MDR/ XDR TB
KZN Update

Dr I H Master
King George V Hospital
Department of Health (KZN)
06/10/2011
Estimated absolute number of MDR-TB cases, 2009

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 2011. All rights reserved
Proportions of MDR among new TB cases, 1994-2010

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 2011. All rights reserved.
Countries that had reported at least one XDR-TB case by end 2010

Argentina, Armenia, Australia, Austria, Azerbaijan, Bangladesh, Belgium, Botswana, Brazil, Burkina Faso, Bhutan, Cambodia, Canada, Chile, China, Colombia, Czech Republic, Ecuador, Egypt, Estonia, France, Georgia, Germany, Greece, India, Iran (Islamic Rep. of), Ireland, Israel, Italy, Japan, Kazakhstan, Kenya, Kyrgyzstan, Latvia, Lesotho, Lithuania, Luxembourg, Mexico, Mozambique, Myanmar, Nepal, Netherlands, Norway, Pakistan, Peru, Philippines, Poland, Portugal, Qatar, Republic of Korea, Republic of Moldova, Romania, Russian Federation, Slovenia, South Africa, Spain, South Korea, Sweden, Togo, Tunisia, Ukraine, United Arab Emirates, United Kingdom, United States of America, Uzbekistan, Viet Nam, Thailand

The boundaries and names shown 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 2011. All rights reserved.
<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled MDR Cases 2009</td>
<td>9600</td>
</tr>
<tr>
<td>MDR in New TB</td>
<td>5200</td>
</tr>
<tr>
<td>MDR in Retreatment TB</td>
<td>4400</td>
</tr>
<tr>
<td>% MDR in New Cases</td>
<td>1.8%</td>
</tr>
<tr>
<td></td>
<td>(1.5-2.3) 2002</td>
</tr>
<tr>
<td>% MDR in Retreatment Cases</td>
<td>6.7%</td>
</tr>
<tr>
<td></td>
<td>(5.5-8.1) 2002</td>
</tr>
</tbody>
</table>
MDR TB Beds in KZN (+/- 745 beds)

- **KGV (224 beds)** - exclusive provincial MDR TB facility (2000)
- Decentralized MDR care in KZN due to bed crises of (2007)
  - **FOSA (2007) stepdown for KGV (187 beds)**
  - 6 Decentralized MDR units now functioning - began March 2008
    - Thulasizwe - 2008 (107 beds)
    - Greytown - 2008 (37 beds)
    - Murchison - 2008 (40 beds)
    - Manguzi - 2008 (40 beds)
    - Catherine Booth - 2010 (40 beds)
    - Doris Goodwin - 2011 (70 beds)

Outpatient MDR treatment program

- Satellite units - If KGV initiates therapy these sites supervise them
- Mosvold, Hlabisa, Madadeni, Charles James, Don Mackensie
- Reviewed monthly at KGV
- Some are at clinic level
- Pilot project Tugela Ferry
KZN/KGV – Management policy

- 2 streams of care at KGV for new patients
- **Admitted cases** - kept for 6 months.
  - XDR and ill patients are prioritized
  - Discharges are allowed for
    - Urgent social issues
    - Aggressive patients
    - Extreme pressure on beds
- **Outpatients** – Started on MDR treatment at our Clinic
  - Some admitted to district hospital / TB centres (a period)
  - Some treated purely at clinic level
  - Refuse to be admitted
  - Needs commitment from referring party to supervise treatment
  - Most are self supervised

National has drafted a policy to implement decentralized care
The Current & Future KGV Complex (930 Beds)

The Completed Hospital complex will comprise of a

- District Hospital – 400 Beds
- MDR/XDR TB Unit - 320 Beds
- TB Spinal & Thoracic Unit – 80 Beds
- Psychiatric Hospital – 130 Beds
## Current Waiting List

