Epidemiology of TB: A Local and National Overview

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Tuberculosis in New York City: The Last Decade

Tuberculosis Cases and Rates New York City, 1978 - 1991

Tuberculosis rates by borough New York City, 1991

Rates of natural resistance in M. tuberculosis

- Isoniazid 1 in $10^6$
- Rifampin 1 in $10^8$
- Ethambutol 1 in $10^6$
- Streptomycin 1 in $10^5$
- INH & RIF 1 in $10^{14}$

Number of organisms in a TB cavity = $10^8$-$10^{11}$
Pathogenesis of Drug Resistance I

INH
RIF
PZA

INH

Pathogenesis of Drug Resistance II

IR

R

INH
RIF

How to get MDRTB

• Acquired resistance
  • Non adherence to therapy
  • inappropriate therapy
• Primary resistance
  • nosocomial transmission
  • community transmission

Emergence of Resistance (Inappropriate Therapy)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>6/90</th>
<th>9/90</th>
<th>2/91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Smear: + + + + +
Culture: + + + + +
Susceptibility
Isoniazid: R R R
Rifampin: S R R
Ethambutol: S S R

Evolution of Drug Resistance in a Community

First (mis) treatment 3-8 years
Acquired resistance 7-12 years
New Infection 10-15 years
Disease with primary resistance 13-18 years
Causes of resurgent tuberculosis in New York City

- Poverty, homelessness, crowding, substance abuse
- TB abroad on the rise; immigration from high prevalence countries
- HIV/AIDS epidemic
- Decline of public health infrastructure; lack of accessible health care
- Marked reduction in TB control program staff and clinic facilities
- By 1989, less than half of patients who began treatment were cured

Patients with resistant isolates
New York City, 1991 (N=466)

<table>
<thead>
<tr>
<th>Percent resistant</th>
<th>Any Anti-TB agent</th>
<th>INH</th>
<th>INH/RIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never treated</td>
<td>23</td>
<td>43</td>
<td>38.6</td>
</tr>
<tr>
<td>Previously treated</td>
<td>12.5</td>
<td>6.5</td>
<td>34</td>
</tr>
</tbody>
</table>

Nosocomial, HIV-related outbreaks of multidrug-resistant TB as of October, 1992

<table>
<thead>
<tr>
<th>Facility</th>
<th>Location</th>
<th>Time Period</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td>Miami</td>
<td>1988-91</td>
<td>65</td>
</tr>
<tr>
<td>Hospital B</td>
<td>NYC</td>
<td>1989-91</td>
<td>51</td>
</tr>
<tr>
<td>Hospital C</td>
<td>NYC</td>
<td>1989-92</td>
<td>70</td>
</tr>
<tr>
<td>Hospital D</td>
<td>NYC</td>
<td>1990-91</td>
<td>29</td>
</tr>
<tr>
<td>Hospital E</td>
<td>NYS</td>
<td>1990-91</td>
<td>7</td>
</tr>
<tr>
<td>Hospital F</td>
<td>NYC</td>
<td>1990-91</td>
<td>16</td>
</tr>
<tr>
<td>Hospital I</td>
<td>NJ</td>
<td>1990-92</td>
<td>13</td>
</tr>
<tr>
<td>Hospital J</td>
<td>NYC</td>
<td>1991-92</td>
<td>28</td>
</tr>
<tr>
<td>Prisons*</td>
<td>NYS</td>
<td>1990-92</td>
<td>42</td>
</tr>
<tr>
<td>Total Cases</td>
<td></td>
<td></td>
<td>297</td>
</tr>
</tbody>
</table>

* 24 prison cases are also counted with Hospital C

Prevalence of HIV and mortality of patients with multidrug-resistant TB as of Oct., 1992

<table>
<thead>
<tr>
<th>Facility</th>
<th>HIV+</th>
<th>Mortality</th>
<th>Median Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td>93%</td>
<td>72%</td>
<td>7 weeks</td>
</tr>
<tr>
<td>Hospital B*</td>
<td>100%</td>
<td>89%</td>
<td>16 weeks</td>
</tr>
<tr>
<td>Hospital C</td>
<td>95%</td>
<td>77%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hospital D</td>
<td>91%</td>
<td>83%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hospital E</td>
<td>14%</td>
<td>43%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hospital F</td>
<td>82%</td>
<td>82%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hospital I</td>
<td>100%</td>
<td>85%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Hospital J</td>
<td>96%</td>
<td>93%</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Prison System **</td>
<td>98%</td>
<td>79%</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

* HIV infection was part of case definition
** Includes 24 cases also counted with Hospital C

Nosocomial Tuberculosis
Common Characteristics

- Diagnosis was not considered or late diagnosis
- CXR often “atypical” for TB
- Ineffective or inadequate isolation
- Most cases in HIV seropositive patients
- Multidrug-resistant strains
  - Standard treatment not effective
  - Appropriate treatment also often ineffective for prolonged periods
  - Laboratory results delayed

