>164</td>
<td>115</td>
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<td>336</td>
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<td>253</td>
<td>175</td>
<td>118</td>
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<td>50–59</td>
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<td>325</td>
<td>267</td>
<td>252</td>
<td>171</td>
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<tr>
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<td>346</td>
<td>304</td>
<td>246</td>
<td>172</td>
<td>95</td>
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<tr>
<td>70+</td>
<td>672</td>
<td>396</td>
<td>343</td>
<td>163</td>
<td>127</td>
<td>95</td>
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<tr>
<td><strong>Females</strong></td>
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<tr>
<td>0–4</td>
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<td>595</td>
<td>354</td>
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<td>101</td>
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<tr>
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<tr>
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<tr>
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<td>40–49</td>
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<td>50–59</td>
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<td>234</td>
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<td>130</td>
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<td>47</td>
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<tr>
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<td>70+</td>
<td>584</td>
<td>375</td>
<td>296</td>
<td>126</td>
<td>68</td>
<td>40</td>
</tr>
</tbody>
</table>
Reported Tuberculosis (TB) Cases United States, 1982–2016*

No. of cases

26,673 TB cases in 1992

9,287 TB cases in 2016

*Provisional data, as of February 17, 2017.
## TB Morbidity United States, 2010–2015

<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Rate*</th>
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</thead>
<tbody>
<tr>
<td>2010</td>
<td>11,159</td>
<td>3.6</td>
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<tr>
<td>2011</td>
<td>10,510</td>
<td>3.4</td>
</tr>
<tr>
<td>2012</td>
<td>9,942</td>
<td>3.2</td>
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<td>2013</td>
<td>9,550</td>
<td>3.0</td>
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<tr>
<td>2014</td>
<td>9,406</td>
<td>2.9</td>
</tr>
<tr>
<td>2015</td>
<td>9,557</td>
<td>3.0</td>
</tr>
</tbody>
</table>

* Cases per 100,000 population; as of June 9, 2016.
TB Case Rates,* United States, 2015

*Cases per 100,000 population; as of June 9, 2016.

www.cdc.gov/tb
Map of U.S.-Affiliated Pacific Islands, by TB Case Rates,* 2015

* Cases per 100,000 population; as of June 9, 2016.
TB Case Rates,* by Age Group, United States, 1993–2015

* As of June 9, 2016.
## TB Case Rates, by Age Group and Sex, United States, 2015*

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>5–14</td>
<td>0.2</td>
<td>0.2</td>
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<tr>
<td>15–24</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>25–44</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>45–64</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>≥65</td>
<td>7.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>

*As of June 9, 2016.

[www.cdc.gov/tb](http://www.cdc.gov/tb)
TB Case Rates by Race/Ethnicity,*
United States, 2003–2015†

* All races are non-Hispanic.
† As of June 9, 2016.
Number of TB Cases Among U.S.-Born versus Foreign-Born Persons, United States, 1993–2015*

* As of June 9, 2016.
Trends in TB Cases Among Foreign-Born Persons, United States, 1993–2015*

No. of cases

Year

Percentage

* As of June 9, 2016.

www.cdc.gov/tb
Reported TB Cases, by Origin and Race/Ethnicity, United States, 2015

U.S.-born persons
- Hispanic/Latino: 21%
- Native Indian/Alaska Native: 4%
- Asian: 4%
- Native Hawaiian/Pacific Islander: 3%
- White: 31%
- Multiple race: 1%

Foreign-born persons
- Hispanic/Latino: 32%
- Asian: 48%
- Black/African American: 13%
- White: 4%
- Multiple race: 2%

www.cdc.gov/tb
Countries of Birth Among Foreign-Born Persons Reported with TB, United States, 2015*

* As of June 9, 2016.
Primary Anti-TB Drug Resistance, United States, 1993–2015*
Primary Isoniazid Resistance Among U.S.-Born versus Foreign-Born Persons, United States, 1993–2015
Primary MDR-TB Among U.S.-Born versus Foreign-Born Persons, United States, 1993–2015*

Year

1993 1995 1997 1999 2001 2003 2005 2007 2009 2011 2013 2015

Resistant (%)
XDR-TB Case Count, Defined on Initial DST, by Year, 1993–2015

Year of diagnosis

Case count

www.cdc.gov/tb
Epidemiology of MDR TB in the U.S.

- 168 cases in 8 states, 86% foreign-born, 15% with clustered isolates by genotyping
- 92 in-depth interview:
  - 22% imported active MDR TB (within 3 mo.)
  - 22% due to transmission within USA
  - 41% due to reactivation of latent TB infection, with 15% previously treated outside USA
  - 5% relapse of TB previously treated in USA
  - 10% unknown

Moonan P, et al Lancet Infection 2013: TBESC TO 8
TB Cases in Foreign-born Persons 2004

- 7,806 cases, 54% of total
- Most (50%) within 5 yrs of arrival
  - 24% within 1 year
  - 26% next 4 years; 50% later
- Rate ($10^5$/yr) 21.5 FB vs 2.7 US-born
  - First year 1,620 cases rate 121
  - Yr 1-5 1,767 cases rate 30
  - Over 5 yr 3,444 cases rate 12

Cain K. Am J Resp Crit Care Med 2007;175:75
25 yr old woman, 8 mm TST, not ill

Radiology reading: Fibrotic opacity in the right upper lobe with pleural thickening consistent with scarring from old TB
25 yr old woman

- No other PMHx
- HIV (-)
- Sputum AFB smear (-) x 3

Because she has an infant at home, she is started on I/R/Z/E

All 3 Sputa are Culture (+) for MTB
Reduced importation of TB in California after culture-based pre-immigration screening (2007 Technical Instructions)
P. Lowenthal, et al IJTLD 2011;15:761

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention cohort (n = 2049)</th>
<th>Post-intervention cohort (n = 1430)</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TB cases among immigrant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>arrivals</td>
<td>86 (4.2)</td>
<td>22 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Country of origin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>2 (1.4)</td>
<td>1 (0.6)</td>
<td>0.59</td>
</tr>
<tr>
<td>Philippines</td>
<td>65 (4.0)</td>
<td>17 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>19 (7.1)</td>
<td>4 (2.8)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Excess Early Reported TB Cases in Filipino Immigrants to California Is Due to Imported Cases: Stable TB Rates due to LTBI

793 TB cases in 123,000 immigrants to CA
N. Walter Am J Resp Crit Care Med 2014;189:88
Estimated TB Infection in the U.S.

Between 6 million and 13 million people infected with TB in the U.S.

Foreign-born: 9.3%-20.5%

US-born: 0.6%-2.8%

<table>
<thead>
<tr>
<th>TST Status Combination</th>
<th>Overall Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST Positive/IGRA Positive</td>
<td>2.1</td>
</tr>
<tr>
<td>TST Positive/IGRA Negative</td>
<td>2.6</td>
</tr>
<tr>
<td>TST Negative/IGRA Positive</td>
<td>2.9</td>
</tr>
<tr>
<td>TST Negative/IGRA Negative</td>
<td>92.4</td>
</tr>
</tbody>
</table>
Prospects for TB Elimination

TUBERCULOSIS IS CURABLE AND PREVENTABLE

If You are Rundown or have a Cough get a Medical Examination

Maritime Tuberculosis Educational Committee.