50 Years of Tuberculosis Control in India: Progress, Pitfalls and the Way Forward

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India established the National Tuberculosis Control Project (NTCP) 50 years ago and re-designed it as Revised NTCP (RNTCP) 19 years ago. Tuberculosis (TB) control was beset with obstacles — BCG vaccination was found ineffective in TB control in 1979; human immunodeficiency virus began spreading in India since 1984 with TB as the commonest opportunistic disease; multi-drug resistance was found to be prevalent since 1992. The World Health Organization declared TB as global emergency in 1993. Yet, RNTCP was extended to the whole nation very slowly, taking 13 years from inception. The first objective of RNTCP, namely 85% treatment success has been achieved and case-fatality had dropped by 90%. Still, TB burden continues to remain huge; about half the cases are not getting registered under RNTCP; pediatric TB is neglected; TB drains national economy of US$ 23 billion annually. Therefore, TB control is in urgent need of re-design and re-invigoration, with additional inputs and system re-organization to cover all such gaps. We highlight the need for Public Health infrastructure under which all vertical disease control projects such as RNTCP should be synergized for better efficiency and for establishing Public Health Surveillance for collecting denominator-based data on incidence and prevalence to guide course corrections. India ought to spend 3 to 5 times more on TB control than at present. Control needs clear epidemiologic definition and measurable parameters for monitoring the level of control over time. TB control is both a measure of, and a means to, socioeconomic development.

Keywords: *Annual Risk of TB infection (ARTI), Pediatric TB, Public Health, Revised National TB Control Project (RNTCP), Tuberculosis (TB), TB Control.*

India launched the National Tuberculosis Control Project (NTCP) 50 years ago, in 1962 [1]. Much progress has been achieved since then, but many problems also persist. About 60% of world's tuberculosis (TB) cases are in the South-East Asia and Western Pacific regions, and India and China together account for almost 40% of them [2]. We bear an unfair burden of TB-17% of global population with 26% of global TB [3]. A decade ago we were 16% of global population with 20% of global TB [4]. The proportional increase reflects poor control in India and better control elsewhere, particularly in China where TB burden has declined to 14% of global total [3,5].

Countries with Public Health infrastructure had remarkable reduction in TB mortality and transmission of *Mycobacterium tuberculosis* (MTb) beginning in the 19th century long before anti-TB drugs became available [6]. Success resulted from amelioration of the social determinants of TB [6]. India, without Public Health Surveillance (PHS), remains even today without validated denominator-based incidence, prevalence or mortality data. The secular downward trend due to economic improvement remains un-measured. NTCP depended on bio-medical interventions for TB control. The battle was unequal–MTb is contagious, highly prevalent, with latent infection in children, adolescents and adults. About 60% of men cumulatively become latently infected [7]. TB control does not directly follow treatment of disease, unless socio-behavioral determinants are redressed or the 'pool' of latently infected is reduced [8]. For the latter, effective management of childhood TB, both infection and disease, particularly the former, is key [8-10]. Detection of infection requires close links with healthcare, precluded by the vertical design [8-10]. India has a long way to go to reach the level of TB control achieved by developed countries in the last century. Drug treatment without achieving control resulted in development of drug resistance – both multi-drug resistance (MDR) and lately extensive drug resistance (XDR) [11,12]. MDR and XDR MTb breeds true through secondary infections – making future prospects of control more difficult.

The synergy of human immunodeficiency virus (HIV) infection and TB exacerbates morbidity and accelerates mortality. HIV pandemic reached India two decades after the launch of NTCP [13]. India would have been in happier situation had we substantially reduced TB

incidence before HIV reached India. Developed countries also had a setback in TB control when HIV pandemic hit them, but their Public Health infrastructure was robust enough to resolve it fairly fast.

Challenged with unrelenting TB problem, the project was improved as the Revised NTCP (RNTCP) in 1993 [1]. Using treatment protocols India has achieved drastic reduction in case fatality, which is only one element in control. In epidemiological terms control is reduction of incidence to a pre-defined level, within a stipulated period.

Epidemiology is the foundation science of public health; its systematic application requires functional public health infrastructure, lacking in India [14]. Epidemiology, therefore, remains in research and teaching modes. In this communication, we will explore the gaps in TB control efforts and suggest the way forward.

