DRUG-RESISTANT TUBERCULOSIS

WHAT HAVE WE LEARNED?

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INTERNATIONAL WORKSHOP ON MDR-TB
BEIJING, PEOPLES REPUBLIC OF CHINA
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The Crisis in Antibiotic Resistance

Harold C. Neu

The synthesis of large numbers of antibiotics over the past three decades has caused concern about the threat of bacterial resistance. Bacteria have become resistant to antimicrobial agents as a result of chromosomal changes or the exchange of genetic material via plasmids and transposons. Streptococcus pneumoniae, Streptococcus pyogenes, and staphylococci, organisms that cause respiratory and cutaneous infections, and members of the Enterobacteriaceae and Pseudomonas families, organisms that cause diarrhea, urinary infections, and sepsis, are now resistant to virtually all of the older antibiotics. The extensive use of antibiotics in the community and hospitals has fueled this crisis. Mechanisms such as antimicrobial control programs, better hygiene, and synthesis of agents with improved antimicrobial activity need to be adopted in order to limit bacterial resistance.

Staphylococci

In 1994, virtually all strains of Staphylococcus aureus worldwide were susceptible to penicillin G, but by 1994 3. aureus was

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Fig. 1. Sites of action of various antimicrobial agents. mRNA, messenger RNA; RNA, transfer RNA; PABA, p-aminobenzoic acid; DHFR, dihydrofolate reductase; THFA, tetrahydrofolic acid.
Decline in TB rates before chemotherapy, USA

Source: Snider GL. Annals of Internal Medicine 1997
TB Funding History
US Public Health Service
United States Centers for Disease Control and Prevention
1944-1976

Categorical Grants Ceased
1972-1982

Adapted from: Dr. Ken Castro, U.S. Centers for Disease Control and Prevention, Presentation, Harvard University, June 2012
Tuberculosis in New York City

- Incidence of TB in U.S. began to rise in late 1980s; AIDS epidemic believed to have central role in rise
- Other causes: homelessness, poverty, immigration, weakened public health infrastructure, and limited access to medical care
- Incidence in NYC increased 132% from 1980 to 1990
- NYC reported 14% of all TB cases in the US in 1990
Tuberculosis cases and rates: New York City, 1978-2009*
760 cases in 2009

* Rates based on official Census data and intercensal estimates prior to 2000. Rates for 2000 to 2008 are based on intercensal estimates.

• # of cases of TB had nearly tripled in 15 years
• In central Harlem, case rate of >100 per 100,000 people
• Nearly 1 in 5 patients in NYC with TB had MDR-TB
• Proportion of patients with MDR-TB had more than doubled in 7 years
• In 1991, with 3% of the country’s population, NYC accounted for 61% of all MDR-TB cases in U.S.

• Diagnosis using mycobacterial culture
• Access to quality-assured second-line anti-TB medications
• Proper infection control
• Delivery of care under direct observation, with management of adverse events
THE WAR ON TUBERCULOSIS: DOTS IN NEWARK, NJ, USA

Am J Nursing, July 2010
Table 3. WHO/IUATLD-designated “hot spots,” where at least 5% of all TB cases studied were MDR-TB, ranked by reported proportion

<table>
<thead>
<tr>
<th>Country, Region</th>
<th>Year of survey</th>
<th>Proportion of all TB cases that are MDR-TB</th>
</tr>
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<tbody>
<tr>
<td>Latvia</td>
<td>1996</td>
<td>22.1%</td>
</tr>
<tr>
<td>India, Delhi state</td>
<td>1995</td>
<td>13.3%</td>
</tr>
<tr>
<td>Estonia</td>
<td>1994</td>
<td>11.7%</td>
</tr>
<tr>
<td>China, Henan province</td>
<td>1996</td>
<td>11.3%</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>1994-1995</td>
<td>8.6%</td>
</tr>
<tr>
<td>Argentina</td>
<td>1994</td>
<td>8.0%</td>
</tr>
<tr>
<td>Russia, Ivanovo oblast</td>
<td>1995-1996</td>
<td>7.3%</td>
</tr>
<tr>
<td>Ivory Coast</td>
<td>1995-1996</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

Source: WHO and IUATLD, 1997

Source: The Global Impact of Drug-Resistant Tuberculosis, 1999
August 1996
DOTS-Plus project initiated in Lima’s Northern Cone by PIH/SES and Harvard Medical School, with the Peruvian National TB Program
Outcomes in 66 MDR TB patients in Lima, Peru receiving at least four months of therapy

All patients initiated therapy between August 1996 and February 1999.