A Multi-institutional Outbreak of Highly Drug-Resistant Tuberculosis

Frieden et al. JAMA 1996;276:1229-1235
Characteristics of strain W outbreak

**Patient Selection**
- Patients were selected from those cared for at public and nonpublic institutions from January 1, 1990 to August 1, 1993
- Patients had to have isolates resistant to at least I/R/E/S and RBT, if testing included it
- For those suspected of having strain W TB, results of isolate testing by RFLP had to have an identical or closely related pattern to strain W

**Results**
- 357 patients met case definition, 267 had isolates for RFLP
- 78% were sputum AFB smear positive
- Of 249 with known serostatus, 230 (92%) were HIV+
- Median survival for the 230 HIV+ patients was 66 days
- 221 HIV+ patients had positive cultures from a pulmonary source
- Patients with strain W had more documented HIV infection than other CX+ TB patients (86% vs. 37%; P<.001)

Characteristics of strain W outbreak

**Epidemiological links-1**
- 267 (75%) had isolates available for RFLP testing
- 237 isolates had an identical RFLP pattern (strain W)
- 30 isolates had RFLP patterns that were very similar to strain W
- Patients resided in all boroughs and most zip codes in NYC
- Cared for at 41 hospitals and hospitalized for 19,740 days

**Epidemiological links-2**
- 186 (70%) of 267 were epidemiologically linked
- 178 (96%) occurred in 11 different hospitals (range 1-76 case/hospital)
- 3 (2%) were linked in the correctional system
- 5 (3%) were linked in the community
- Outbreaks lasted up to 38 months and most took place in 4 hospitals
- Median time from exposure to disease was 17 weeks

MDRTB Transmission in a Hospital Nursery

TB Control: The 5 components of DOTS
- Political commitment
- Diagnosis by microscopy
- Adequate supply of the right drugs
- Directly observed treatment
- Accountability
Programmatic measures used to control TB in NYC

- DOT as standard of care
- Intensive case management
- Detention until cure for least adherent
- Improved Infection Control
  - Hospitals
  - Correctional facilities
- Changes in empiric treatment regimens
- Mandatory susceptibility testing and reporting

Tuberculosis Cases and Rates New York City, 1978 – 2002*

Trends in Tuberculosis - 1
New York City, 1992-2002

- 71.6% fewer cases since 1992
- 93.9% fewer MDRTB cases
- 88.4% fewer US-born cases
- 76.9% fewer cases in 25-44 year age group

Trends in Tuberculosis - 2
New York City, 1992-2002

- HIV-infected cases decreased from 34% in 1992 to 15% in 2001, increasing to 18% in 2002
- Females increased from 28% in 1986 to 39% in 2002
- Non-US-born cases increased from 18% in 1992 to 66% in 2001, decreasing to 65% in 2002

Tuberculosis Cases New York City, 1978-1998

* Rates since 2000 are based on 2000 Census data.
Cluster size among NYC TB patients during three surveys

Cluster size (Patients per Cluster)

Number of patients per cluster

Number and Size of DNA Clusters (N=132 clusters)

DNA Clustering by country of origin, NYC 1991-2002

US-Born Patients Non-US-Born Patients

Cross-Sectional Surveys (NYC April Studies)

RFLP alone for cases >3 bands

RFLP and Spoligol for ALL Cases

NYC 2001-2002 Incident ME Project cases (2 years)

DNA Clustering by country of origin, NYC 1991-2002

DNA Clustering by country of origin, NYC 1991-2002

Multivariate Analysis Clustering

Variable | OR Adjusted | (95% CI)
--- | --- | ---
Age <60 | 1.79 | 1.28 – 2.51
US-Born | 2.46 | 1.83 – 3.29
Asian | 0.41 | 0.29 – 0.59
History of TB or LTBI | 2.00 | 1.09 – 3.66
Low band RFLP | 9.33 | 6.47 – 13.46
### Health Districts with Case Rate* $20
New York City, 2002

<table>
<thead>
<tr>
<th>Health District</th>
<th>Case Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Harlem</td>
<td>38.5</td>
</tr>
<tr>
<td>Corona</td>
<td>28.5</td>
</tr>
<tr>
<td>East Side</td>
<td>21.8</td>
</tr>
<tr>
<td>Bushwick</td>
<td>28.7</td>
</tr>
<tr>
<td>Astoria-LIC</td>
<td>20.3</td>
</tr>
<tr>
<td>Fort Greene</td>
<td>20.3</td>
</tr>
</tbody>
</table>

* Rates per 100,000 based on 2000 Census data.