Early History of TB Control

During the early 20th century, TB could be diagnosed microbiologically, but there was no anti-TB drug. For rest and fresh air, sanatoria were established in Europe. India's early TB sanatoria were in Tiluania (near Ajmer, 1906), Almora (1908), Shimla (1909) and Madanapalle (Andhra Pradesh, 1914) [15-17]. Johannes Frimodt-Moller became medical superintendent in Madanapalle in 1940 [15-17]. He introduced BCG vaccination in 1948; the Government of India (GoI) established a BCG production unit in Chennai [15-17]. One of us (TJJ) learned TB epidemiology from Frimodt-Moller [18].

BCG was believed to prevent MTb infection [7,15, 16]. The Indian Council of Medical Research (ICMR) and Government of India (GoI) had conducted country-wide surveys and found TB rampant everywhere. In 1951 mass BCG campaign was begun. During 1949-1952, soon after their discovery, Para amino salicylic acid (PAS), streptomycin (SM) and isoniazid (INH) were introduced in India and GoI established a TB Chemotherapy Centre (renamed TB Research Centre and today National Institute for Research in TB) in Chennai in 1956 [15-17]. In 1961 a district TB diagnosis and treatment Programme was designed, using which NTCP was launched in 1962 [15-17].

Post-independence, GoI re-designed health ministry abolishing the posts of Public Health Commissioner at GoI and Directors of Public Health in most States [18]. Public Health functions were assigned to Directorate of Health Services (DHS) [18]. Thus, disease control, including NTCP, came under DHS as vertical and single-disease oriented [4,18]. Since then, attempts to re-establish a Public Health Service in India have been unsuccessful [14,18,19]. National leaders understand biomedical advances, not the value of Public Health [14, 18,19].

NATIONAL TB CONTROL PROJECT (NTCP)

NTCP was designed for a two pronged attack on TB – BCG vaccination and TB treatment. State government (responsible for healthcare) and GoI (responsible for disease control) had to be full partners. The policy was to give treatment free of charge. Chemoprophylaxis (for latent TB) was considered impractical because of the massive numbers of subjects, and non-essential as BCG was believed sufficient to control MTb infection [16]. To measure vaccine efficacy of BCG, a large trial was designed in Chingleput District (Tamil Nadu) under the TB Research Centre [16,20].

In 1961, treatment demonstration was established in Anantapur district (Andhra Pradesh) [16]. *"The Anantapur DTC [district TB control] became operational quickly and functioned well because, in addition to the state government's component, NTI [National TB Institute, Bangalore] staff also worked. By October 1961 the NTI trainers and trainees withdrew. From then on, there was a decline in the services of this DTP. The Anantapur project suffered from not being recognized by the Andhra State government as essentially their responsibility"* [16].

Yet, unmodified NTCP was launched nationally in 1962. Retrospectively, TB treatment in project mode, separated from healthcare, was not optimal for success. This flaw, recognized in 1961, has not been rectified, for which the sharing of health management responsibilities between GoI and State governments must be re-designed [14, 18, 19].

Tuberculosis Control in Crisis, 1980s and 1990s

In 1978, BCG vaccination was shifted under the Expanded Programme on Immunisation. In 1979, preliminary results of the BCG trial showed no protection against MTb infection [20, 21]. This unexpected finding evoked scientific discussion but no GoI response [20-22]. NTCP was now without an effective vaccine to control TB. The HIV pandemic of early 1980s also did not evoke GoI response until academic investigators detected it in India in 1986 [13,23,24]. These glaring omissions of non-response to two major factors adversely affecting TB control illustrate why Public Health infrastructure, capable of recognition of all diseases, is unavoidable for their successful control.

HIV infection was spreading in India since 1984 [13, 23,24]. Volunteer blood donors, and even pregnant women without behavioral risk factors, were found infected in

1988/89–the epidemic was getting into general population [24,25]. West was by then aware of HIV-TB synergy; in 1992 the first report of clinical profile of AIDS in India showed TB as the commonest secondary infectious disease [26].

