

# **Multi-drug resistant and Extensively drug resistant TB in India**

## **Consensus statement on the problem, prevention, management and control**

**From the consultative meeting of national experts organized by the TB Research Centre, ICMR, Govt. of India, on 14-15 September 2007, at Chennai**

Based on the review of published evidence, international and national guidelines, and the experience of participants and their institutions in the management of multi-drug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB), the following consensus was reached.

### **Epidemiology**

As per the estimates from the State representative drug resistance surveillance (DRS) survey in Gujarat and various district level DRS studies, the prevalence of MDR-TB in new smear positive pulmonary TB (PTB) cases is  $\leq 3\%$  and 12 to 17% amongst smear positive previously treated PTB cases. Review of studies with representative samples do not indicate any increase in India of the prevalence of drug resistance over the years.

Although isolated reports, both published and unpublished, indicate the existence of XDR-TB in the country, it is not possible as yet to estimate its magnitude and distribution from the available data.

### **Definitions**

MDR-TB is defined as resistance to isoniazid and rifampicin, with or without resistance to other anti-TB drugs.

XDR-TB is defined as resistance to at least Isoniazid and Rifampicin (i.e. MDR-TB) plus resistance to any of the fluoroquinolones and any one of the second-line injectable drugs (amikacin, kanamycin, or capreomycin).

### **Prevention of MDR-TB and XDR-TB**

The use of inadequate regimens and the absence, or inappropriate application, of directly observed treatment can lead to the development of drug resistance and potentially to an increase in drug resistance levels amongst the community. The implementation of a good quality DOTS programme will prevent the emergence of MDR and XDR-TB in the community. Therefore the highest priority is to further improve the quality and reach of DOTS services in the country. For this, all health care providers managing TB patients need to be linked to RNTCP and operational challenges in implementing DOTS needs to be addressed. The proportion of TB patients being treated outside the DOTS strategy needs to be minimized. The International Standards of TB Care need to be used by RNTCP and professional medical associations as a tool to improve TB care in the country. The fluoroquinolone group of drugs are not as yet recognized, nor recommended, as first line anti-TB drugs, and their use should be restricted only to the treatment of confirmed MDR-TB cases.

### **Management of MDR-TB**

National guidelines and plans for scaling up management of MDR-TB have been developed under RNTCP. In the interim, while RNTCP DOTS-Plus services are being expanded across the

country, all health care providers in the public and private sector managing MDR TB cases, need to adhere to the following:

- MDR-TB management to be preferably undertaken only at selected health institutions with experience, expertise and availability of required diagnostic and treatment facilities
- Diagnosis of MDR-TB
  - Drug resistance may be suspected based on history of prior treatment (e.g. smear positive case after repeated treatment courses, Cat II failure etc.) and/or close exposure to a possible source case confirmed to have drug-resistant TB
  - For patients in whom drug resistance is suspected, diagnosis of MDR-TB should be done through culture and drug susceptibility testing from a quality-assured laboratory.
- Interpretation of DST Results
  - Drug susceptibility test results of the 1<sup>st</sup> line anti-TB drugs pyrazinamide, streptomycin, and ethambutol should be interpreted with caution due to the poor reproducibility of these results even under optimal laboratory conditions.
  - Drug Susceptibility Test (DST) results of 2<sup>nd</sup> line anti-TB drugs\* should be interpreted with great caution due to limited capacity of laboratories, absence of quality-assurance, and lack of standardized methodology.
- Treatment regimen
  - All relevant investigations to be performed prior to treatment initiation
  - Preferably the standardized regimen as recommended in the national DOTS-Plus guidelines should be used [6(9) Km Ofx Eto Cs Z E / 18 Ofx Eto Cs E] †
  - If results of 2<sup>nd</sup> line DST from an accredited laboratory are available, an individualized regimen may be used in such patients after obtaining a detailed history of previous anti-TB treatment
- Duration of treatment
  - At least six months of Intensive Phase (IP) should be given, extended up to 9 months in patients who have a positive culture result taken at 4<sup>th</sup> month of treatment
  - Minimum 18 months of Continuation Phase (CP) should be given following the Intensive Phase
- Follow-up schedule
  - Smear examination should be conducted monthly during IP and at least quarterly during CP
  - Culture examination should be done at least at 4, 6, 12, 18 and 24 months of treatment
  - Relevant additional investigations should be performed as indicated
- Treatment adherence and support

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\* Fluoroquinolones (Ciprofloxacin, Ofloxacin, Levofloxacin, Moxifloxacin, Gatifloxacin, Sparfloxacin, Pefloxacin); Kanamycin, Amikacin, Capreomycin, Ethionamide, Prothionamide, Cycloserine and PAS

† Km = Kanamycin; Ofx=Ofloxacin; Eto=Ethinamide; Cs=Cycloserine; Z=Pyrazinamide; E=Etambutol

- All patients initiated on treatment and their family members should be intensively counseled prior to treatment initiation and during all follow-up visits
- To reduce the risk of development of resistance to second-line anti-TB drugs and promote optimal treatment outcomes, all efforts should be made to administer treatment under direct observation (DOT) over the entire course of treatment
- If DOT is not possible, attempts to ensure treatment adherence should be made by
  - Checking empty blister packs; and
  - Follow up visits at least every month
- Documentation of treatment
  - Health care facilities/practitioners managing MDR-TB patients should maintain a systematic record of treatment regimen, doses, duration, side-effects, investigation results and treatment outcome for all patients initiated on second-line treatment.

### **Public health responsibilities of health care providers**

- Health care facilities/practitioners managing confirmed MDR-TB patients should inform their respective District TB Officer regarding treatment initiation and outcome of all MDR-TB cases
- Prior to treatment initiation and on all follow up visits the patient and family members should be counseled on all aspects of MDR-TB
- All house hold contacts of the MDR-TB patients should be screened for active TB disease
- Infection control measures
  - All large health care facilities need to have an infection control (including air-borne infection) plan and a team for implementation of measures to prevent nosocomial transmission of TB and other air-borne infections
- Statements to the press/media on MDR-TB and XDR-TB should be made with extreme caution and after requisite verification and authentication