<table>
<thead>
<tr>
<th>Waiting List</th>
<th>Pat. Nos.</th>
<th>Waiting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>03/10/2011</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males – awaiting beds</td>
<td>30</td>
<td>3 Weeks</td>
</tr>
<tr>
<td>Females – awaiting beds</td>
<td>50</td>
<td>4 Weeks</td>
</tr>
<tr>
<td>New Outpatients awaiting Rx</td>
<td>26</td>
<td>2 Weeks</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>106</strong></td>
<td></td>
</tr>
</tbody>
</table>

- The reality is there will never be enough beds
- An outpatient program is the only rational option.
MDR TB Clinic

- Aprox. 150 MDR patients started on Rx per month
  - Averaging 40 per week
  - Up to 30 as outpatients / week
  - Up to 20 admissions / week

- See up to 400 patients in biweekly clinic (2500/month)

- Transport issues – difficulty accessing KGV
  - Vital to decentralize MDR care
**DR TB Management - guidelines** (since March 2007)

- National Plan based on **WHO Guidelines** of 2008
- Intensive phase (with injectable) for minimum of **6 months** & at least 4 months after culture conversion.
- Continuation phase - at least **18 months** after culture conversion.
- Treat for at least 24 months if extensive Disease

**New WHO guidelines – 2011 advocate 8/12 injectable phase**

- Decisions to be made by SA TB program on way forward
  - ? Injection period to remain as is (6/12)
  - ? Moxifloxacin for all MDR/XDRs
  - ? Response to Gene Expert results
Standardized MDR Treatment Regimen

6/12 months injectable (minimum)
- Kanamycin (Amikacin)
- Ofloxacin
- Ethionamide
- Terizidone (with Pyridoxine)
- Pyrazinamide
- +/- Ethambutol

18 months (minimum)
- Ofloxacin
- Ethionamide
- Terizidone (with Pyridoxine)
- Pyrazinamide
- +/- Ethambutol
MDR OUTCOMES 2000 TO 2006

- Cured: 44%
- Died: 20%
- Failed: 10%
- Not Evaluated: 7%
- Not treated: 3%
- Defaulted: 16%

Legend:
- Defaulted
- Cured
- Died
- Failed
- Not Evaluated
- Not treated
Standardized XDR Treatment Regimen

6/12 months injectable (minimum)
- Capreomycin
- Moxifloxacin
- Ethionamide
- Terizidone (with Pyridoxine)
- Pyrazinamide
- PAS
- Clofazamine

18 months (minimum)
- Moxifloxacin
- Ethionamide
- Terizidone (with Pyridoxine)
- Pyrazinamide
- PAS
- Clofazamine

Treatment may be modified based on DST results & previous 2\textsuperscript{nd} line drug exposure

Use group 5 drugs to make a regimen

Individualize in MDR treatment failures
Progress of XDR Cohort (60) since 2006

XDR OUTCOMES

- Died: 51%
- Cured: 18%
- Failed: 18%
- Defaulted: 10%
- Unknown: 3%

Data courtesy of Max O Donnel
Male vs female for All TB KGV

- Females: 53%
- Males: 47%

Graph showing the trend from 2000 to 2010 for males and females with specific numbers for each year.
MDR/XDR Age Distribution over the years 2008 - 2010

The chart shows the distribution of MDR/XDR cases by age group over the years 2008 to 2010. The age groups are represented as follows:

- 0-4
- 5-14
- 15-24
- 25-34
- 35-44
- 45-54
- 55-64
- >64

The vertical axis represents the number of cases, with a scale from 0 to 2500. The bars indicate the number of cases for each age group, with the highest number of cases occurring in the 25-34 age group.
HIV in King George Patients 2010

- Positive: 69%
- Negative: 23%
- Unknown: 8%
HIV + MDR TB

- Adverse events are commoner
- Mortality is higher
  - (advanced HIV, advanced TB disease and OIs)
- Often smear neg. making diagnosis difficult
- **HIV + MDR/XDR- add ARVs in ± 2 weeks on** (90%)
- On ARVs – just add MDR treatment
- Cure rates appear to be better with ARVs

Complicating Treatment

- Drug-drug interactions;
- Overlapping toxicities;
- Adherence to multiple medicines
Renal Insufficiency