In 1992, the Swedish International Development Agency, WHO and GoI evaluated NTCP and found reduction in mortality, but no reduction of TB burden [7]. Also multi-drug resistance (MDR) in TB was widely recognized in India [11, 27]

Thus, 5 factors signaled crisis – (*i*) BCG without role in TB control; (*ii*) no alternate primary prevention tool; (*iii*) failure of NTCP in reducing TB burden; (*iv*) HIV pandemic; and (*v*) increasing prevalence of drug resistance.

REVISED NTCP (RNTCP)

In 1993, the WHO declared TB as a global emergency, devised the directly observed treatment – short course (DOTS), and recommended it for all countries [1,7,17]. The NTCP evaluation partners jointly designed RNTCP the same year. The objectives of RNTCP were to achieve at least 85% cure rate among the new smear-positive (NSP) cases of pulmonary TB, and a case detection rate of at least 70% [1,7]. NTCP had created wide public awareness of TB, 446 district TB centres, 330 TB clinics and 47,600 hospital beds for TB, treating over 1.3 million cases annually [7]. In spite of these advantages, there was delay in achieving RNTCP and DOTS coverage throughout the country–piloted in 1993, launched in 1997, 50% districts covered in 2003 and all districts covered by 24 March 2006 [1,7, 16,17]. The opportunity of WHO declaring TB as emergency was not used to put RNTCP on war footing. Instead it took 13 years to build up; meanwhile HIV was spreading; drug resistance was increasing; and NSP cases were not declining.

The Current Status of TB Situation in India

RNTCP has achieved very high cure rates. For those diagnosed as NSP TB at the designated microscopy centres (DMS) and put on DOTS, case fatality has dropped to 4.2 to 4.7% during 2000 to 2003 [7]. Without treatment the case fatality is believed to be about 80%, suggesting 90% reduction in case fatality. Thus the first objective of RNTCP is being achieved. WHO estimates overall TB mortality of 26 and 24/100,000 in 2010 and 2011, respectively [2,3]. This translates to about 1000 deaths a day, or 2 deaths every 3 minutes. TB accounts for 17.6% of all deaths from communicable disease, and for 3.5% of all cause-mortality, in India [3]. TB continues as India's public health emergency.

The proportion of persons with pulmonary TB getting treatment is between 59% (WHO) and 70% (RNTCP) [7, 3]. The WHO estimates that annually there are 2.2 million cases (181/100,000 population), without appreciable decline over the years [2]. An estimated 40-50% of those with pulmonary TB seek care in private sector healthcare clinics [7,3]. They pay for diagnosis and treatment, but get non-standard drug regimen for less than recommended duration and are believed to contribute to high case fatality and drug resistance [28].

The current estimates are that at least 3% NSP cases and 12% those with relapse have MDR TB [11,29]. Only after failure of DOTS to cure TB is sputum cultured for drug sensitivity test (DST) under RNTCP, thus delaying detecting drug resistance. Recently extensively drug resistant (XDR) TB has been detected in several tertiary care institutions in India [12].

The current annual economic loss to the country on account of TB is estimated to be Rs. one lakh and two thousand crores ($ 23.7 billion) [30]. But India had been spending only about Rs. 500 crores ($ 100 million) on TB control [5, 30] which was raised to around $ 200 million recently [2]. Independent assessment puts the requirement for effective TB control as over Rs. 3000 crores ($ 600 million) [5]. Thus TB acts as a spotlight on several deficiencies of the health management system: the lack of public health infrastructure; failure to apply epidemiology in disease control; the neglect of health economics resulting in unwillingness to allocate sufficient funds to face a national health emergency like TB.

Pediatric TB, the Achilles Heel of TB Control

When RNTCP was designed, the final result of the 15-year Chingleput BCG trial had not been fully analyzed and published [31]. There was lingering hope that the interim data analysis (1978-79) was incomplete and that the final results would prove BCG a tool of primary prevention. However, BCG showed no efficacy against MTb infection or reactivation of latent infection [31]. Thus, TB control had to be re-designed [8]. The objective of 70% case detection and 85% cure were set on modeling but not field evaluation [9]. We do not believe DOTS alone will control TB, even if rates of case detection and cure increased further [8,10]. Addressing childhood MTb infection is key to TB control [8-10].

