Underreported threat of MDR-TB in Africa

Forum on Drug Discovery, Development and Translation

Yanis BEN AMOR
MDR-TB among new cases 1994-2007

* Sub-national averages applied to China, Russia, Indonesia

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

© WHO 2006. All rights reserved
MDR-TB among new cases 1994-2007

WHO, 2008
Countries with no data

- Despite high TB incidence and prevalence, and high HIV prevalence, MDR-TB is considered low in Africa
- NTP are operating well
- Rifampicin introduced later
Performance of NTP (1997-2008)

<table>
<thead>
<tr>
<th></th>
<th>Case Detection</th>
<th>Treatment Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estonia</td>
<td>69%</td>
<td>68%</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>76%</td>
<td>76%</td>
</tr>
<tr>
<td>Latvia</td>
<td>73%</td>
<td>70%</td>
</tr>
<tr>
<td>Lithuania</td>
<td>78%</td>
<td>78%</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>43%</td>
<td>64%</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>42%</td>
<td>79%</td>
</tr>
<tr>
<td>AFRO</td>
<td>51%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Source: WHO reports 1997 - 2008
Introduction of Rifampicin

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>1979</td>
</tr>
<tr>
<td>Tanzania</td>
<td>1982</td>
</tr>
<tr>
<td>Botswana</td>
<td>1986</td>
</tr>
<tr>
<td>Gambia</td>
<td>1986</td>
</tr>
<tr>
<td>Mozambique</td>
<td>1986</td>
</tr>
<tr>
<td>Zambia</td>
<td>1989</td>
</tr>
</tbody>
</table>
Countries with no data

- One might speculate that the countries capable of providing DRS data may have been the ones most likely to have a well functioning NTP, laboratory structures and transport networks.
- MDR-TB rates are likely higher in the African countries which were never surveyed than in the countries already surveyed.
Countries with known MDR-TB rate

Underreported Threat of Multidrug-Resistant Tuberculosis in Africa
Yanis Ben Amor, Bennett Nemser, Angad Singh, Alissa Sankin, and Neil Schügger

Multidrug-resistant tuberculosis (MDR TB) in Africa may be more prevalent than previously appreciated. Factors leading to development of drug resistance need to be understood to develop appropriate control strategies for resistance programs. We performed a retrospective analysis of MDR-TB rates and independent factors were analyzed by using correlation and linear regression models. Our findings indicate that drug resistance surveys in Africa are critically needed. MDR-TB rates must be assessed in countries without these surveys. It is clear that countries that have conducted drug resistance surveys with adequate follow-up of drug resistance rates, are currently experiencing lower levels of MDR-TB rates and TB incidence. WHO guidelines on TB control programs in Africa. Eighty-nine percent of the population in the WHO-defined Region of Africa is covered by a national TB program, which is similar to the global average. (4) However, there is a discrepancy between reported DOTs coverage and national TB program (NTP) efficacy. Each year countries with the lowest case detection and cure rates are clustered in the WHO-defined Regional Office for Africa (AFRO) region. This suggests that NTPs in Africa are not performing better than their European or South American counterparts, where MDR-TB rates have already reached alarming levels. The functional status of many programs in Africa is difficult to assess with certainty, and we are unable to develop accurate projections for the near future. However, the more general problem of MDR-TB, with an estimated 450,000 cases worldwide annually, has been recognized since the first World Health Organization (WHO) global survey on drug resistance is the 1990s. (5)

According to the WHO Global Report on Anti-tuberculosis Drug Resistance in the World (1), MDR-TB strains have emerged in all regions of the world. However, the dramatic increase in TB rates in Africa, MDR-TB appears nearly absent from the continent, which, until recently, reported the lowest median levels of drug resistance. Two explanations have been most commonly put forward to explain these reported low levels of MDR-TB in Africa. The first explanation is the presence of well-functioning control programs in Africa. Eighty-nine percent of the population in the WHO-defined region of Africa is covered by a national TB program, which is similar to the global average. (4) However, there is a discrepancy between reported DOTs coverage and national TB program (NTP) efficacy. Each year countries with the lowest case detection and cure rates are clustered in the WHO-defined Regional Office for Africa (AFRO) region. This suggests that NTPs in Africa are not performing better than their European or South American counterparts, where MDR-TB rates have already reached alarming levels. The functional status of many programs in Africa is difficult to assess with certainty, and the high incidence rates on the continent indicate that programs may not be functioning well. Low case-detection rates alone may not lead to development of MDR TB. Other factors that might favor development of MDR TB include the availability of drugs on the open market and a private sector that delivers drugs to its population in an unregulated fashion.

The second explanation is the recent introduction of rifampin in Africa. It is often stated that because rifampin was only recently introduced in Africa on a large scale, there has been relatively little time for resistance to develop. However, development of rifampin resistance may be present at high incidence rates have been relatively high.

WHO, 2008
Countries with known MDR-TB rate

Most new countries surveyed are either moderate or high MDR levels
Countries with known MDR-TB rate

- 14/21 surveys are older than 5 years
- Few settings in Africa with repeat surveys show rising MDR-TB rates (Botswana)
- We can assume that current rates of MDR-TB in repeat surveys would be higher
Countries with known MDR-TB rate

Matteo Zignol, Paul Nunn J. Infect Dis 2006
Countries with known MDR-TB rate

- Current DRS only include SS+ TB cases
- 2 countries (Latvia and Ukraine) with MDR-TB rates segregated based on HIV status show significant association between HIV+ and MDR-TB
- HIV+ are more likely to be SS-
- In high HIV prevalence settings, current DRS protocol may underestimate actual MDR-TB levels
Indicators of MDR-TB rates

- Investigate association between country specific factors and MDR-TB levels in Africa
- No linear relationship between MDR-TB rates and average case detection rate, average TB incidence rate or TB prevalence
- Retreatment failure rate was the most predictive indicator of MDR-TB rates
  - Association without causation
  - Current retreatment regimen may cause MDR-TB
Conclusions

- MDR-TB likely to be underestimated
- Diagnosis of MDR-TB not widely available
- Second line drugs not available
- Current Category II regimen may be creating MDR-TB
Acknowledgements

- Bennett Nemser
- Neil Schluger
- Angad Singh
- Alyssa Sankin
- Institute of Medicine