Multi-drug resistant Tuberculosis in Low resource settings:
A case vignette from India
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Glossary:

- **RNTCP**: Revised National Tuberculosis Control Programme (based on DOTS strategy).
- **NTP**: National Tuberculosis Programme (predecessor to RNTCP)

**FIGURE 1.6**
Countries with the highest numbers of estimated MDR-TB cases, 2007. Horizontal lines denote 95% confidence intervals. The source of estimates is drug resistance surveillance or surveys (DRS, in red) or modelling (in grey).

Source: Global Tuberculosis Control 2009, WHO.
34 year old, non-smoker
Has 2 young children.
Drives an autorickshaw.
History of symptoms of Pulmonary TB off and on since ..........years.

1990s: recurrence of disease


2000: Rxed with Rifampicin containing regime.

2004: Retreatment regime of RNTCP + ethionamide + quinolone. Interrupted therapy because of cost.

No lasting improvement in symptoms.

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The type of regimes received by patient in NTP/RNTCP

<table>
<thead>
<tr>
<th>Pre 1993</th>
<th>TYPE OF REGIME</th>
<th>INTENSIVE PHASE</th>
<th>MAINTENANCE PHASE</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-1993</td>
<td>New Cases</td>
<td>Streptomycin, INH and Thiacetzone</td>
<td>INH and Thiacetzone</td>
<td>12 months</td>
</tr>
<tr>
<td>Post 1993</td>
<td>Retreatment regime</td>
<td>2 SHRZ</td>
<td>4 (SHRZ)₂</td>
<td>6 months</td>
</tr>
<tr>
<td>Post 1997</td>
<td>Retreatment regime</td>
<td>2 SHRZ</td>
<td>4 (SHRZ)₂</td>
<td>6 months</td>
</tr>
<tr>
<td>Post 2002</td>
<td>Retreatment regime</td>
<td>2 (SHRZE)₂, 1 (HRZE)₃</td>
<td>5 (HRE)₃</td>
<td>8 months</td>
</tr>
</tbody>
</table>

H: Isoniazid, R: Rifampicin, Z: Pyrazinamide, E: Ethambutol
6 DRUG RESISTANCE on DST:
STREPTOMYCIN, INH, RIFAMPICIN, ETHAMBUTOL, ETHIONAMIDE
OFLOXACIN
Sputum smear conversion at 2 months.
Sputum culture negative at 3 months.
Monthly smear examinations negative
Surgery on Rt Upper Lobe advised but couldn’t be done for logistical reasons. Children TST positive, on close follow up.

Drug resistance in India: post-1990s

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>10.1%-23.4%</td>
<td>47.0%-87.1%</td>
</tr>
<tr>
<td>RIF</td>
<td>1.7-8.5 %</td>
<td>6.1-67%</td>
</tr>
<tr>
<td>MDR</td>
<td>0.7-5.3</td>
<td>6.1-67 %</td>
</tr>
</tbody>
</table>

Sources: Paramesivan CN. Drug Resistance in India. Ind J Med Res 2004
Chaddha VK. Tuberculosis Epidemiology in India: A review. IJTLD 2005
Points to ponder: Journey from ? Initial INH resistance to pre-XDR tuberculosis

- Pathways to development of drug resistance, and its amplification:
  - 1. Non-adherence.
  - “those least comply, who are least able to comply.” Paul Farmer.
  - 2. Adding a single drug to a failing regime.
  - 3. Failure to add a sufficient number of effective drugs when drug resistance is expected.

Drug regimes in RNTCP:
Formulated in 1997: resistant to change

<table>
<thead>
<tr>
<th>Category of Treatment</th>
<th>Type of Patient</th>
<th>Regimen*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>New sputum smear-positive</td>
<td>2H3RZ(E3)E</td>
</tr>
<tr>
<td></td>
<td>new sputum smear-negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seriously ill* new sputum smear-negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seriously ill* new extra-pulmonary</td>
<td></td>
</tr>
<tr>
<td>Category II</td>
<td>Sputum smear-positive Referee</td>
<td>2H3RZ(E3)E</td>
</tr>
<tr>
<td></td>
<td>Sputum smear-positive Failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sputum smear-positive Treatment After Default</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others***</td>
<td></td>
</tr>
<tr>
<td>Category III</td>
<td>New Sputum smear-negative, not seriously ill</td>
<td>2H3RZ(E3)E</td>
</tr>
<tr>
<td></td>
<td>New Extra-pulmonary, not seriously ill</td>
<td></td>
</tr>
</tbody>
</table>

Source: Managing the RNTCP in your area: Module 1-4, April 2005. Central TB Division. GOI.

RNTCP CATEGORY IV REGIMEN: 6 (9) Km Ofk (Lvir) Etob Cz E / 18 Ofk (Lvir)Etob Cz E

• This Patient failed on SHRZ ---- treated with SHRZE under the RNTCP

• If a new patient fails on HRZE --------
  Retreatment regime : S HRZE

• The **first commandment** of treating potential MDR-TB “Never add a single drug to a failing regime- MD Iseman”


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**If Not Now When?**

• Access to Drug Susceptibility testing for patients failing on regime for new cases, retreatment cases.

• Access to regimens effective against drug resistant TB.

• “It is too expensive not to treat MDR-TB now, when a small fraction of all TB patients are resistant to our best drugs.”

The question of resources:

70 million dollars per jet