Recognizing this need, a workshop on childhood TB was organized in 2003 by TB experts of RNTCP and Indian Academy of Pediatrics. Its recommendation was: "*Asymptomatic children under 6 years of age, exposed to an adult with infectious (smear positive) tuberculosis, from the same household, will be given 6 months of isoniazid (5 mg per kg daily) chemoprophylaxis*" [32]. It was agreed that "*pediatric-focused monitoring may*

preferably be an integral part of the programme" and that "*A revision of the RNTCP training modules will be undertaken to include pediatric TB issues*" [32].

Thus, tracing of household contacts of NSP cases is an added intervention; all under-6 children are to be screened for symptomatic TB and treated if so diagnosed. All others ought to be offered INH preventive treatment. The underlying assumption is that all such children would already have been infected by the NSP case of pulmonary TB. In a study with careful search, 100 at-risk children were screened; 99 were infected, among whom 55 had chest radiographic signs of TB [33,34]. The assumption that all <6 children would have been infected may reflect reality [35]. If given prophylaxis, they will be cured of infection. The critical value of this intervention has not been widely appreciated [36]. In Krishna district (Andhra Pradesh), among 825 NSP case households 172 contacts <6 were enumerated; two-thirds had been screened for TB disease and none found [36]. Ninety seven children (84%) were initiated on Isoniazid preventive therapy but the remaining 16 children were not treated for want of drugs at the health centre [36]. In the former study pediatricians, and in the latter paramedical workers screened children for symptomatic TB. The contrast is striking; unfortunately RNTCP does not have sufficient medical officers to do follow-up in families of NSP TB patients. These two studies illustrate the complexity of contact tracing, screening, and preventive therapy. Currently coverage is less than optimal. About half of TB cases are seen in private sector and lost from TB Registry; children in such households are not even identified. If screening is suboptimal, children with early TB disease may receive INH monotherapy, which is unsound medical care [36].

Preventive treatment can sterilize latent infection. From this viewpoint, preventive chemotherapy is the only biomedical TB control intervention we have, while DOTS is the mortality reduction intervention that will enable the buy-in of TB control by the public. Detection of pediatric MTb infection has to be brought under systematic management; pediatric TB disease has to be kept under close clinical scrutiny. In countries practicing Public Health surveillance, 20-25% of all TB is in children. In India the proportion of childhood TB is a mere 2%, illustrating its gross neglect [4].

The magnitude of childhood TB disease is unknown in India. Regional data from the WHO in 2007 showed that smear-positive TB in children aged <14 years accounted for 0.6%–3.6% of reported cases. However, because <95% of cases in children <12 years of age are smear negative, these data underestimate the true burden of TB [37]. It is estimated that in developing countries, nearly 8-20% of the deaths are caused by pediatric TB [38].

Infected children accumulate in the 'pool' of latent infection, from which individuals exit with disease [39]. TB control requires shrinking of the magnitude of the pool. If detection of pediatric MTb infection has to be brought under systematic management, pediatric TB disease has to be kept under close clinical scrutiny. Only in May 2012 has TB been made "notifiable," endorsing the arguments about the critical need for complete data on TB cases [8, 40].

We have proposed the definition of TB control as 5-10% annual reduction of the incidence of MTb infection in children, monitored through tuberculin skin testing [9, 10]. This is realistically achievable. A nation-wide survey in India among young children showed very high figures of annual risk of MTb infection (ARTI) in almost all the regions- highest in north zone (1.9%) followed by west zone (1.8%), east zone (1.3%) and lowest in the south zone (1.0-1.1%) [41]. Under NTCP the goal of achieving a level of ARTI of 1% during the first 14 years of life had been mooted [8]. That translates as ARTI of 0.07% from infancy till 14 years. Reduction by 5% annually will result in 0.07% incidence of infection in 20 years; reduction by 10% will achieve it in 10 years [9,10].

THE WAY FORWARD FOR TB CONTROL IN INDIA

Controlling TB is an extremely complex task but it is extremely urgent also. Under India's Constitution, responsibility for disease control belongs to GoI and healthcare to State. Although TB control is a GoI project, the tool of intervention is healthcare– case diagnosis and treatment. All healthcares are shared between public and private sectors; hence the success of TB control will depend upon how well these 3 partners cooperate in managing and monitoring TB in a seamless manner. Thus, TB control is in urgent need of re-design.

