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

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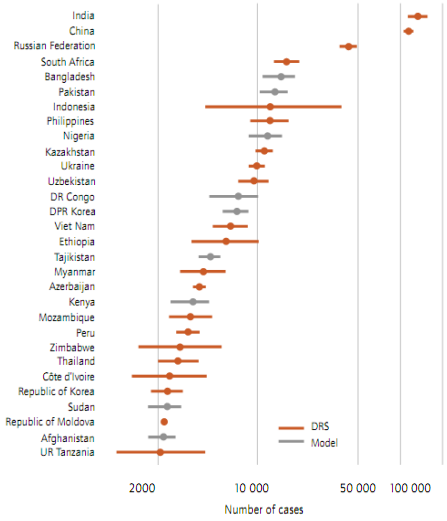
Glossary:

- 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.

MDR-TB in India: Access to treatment vs.Denial :

MDR-TB, TB/HIV AND OTHER CHALLENGES

Multidrug-resistant TB (MDR-TB)	2005	2006	2007
	Number (% of estimated ss+ MDR-TB)		
Estimated incidence of ss+ MDR cases	96 663	98 155	99 639
Diagnosed and notified	34 (0.04%)	33 (0.03%)	146 (0.15%)
Registered for treatment	34 (0.04%)	33 (0.03%)	88 (0.09%)
GLC	0	0	0
non-GLC	34	33	88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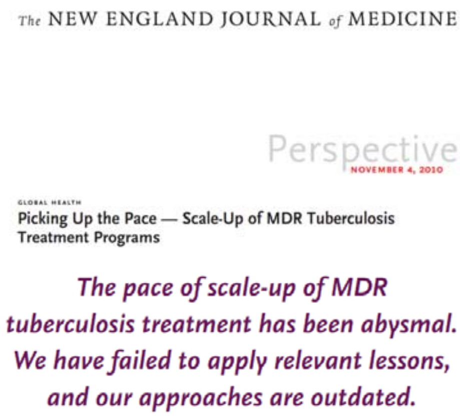
Medicine and Society

The Revised National Tuberculosis Control Programme in India: Time for revision of treatment regimens and rapid upscaling of DOTS-plus initiative

ANURAG BHARGAVA, YOGESH JAIN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Perspective
NOVEMBER 4, 2010

GLOBAL HEALTH

Picking Up the Pace — Scale-Up of MDR Tuberculosis Treatment Programs

The pace of scale-up of MDR tuberculosis treatment has been abysmal. We have failed to apply relevant lessons, and our approaches are outdated.

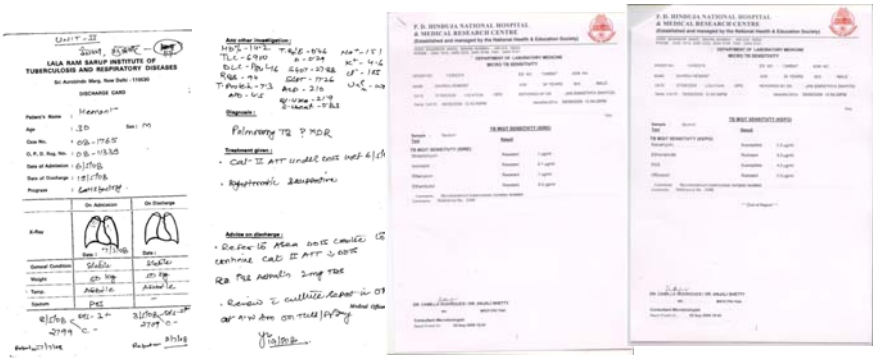
34 year old, non-smoker
Has 2 young children.
Drives an autorickshaw.
History of symptoms of Pulmonary TB off and on since ………..years.

- Ist episode of treatment :1989.
- 1990s: recurrence of disease
- 1992,1996,1998.
- 2000: Rxed with Rifampicin containing regime.
- 2004: Retreatment regime of RNTCP + ethionamide + quinolone . Interrupted therapy because of cost.
- No lasting improvement in symptoms.

The type of regimes received by patient in NTP/RNTCP

Pre 1993	TYPE OF REGIME	INTENSIVE PHASE	MAINTENANCE PHASE	DURATION
Pre-1993	New Cases	Streptomycin, INH and Thiacetazone	INH and Thiacetazone	12 months
Post 1993	Retreatment regime	2 SHRZ	4 $(SHRZ)_2$	6 months
Post 1997	Retreatment regime	2 SHRZ	4 $(SHRZ)_2$	6 months
Post 2002	Retreatment regime	2 $(SHRZE)_3$ 1 $(HRZE)_3$	5 $(HRE)_3$	8 months

H: Isoniazid, R : Rifampicin, Z: Pyrazinamide, E: Ethambutol



6 DRUG RESISTANCE on DST:
STREPTOMYCIN, INH,RIFAMPICIN,ETHAMBUTOL, ETHIONAMIDE OFLOXACIN

- **On Pyrazinamide, Inj. Amikacin, Moxifloxacin, PAS, Cycloserine, Clofazimine since 2009.**
- **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

Drug	Initial	Acquired
INH	10.1%-23.4%	47.0%-87.1%
RIF	1.7-8.5 %	6.1- 67%
MDR	0.7-5.3	6.1- 67 %

Sources: Paramsivan 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

Treatment Regimens

Category of Treatment	Type of Patient	Regimen*
Category I	New sputum smear-positive Seriously ill** new sputum smear-negative Seriously ill** new extra-pulmonary	$2H_3R_3Z_3E_3+$ $4H_3R_3$
Category II	Sputum smear-positive Relapse Sputum smear-positive Failure Sputum smear-positive Treatment After Default Others***	$2H_3R_3Z_3E_3S_3+$ $1H_3R_3Z_3E_3+$ $5H_3R_3E_3$
Category III	New Sputum smear-negative, not seriously ill New Extra-pulmonary, not seriously ill	$2H_3R_3Z_3+$ $4H_3R_3$

Source : Managing the RNTCP in your area: Module 1-4, april 2005. central TB division . GOI.

RNTCP CATEGORY IV REGIMEN: 6 (9) Km Ofx (Lvx) Eto Cs Z E / 18 Ofx (Lvx)Eto Cs E

DOTS Plus Guidelines January 2010.

- This Patient failed on SHRZ ---- treated with SHRZ **E** 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"

Espinal MA. Time to abandon the standard retreatment regimen with first-line drugs for failures of standard treatment. *Int J Tuberc Lung Dis* 2003;**7**:607–8.

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."

Farmer P, Bayona J, Becerra M, Furin J, Henry C, Hiatt H, *et al.* The dilemma of MDR-TB in the global era. *Int J Tuberc Lung Dis* 1998;**2**:869–76.

The question of resources:

70 million dollars per jet