- Abandoned therapy: 1.52%
- Failed therapy: 7.58%
- Died: 7.58%
- Cured: 83.33%

TB Centers of Excellence
Peru, 2006
Retrospective of 651 TB patients in metropolitan Lima, Peru from Feb 1999 – Aug 2002

• XDR-TB was identified in 7.4% (48); MDR-TB in 92.6% (603)

• Comprehensive treatment included: aggressive management of adverse events; nutritional support, group therapy, & opportunity for participation in microfinance initiatives; follow-up screening for recurrent disease; efforts to reduce household transmission.

  • 29 (60.4%) XDR-TB patients completed treatment or were cured
  • 412 (67.6%) MDR-TB patients completed treatment or were cured

• Outcomes were better than most reported from hospitals in Europe, the US, & Korea, where cure was achieved in < 50% of XDR-TB patients.

<table>
<thead>
<tr>
<th>ITR Outcome</th>
<th>XDR-TB</th>
<th>MDR-TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good outcomes</td>
<td>29 (60.4)</td>
<td>400 (66.9)</td>
</tr>
<tr>
<td>Cured</td>
<td>29 (60.4)</td>
<td>395 (65.6)</td>
</tr>
<tr>
<td>Completed</td>
<td>0 (0.0)</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Poor outcomes</td>
<td>19 (39.6)</td>
<td>198 (33.1)</td>
</tr>
<tr>
<td>Defaulted</td>
<td>3 (6.3)</td>
<td>62 (10.3)</td>
</tr>
<tr>
<td>Treatment Failed</td>
<td>5 (10.4)</td>
<td>13 (2.2)</td>
</tr>
<tr>
<td>Died</td>
<td>11 (22.9)</td>
<td>123 (20.6)</td>
</tr>
<tr>
<td>Median days to culture conversion (95% CI)</td>
<td>90 (57,115)</td>
<td>61 (59, 67)</td>
</tr>
</tbody>
</table>

Building platforms for management of chronic diseases

Resources for AIDS

A Community-Based AIDS Treatment Program in Rural Rwanda

1041 Patients - 2yr Follow-Up

- Retained in care (92.3%)
- Died (5.0%)
- Lost to follow-up/defaulted (2.7%)

Towards universal access to ART in Rwanda

More than 90,000 Rwandans on ART (>80% of PLWA)

ART coverage vs. GDP per capita in sub-Saharan Africa, 2009

Source: World Bank DataBank (2012) and UN MDG Indicators (2011)
Outcome of MDR-TB Treatment in Rwanda
(N=224 confirmed MDR-TB patients enrolled from Jul 05 – Sep 08)

SUCCESS RATE: 87%
“Enabling Platforms”

Community-based

Hospital-linked

Health-center enriched
Figure 2. Child mortality in Rwanda, 1990 – 2011

Probability of child dying by age 5 per 1,000 live births

- Rwanda
- Sub-Saharan Africa
- World

MDG Target
“It appears that much of the poverty reduction in the last couple of decades almost exclusively comes from China:

- China’s poverty rate fell from 85% to 15.9%, or by over 600 million people
- China accounts for nearly all the world’s reduction in poverty
- Excluding China, poverty fell only by around 10%.”

Anup Shah, Global Issues, 2013
(From World Bank 2008)
TB Funding History
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Adapted from: Dr. Ken Castro, U.S. Centers for Disease Control and Prevention, Presentation, Harvard University, June 2012
WE ASPIRE TO A WORLD WITH ZERO TB DEATHS

Thank you

Photo: Open Society Institute/Pep Bonet