Healthcare functions on the basis of personal demand. TB treatment also, if in healthcare, is demand-driven. In RNTCP the intention is to shift it to project-driven, free, full course treatment, for which supervisory responsibility is assumed. Yet, half of lung TB cases and the lion's share of extra-pulmonary and pediatric TB cases are managed outside RNTCP [28]; if we should bring protocol-based diagnosis and treatment, healthcare has to be supervised, regulated and also helped by locally present and overarching Public Health. Public Health laboratories must be equipped and ready to assist with control of TB and other diseases.

The obvious way to achieve this is to reinstate Public Health department under GoI with functional presence and mandate in all States and districts [14,19]. All vertical

disease control projects should then be shifted under Public Health. We do not see any alternative to such re-engineering of health management in India for not only efficient TB control but also control of all diseases.

Public participation needs to be built into TB control. Innovative ways of public education and empowerment are essential. Citizens should know TB is infectious and treatment is of long duration; completion of treatment is in the interests of all – affected and unaffected individuals including children. We must educate the public to adopt hygienic behaviours – of not spitting in public spaces and observing cough/sneeze etiquette.

Case detection has to reach as near 100% as possible; for this, innovative ways of building public-private partnering has to be accomplished in every community, especially in sub-districts, under supervision of the district RNTCP unit. Anti-TB drugs should be restricted from over-the-counter dispensing; alternatively such prescriptions should be notified on par with TB cases.

TB may affect any organ system; therefore, all medical and surgical subspecialties that treat TB must be brought under Public Health surveillance. Such gathering of information is not realistic for just one pathogen; all pathogens under Public Health purview must be made notifiable. A model for decentralized and response-demanding disease surveillance has been tested successfully in India [42]. The Integrated Disease Surveillance Project, as currently conducted, unfortunately, does not satisfy the definition or requirements of Public Health surveillance or of disease control [43].

TB diagnosis and treatment in the private sector ought to be registered with RNTCP and monitored for quality and outcomes. Around every diagnosed person with TB, adult and child, active search and standard management for latently infected and symptomatic cases must be enforced. All data should be supported by information technology for ready access and follow up.

Currently there are built-in delays in TB diagnosis and also detection of MDR TB. There are newer techniques available to shorten such intervals and they should be systematically included in RNTCP. Under RNTCP, a second sputum screening to detect treatment failure (for MDR TB) is collected after 2 months of therapy. This interval ought to be reduced to 2 weeks to detect MDR status at the earliest. Healthcare deserves assistance in access to diagnostics – both classical and modern. GoI ought to invest at least $ 600 million, if not 1 billion, annually for TB control as we are losing >23 billion from national wealth. Budgeting 100-200 million appears to be indicative of inadequate seriousness given for TB control [2].

All pediatric clinics should be linked to RNTCP so that case-detection rate is increased. As part of 'well baby' checks, all children ought to be tuberculin tested at 5 and 10 years and appropriate management applied if found positive. Until this intervention becomes operational, annual skin test surveys should be conducted to document and monitor ARTI and its annual decline.

TB control is both a means to, and a measure of, economic and social development. These many additions to the DOTS strategy require a reorganization of the health management approach in India. TB control must be owned by States and Districts – for which flexibility in interventions and freedom to innovate must be given to them, while regularly auditing the performances at the district level. Such external auditing should be in addition to internal (within district) auditing of the performance by the district RNTCP staff themselves. All tools and parameters for auditing have to be developed urgently.

To conclude, there is an urgent need to relook at the strategies of TB control in India with openness to accept the need for redesigning, particularly the way pediatric TB is dealt with. The efforts to control TB must be comprehensive, addressing all the elements necessary in this national massive initiative. They include effective health education, strong Public Health, functional surveillance, sound public-private partnership, and more liberal financial support.

