Revisions to RNTCP, to Keep Pace with the Changing Needs, Evidence and Global Recommendations – Part 1

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Tuberculosis history is one of the political, scientific, and medical failures.[1] The growing importance of TB as a public health problem and the potential for cost-effective control using currently available tools was recognized by World Health Organization (WHO) in 1991, led to a reassessment of ongoing global TB control efforts. The persistence of TB has been due chiefly to the neglect by governments, poorly managed TB control programmes, poverty, population growth and migration, and rise of TB cases in HIV endemic areas.[2] To help address the situation, a new framework for effective TB control was then developed and a global strategy called *Directly Observed Treatment Short-course* (DOTS) was introduced. The five elements of the DOTS strategy, considered essential for global TB control are

(i) Political commitment,

(ii) Case detection using sputum microscopy among persons having symptoms of TB (most importantly prolonged cough),

(iii) Standardized short-course chemotherapy to all cases of TB under proper case-management conditions including direct observation of treatment (DOT),

(iv) Uninterrupted supply of quality-assured drugs, and

(v) Standardized recording and reporting system enabling outcome assessment of each and every patient and assessment of the overall programme performance. [3, 4, 5]

Based on the findings and recommendations of a joint review conducted by Government of India (GoI), WHO and the Swedish International Development Agency (SIDA), India launched the *Revised National Tuberculosis Control Programme* (RNTCP) in 1992. By incorporating the elements of internationally recommended DOTS strategy, RNTCP is built upon the existing infrastructure of National Tuberculosis Programme (NTP). After successful piloting of DOTS during 1992 – 1997, geographic scaling up of RNTCP was started in 1997, and entire country coverage was achieved by March 2006. [6, 8]

After the development of the DOTS strategy and its wide adoption in the NTPs across the world by most of countries, WHO along with the partners have continually worked on additional complementary policies and strategies to address the remaining major constraints to achievement of global TB control targets. These include expanding access to diagnosis and treatment through community TB care, and public–private mix (PPM) approaches aimed at engaging all care providers - both public and non-public in DOTS implementation. After the declaration of *Millennium Development Goal*s (MDG)[7], the focus shifted to achieve the MDG and the related Stop TB Partnership targets for TB control. In 2006, a coherent global strategy called *'the STOP TB Strategy'* was launched with a vision of *"a world without TB"*. Building on the DOTS strategy, the Stop TB strategy expanded its scope to address remaining constraints and challenges to TB control. The Stop TB Strategy has six principal components:

(i) Pursue high-quality DOTS expansion and enhancement;

(ii) Address TB/HIV and MDR-TB and other special challenges;

(iii) Contribute to health system strengthening;

(iv) Engage all care providers;

(v) Empower people with TB, and communities; and

(vi) Enable and promote research.[8]

When global TB control strategy was revised from DOTS to the Stop TB Strategy, same was immediately adopted in RNTCP. During the second phase (2006–2011), RNTCP focused to improve the quality and reach of services, and reach global case detection and cure targets[9]. DOTS was strengthened by the six-point new Stop TB strategy, mainly to achieve TB-related Millennium Development Goal (MDG) and the Stop TB partnership targets.

To keep pace with the changes in global TB control strategies and recommendations, latest evidence and operational feasibility, time to time RNTCP made efforts to make

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revisions or amendments in the programme.

Some Major Revisions:

Revisions to Objectives:

During first and second phase of RNTCP, the objectives were *to achieve and maintain*

(i) a cure rate of *at least* 85% among newly detected smear-positive (infectious) pulmonary tuberculosis cases; and

(ii) case detection of *at least* 70% of the expected new smear positive Pulmonary TB cases in the community.[6]

However, during second phase, RNTCP shifted the focus to ensure universal access to quality assured TB diagnosis and treatment services under the programme.[9]

The vision of the Government of India is for a *"TB-free India"* with reduction of the burden of the disease until it is no longer a major public health problem. To achieve this vision, the RNTCP has now adopted the new objective of *"Universal Access for quality diagnosis and treatment for all TB patients in the community"*. In addition, RNTCP defined, objectives for 2012–2017 are:

- To achieve 90% notification rate for all TB cases in the community.
- To achieve treat success rate of 90% for all new and 85% for re-treatment TB cases.
- To significantly improve the successful outcomes of treatment of Drug Resistant TB Cases.
- To achieve decreased morbidity and mortality of HIV associated TB.
- To improve treatment outcomes of TB care in the private sector.[10]

Revisions to Diagnostic Algorithms:

As the smear positive pulmonary tuberculosis is the most infectious form of TB, from public health point of view it is important to detect and treat such cases as early as possible on priority so as to cut the chain of transmission of disease in the community. Hence, sputum smear microscopy is the most widely used and acceptable testing tool for diagnosing smear positive pulmonary TB (PTB).[6]