### Percent of Eligible* Tuberculosis Patients on Directly Observed Therapy**
New York City, 2001

<table>
<thead>
<tr>
<th>Classification</th>
<th>% on DOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDR</td>
<td>55.9</td>
</tr>
<tr>
<td>Pulm. smear-positive</td>
<td>75.1</td>
</tr>
<tr>
<td>Any DOHMH Rx</td>
<td>82.6</td>
</tr>
<tr>
<td>All</td>
<td>64.3</td>
</tr>
</tbody>
</table>

* Eligible patients were those diagnosed while alive and who received some treatment on an outpatient basis.
** Ever on DOT as of March of the year after being confirmed as a case of tuberculosis.

### Trend in HIV-Infection and TB
New York City, 1992-2002

- **Number of Cases**: 1,400
- **% of Cases TB/HIV Infected**: 33%

### HIV Infection and Tuberculosis
New York City, 2002

- **% of Cases**
  - Males (N = 667): 42.4%
  - Females (N = 417): 33.6%

### Estimated HIV Coinfection in Persons Reported with TB
United States, 1993-2001

- **% Coinfection**
  - 1993: 7%
  - 1994: 6%
  - 1995: 5%
  - 1996: 4%
  - 1997: 3%
  - 1998: 2%
  - 1999: 1%
  - 2000: 0.5%
  - 2001: 0.2%

Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group. All 2001 cases from California have an unknown HIV status.
HIV-Infected US-Born TB Cases
New York City, 1993-2002

Multidrug-Resistant TB*
New York City, 1991 - 2002

W and related strain epidemic curve in
NYC, 1991-2001

Major multidrug-resistant strains in New York City, 1995-1997

Drug Resistance in
New York City, 1992-2002

Primary Anti-TB Drug Resistance
United States, 1993-2002

*1991 data are incomplete
**multidrug-resistant TB or MDRTB: resistant to at least INH & RIF

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
US* and Non-US Born TB Cases 
New York City, 1980 – 2002

Non-US Born Tuberculosis Cases 
New York City, 1990 - 2002

Tuberculosis Cases by Area of Birth and Borough. 
New York City, 2002

22 High-Burden TB Countries* 

Top 10 Countries of Birth 
NYC TB Cases 2002

22 High-Burden TB Countries*

1. India
2. China
3. Indonesia
4. Nigeria
5. Bangladesh
6. Ethiopia
7. Philippines
8. Pakistan
9. South Africa
10. Russian Federation
11. DR Congo
12. Kenya
13. Vietnam
14. Tanzania
15. Brazil
16. Thailand
17. Uganda
18. Myanmar
19. Mozambique
20. Cambodia
21. Zimbabwe
22. Afghanistan

*Rate per 100,000 based on 2000 Census
*As per the World Health Organization

NYC DOHMH
NYC Population and TB Case Rates:
Top 12 Countries of Origin for TB cases

<table>
<thead>
<tr>
<th>Country</th>
<th>NYC 2000 population</th>
<th>In US &lt;10 years*</th>
<th>Expected TB cases using:</th>
<th>Actual 2001 Cases in NYC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total population</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1,839</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In US &lt;10 years</td>
<td>617</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Actual 2001 Cases in NYC</td>
<td>560</td>
</tr>
</tbody>
</table>

*Includes Mexico and Caribbean

Sources: US Census 2000 and WHO estimated TB case rates

Limitations of Census Data

- 1990 Census denominators - overestimate incidence rate
- Time spent outside US for US-born, and re-entry for non-US born unavailable
- Immigration status of non-US born TB cases not available

Current Prevention Strategies

- Improving LTBI treatment completion for high risk individuals
- Targeted testing in high risk communities
- Screening of immigrants
- Identifying missed opportunities for TB prevention

LTBI Treatment

Treatment for LTBI is resource intensive and has limited success
- Isoniazid treatment for 9-12 months is 75% effective
- Cost per case prevented $14,558
- Cost per TB case $16,391

- But if completion rate is 50%, it is not cost effective

Source: Institute of Medicine, Ending Neglect, 2000
Screening of Immigrants/Refugees

- Immigrants/refugees (>15 years of age) are screened by chest x-ray and sputa before entry
- Non-infectious disease - required to report to health department at destination
- Account for small proportion of foreign-born cases
  - In NYC, on average 20/year
  - 2% of FB cases in 2001
- Excludes majority of foreign-born (tourists, students, temporary workers, undocumented)

Will there always be 1000 TB cases per year in NYC?

- Non-US born population increasing in NYC
- Prevention strategies are resource intensive and have limited success
- Immigrant screening abroad covers small proportion of cases in non-US born
- Case rates in country of origin and recent arrival in US strongest predictors of disease
- Imported TB likely to continue to contribute significantly to NYC cases in near future

Challenges in the Future

- HIV infection and congregate settings
- Continued high immigration from high incidence countries
- Potential for decreased vigilance in hospitals
- Decreased funding
- International TB efforts not moving at the pace needed to fulfill WHO goals