Part I
Tuberculosis (TB): the Once and Future Plague

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Population growth 10,000 B.C. to 2000 A.D.


Most pathogens enter their hosts via mucosal surfaces
“Following infection, the incubation period of TB ranges from a few weeks to a lifetime.”

Stage 1: Primary Lesion
Mycobacterium tuberculosis inhibits phagosome maturation in macrophages

Stage 2: Dissemination
Stage 3: Secondary Lesions
Stage 4: Latent Infection
Stage 5: Reactivation
The tuberculosis granuloma: protection and pathogenesis

Early Granuloma

Late Granuloma
Stage 6: Cavitation
Stage 6: Cavitation
Stage 6: Cavitation
Stage 7: Transmission
The SEIR model of epidemic dynamics

**MEASLES**
Critical community size = 300,000

Susceptible → Exposed → Infectious → Recovered

- 2 weeks
- 1 week
- months-decades
- months-decades

**TUBERCULOSIS**
Critical community size = 100

Exposed to Infectious: 2 weeks & 1 month
Recovered: months-decades
Causes of death worldwide (total: 57 million)


- Respiratory digestive: 5.7 million
- Neoplasms: 7.3 million
- Cardiovascular: 16.7 million
- Maternal perinatal nutritional: 3.5 million
- Injuries: 5.2 million
- HIV/AIDS: 2.8 million
- Malaria: 1.3 million
- Other infections: 9.3 million
- Tuberculosis: 1.6 million
- Other: 3.7 million

TB latency: the iceberg of pathogenesis

- 2.0 million dead
- 16.2 million sick
- 1.9 billion infected
- 3.9 billion uninfected (for now...)
TB in the United States 1989-2000


- US-born
- Foreign-born

Year


0 5 10 15 20
Most TB victims are young adults

Most TB victims are young adults

### Leading causes of global mortality among adults


<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>Deaths (1000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HIV/AIDS</td>
<td>2,279</td>
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<tr>
<td>2</td>
<td>Ischaemic heart disease</td>
<td>1,332</td>
</tr>
<tr>
<td>3</td>
<td><strong>Tuberculosis</strong></td>
<td><strong>1,036</strong></td>
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<tr>
<td>4</td>
<td>Road traffic injuries</td>
<td>814</td>
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<tr>
<td>5</td>
<td>Cerebrovascular disease</td>
<td>783</td>
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<tr>
<td>6</td>
<td>Self-inflicted injuries</td>
<td>672</td>
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<tr>
<td>7</td>
<td>Violence</td>
<td>473</td>
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<tr>
<td>8</td>
<td>Cirrhosis of the liver</td>
<td>382</td>
</tr>
<tr>
<td>9</td>
<td>Lower lung infections</td>
<td>352</td>
</tr>
<tr>
<td>10</td>
<td>COPD</td>
<td>343</td>
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</tbody>
</table>
Leading causes of global mortality among adults

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<th>Cause</th>
<th>DALYs (1000s)</th>
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<tbody>
<tr>
<td>1</td>
<td>HIV/AIDS</td>
<td>68,661</td>
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<tr>
<td>2</td>
<td>Unipolar depressive disorders</td>
<td>57,843</td>
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<td>3</td>
<td><strong>Tuberculosis</strong></td>
<td><strong>28,380</strong></td>
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<td>4</td>
<td>Road traffic injuries</td>
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<td>5</td>
<td>Ischaemic heart disease</td>
<td>26,155</td>
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<td>6</td>
<td>Alcohol use disorders</td>
<td>19,567</td>
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<td>7</td>
<td>Hearing loss, adult onset</td>
<td>19,486</td>
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<td>8</td>
<td>Violence</td>
<td>18,962</td>
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<tr>
<td>9</td>
<td>Cerebrovascular disease</td>
<td>18,749</td>
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<tr>
<td>10</td>
<td>Self-inflicted injuries</td>
<td>18,522</td>
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</tbody>
</table>