In the beginning, RNTCP defined the TB suspect as one who has *3 weeks of cough* and all cases to be subjected for *3 sputum samples examination for AFB*.[6] However, after the introduction of external quality assurance (EQA) for sputum microscopy, the definition was revised as *"persons having cough of 2 weeks or more, with or without other symptoms, are referred to as pulmonary TB suspect and that they should have 2 sputum samples examined for AFB"*. In the same way, the definition of smear positive PTB was also revised as *"a patient with one or two smears being positive for AFB out of the two sputum specimens subjected for smear examination by direct microscopy"*.[11]

During second phase of RNTCP, diagnostic algorithm was introduced for diagnosis of paediatric PTB. During January-February 2012, in consultation with Indian Academy of Paediatrics, the national guidelines on paediatric TB diagnosis and management were revised based on both the recent evidence and the advances. The details of these revised guidelines on paediatric TB diagnosis and treatment recommended under RNTCP can be found at tbcindia.nic.in website.[12]

RNTCP also developed and revised the diagnostic algorithm for diagnosis of lymph node TB, one of the most common types of extra-pulmonary TB both in adults and children, which are adopted in the operational guidelines and training modules of RNTCP.[11, 12]

Revisions to Treatment Regimens:

Using the first line anti-TB drugs, RNTCP introduced the *three standardized thrice-weekly intermittent treatment regimens*. Thus, the TB patients were also classified into 3 different categories for the purpose of the treatment – category I, II and III. The ant-TB drugs being used in the regimens are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) and Streptomycin (S). New TB patients were getting either category I ($2H_3R_3Z_3$ E_3 / 4 H_3R_3) or category III ($2H_3R_3Z_3$ / 4 H_3R_3). Right from the beginning, drugs were supplied through patient wise boxes (PWB), making convenient for drug management as well as for administering Directly Observed treatment (DOT).[6]

In view of the higher levels of INH resistance among new TB patients and lack of facilities for routine testing for INH resistance among, the fourth edition of WHO TB treatment guidelines issued in 2009 recommended against omission of ethambutol during the intensive phase of treatment for patients with non-cavitary, smear-negative pulmonary TB or extra-pulmonary disease who are known to be HIV-negative.[13] Following this, Joint Monitoring Mission 2009 of RNTCP has recommended that *"the Central TB Division (CTD) should proceed with the plan of making a single regimen for all new patients"*.[14]

In the light of these recommendations and following meetings of National Experts (September 2009) and National Task Force for Medical colleges (October 2009), CTD issued e-mail circular to all the states

Table1: Treatment regimen, type of patients and regimens prescribed under RNTCP, with effect from October 2010[15, 11]

Treatment group	Type of patient	Treatment regimen*	
New**	Sputum smear-positive Sputum smear-negative Extra-pulmonary Others	$2(H_3R_3Z_3E_3)$	$4(H_3R_3)$
Previously treated***	Smear-positive relapse Smear-positive failure Smear-positive treatment after default Others	$2(H_3R_3Z_3E_3S_3)$ / $1(H_3R_3Z_3E_3)$	$5(H_3R_3E_3)$

*The number before the letters refers to the number of months of treatment. The subscript after the letters refers to the number of doses per week.
The dosage strengths are as follows: Isoniazid (H) 600 mg, Rifampicin (R) 450mg, Pyrazinamide (Z) 1500mg, Ethambutol (E) 1200mg, Streptomycin (S) 750mg.
• Patients who weigh 60 kg or more receive additional rifampicin 150 mg.
• Patients who are more than 50 years old receive streptomycin 500 mg. Patients who weigh less than 30 kg, receive drugs as per Paediatric weight band boxes according to body weight.
** New includes former categories I and III
*** Previously treated is former category II.

and districts on October 07, 2010 stating that *"it has been decided to have only 2 first line TB treatment regimens in future and discontinue the 3-drug Cat–III regimen from the guidelines. Further, these regimens will be called regimen for 'new' (Category I) and 'previously treated' (Category II) cases. These changes are applicable with immediate effect"*.[15] Details of the revisions to the treatment regimen are shown in Table 1.

In addition, RNTCP also introduced paediatric patient-wise boxes since 2006, making India the first country to do so.[9] In the beginning, there were *4 weight bands and two generic patient-wise boxes* which were used in combination to treat paediatric TB patients in *4 weight bands*.[16, 9]

Based on the recent evidence, RNTCP treatment guidelines for TB in children were revised in 2012. Though intermittent therapy continue to be the mainstay of treating paediatric TB patients under RNTCP, exception is made for a select group of seriously ill admitted patients who should be given daily supervised therapy during their stay in the hospital. The treatment will be shifted to thrice weekly DOT regimen after discharge form hospital in all such cases. Different dosages are recommended for different weight-band groups and also for daily vs. thrice weekly regimen.[12]

Hence, the major revisions made to the paediatric drug dosage are as below:

- There will be *six weight bands and three generic patient wise boxes* will be used in combination to treat patients in the *six weight bands*.
- All paediatric TB patients should be shifted to next weight band if a child gains one kilogram or more, above the upper limit of the existing weight band.
- As mentioned above there will be only two treatment categories – one for treating 'new' cases and another for treating 'previously treated cases'.[12]

Other important revisions to RNTCP, global TB control strategy and the issues and challenges will be discussed in the later parts of the article to be published in the coming issues of this journal.

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