- Renal function needs close monitoring with HIV patients on ARVs (TDF) & Aminoglycosides.
- If GFR is impaired the frequency +/- the dosages must be reduced.
- Diabetics Nephropathy can complicate this.
Paediatric MDR Patients treated 1998 – 2010

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>1</td>
</tr>
<tr>
<td>1996</td>
<td>0</td>
</tr>
<tr>
<td>1997</td>
<td>6</td>
</tr>
<tr>
<td>1998</td>
<td>3</td>
</tr>
<tr>
<td>1999</td>
<td>3</td>
</tr>
<tr>
<td>2000</td>
<td>5</td>
</tr>
<tr>
<td>2001</td>
<td>4</td>
</tr>
<tr>
<td>2002</td>
<td>8</td>
</tr>
<tr>
<td>2003</td>
<td>13</td>
</tr>
<tr>
<td>2004</td>
<td>19</td>
</tr>
<tr>
<td>2005</td>
<td>24</td>
</tr>
<tr>
<td>2006</td>
<td>26</td>
</tr>
<tr>
<td>2007</td>
<td>41</td>
</tr>
<tr>
<td>2008</td>
<td>50</td>
</tr>
<tr>
<td>2009</td>
<td>78</td>
</tr>
<tr>
<td>2010</td>
<td>90</td>
</tr>
</tbody>
</table>
Health Care workers treated at KGV for Resistant TB

- Most of the patients were referred by General Hospitals
- They were not from TB hospitals or from KGV
- Most of the staff were immunocompromised
- The risk of MDR TB may well be higher in a general hospital
Practical Issues around Gene Expert

It is a rapid test to diagnose new TBs
- Important tool to screen for resistant TB
- Cost for diagnosing TB is significant (at present)
- Of value in diagnosing smear negative TB

Limitations
- Little value in a patient with Previous Normal TB
- Little value in a monitoring response to MDR TB Rx
  - Will show Rif res.
  - Results must be confirmed with full sensitivity.
  - It is a genotypic test and needs confirmation
- It cannot distinguish MDR from XDR TB (full DST needed)

Initial Reports suggest high sensitivity
- False positives may be higher than initially thought
Gains Made in MDR Program

↑ MDR TB patient (finding the problem)

↑ in Beds

↑ in Decentralized MDR Units

Positive impact of revised ARV program

♦ ↓ in A/E like neuropathy, lactic-acidosis, Dyslipidaemia’s

Improved outcomes

♦ ↑ ARV enrollment (MDRs on ARVs irrespective of CD)

Advent of Rapid diagnostics – early diagnosis

(Line Probe & Gene Expert)

National Policy on decentralization

Ongoing Research on new Drugs – TMC 207
Challenges in current KGV program

- Delays in Admission - 2-4 weeks (currently)
- Transport Problems - unable to access KGV timeously
- Lack of Rx Supervision – most are self supervised
- Lack of a Plan for treatment failures (? > 300)
- Difficulty accessing other services for MDR/XDRs patients
- Refusal of some to be admitted/isolated
- Refusal of some to stop working
- Frequent passouts taken by patients
- Side effects of Medication - (Deafness/Renal/Electrolyte/CNS)
- Legal Issues - Confidentiality
- Impact of Gene Expert
- Lack of treatment options – esp. for XDRs
Lessons in MDR Management

- Adequately counsel patients
- Treat HIV early
- Actively Monitor & Treat side effects
- Cannot admit everyone
- Social Support Critical
- Working as a Team is Vital
- Empower nurses to take more of a hand
- Be Innovative to overcome problems
- Proper monitoring & Evaluation is Vital
- Treatment support is Crucial

Despite high numbers of MDR & XDR in KZN, with our dedicated and devoted staff we have made a difference.
Acknowledgements

Department of Health
District Office
Management & Staff of KGV

&

A Special Thanks to

All the Health Care workers who tirelessly continue the fight against TB and MDR TB often at great risk to themselves.

Thank You

iqbal.master@kznhealth.gov.za