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REFERENCES

1. Khatri GR. National tuberculosis control programme. J Indian Med Assoc. 1996; 94:370-5.
2. World Health Organization. Global Tuberculosis Report 2012. Available from: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf Accessed on October 20, 2012.
3. World Health Organization. Global Tuberculosis Control 2011: WHO Report 2011 <http://whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf. Accessed August 26, 2012.
4. Park K. Epidemiology of Communicable Diseases. In: Park's Textbook of Preventive and Social Medicine. Jabalpur: B Bhanot; 2009;131-313.
5. Bhatter P, Chatterjee A, Mistry N. The dragon and the tiger: Realities in the control of tuberculosis. Interdisciplinary Perspectives on Infectious Diseases; Volume 2012, Article ID 625459. Doi:10.1155/2012/625459
6. Daniel TM. The history of tuberculosis: past, present and challenges for the future. *In*: Schaaf HM, Zumla AI (*Ed*) Tuberculosis: A Comprehensive Clinical Reference. St Luis: Saunders; 2009. p.1-7.
7. Agarwal SP, Chauhan LS. Tuberculosis control in India. Directorate General of Health Services, Ministry of

Health and Family Welfare, New Delhi, 2005 http://tbcindia.nic.in/pdfs/Tuberculosis%20Control%20in%20India-Final.pdf Accessed on September 8, 2012.
8. John TJ. Tuberculosis control, without protection from BCG. Indian Pediatr. 2000; 37:9-18.
9. John TJ, John SM. Paradigm shift for control of tuberculosis in high prevalence countries. Trop Med Int Health. 2009:4:1-3.
10. John TJ, Vashishtha VM. Tuberculosis control should be scientifically defined and soundly designed. Indian J Med Res. 2010;132:4-8.
11. Jain NK. Drug resistance in India. A tragedy in the making. Indian J Tuberc. 1992;92:145-8.
12. Michael JS, John TJ. Extensively drug-resistant tuberculosis in India. A review. Indian J Med Res. 2012 (In press).
13. John TJ, Babu PG, Jayakumari H, Simoes EAF. Current prevalence and risk groups of HIV infection in Tamilnadu, India. Lancet. 1987;i:160-1.
14. John TJ, Muliyil J. Public health is infrastructure for development. Indian J Med Res. 2009;30:9-11.
15. Anonymous. Indian Journal of Tuberculosis. Leaves from history. Indian J Tuberculosis. 2003;50:124.
16. Directorate General of Health Services, Ministry of Health, Government of India. TBC India. History of TB control. http://tbcindia.nic.in/history.html. Accessed on August 27, 2012.
17. World Health Organisation. A brief history of tuberculosis control in India. 2010 http://whqlibdoc.who.int/publications/2010/9789241500159_eng.pdf. Accessed on August 26, 2012.
18. Park K. Park's Textbook of Preventive and Social Medicine: Chapter 21, Health Planning and Management. B Bhanot, Jabalpur, 2009. p. 771-90.
19. John TJ, Shah NK. Universal healthcare and nation-wide public health. A tale of two declarations from one city. Indian J Med Res. 2011;134:250-2.
20. Tuberculosis prevention trial, Madras. Trial of BCG vaccine in south India for tuberculosis prevention. Indian J Med Res. 1980;72:1-74.
21. Tuberculosis Prevention Trial, Madras. Trial of BCG vaccines for prevention of tuberculosis in south India: First Report. Bull WHO. 1979;57:819-27.
22. World Health Organisation. Report of an ICMR/WHO Scientific Group. Vaccination against tuberculosis. Tech Rep Ser 651, WHO Geneva, 1980. p. 1-21
23. Simoes EAF, Babu PG, Jayakumari HM, John TJ. The initial detection of human immunodeficiency virus 1 and its subsequent spread in prostitutes in Tamilnadu, India. J AIDS. 1993;6:1030-4.
24. John TJ, Babu PG, Pulimood RB, Jayakumari H. Prevalence of human immunodeficiency virus infection among voluntary blood donors. Indian J Med Res. 1989;89:1-3.
25. John TJ, Bhushan N, babu PG, Seshadri L, Balasubramaniam N, Jasper P. Prevalence of HIV infection in pregnant women in Vellore region. Indian J Med Res. 1993;97:227-30.
26. Kaur A, Babu PG, Jacob M, Narasimhan C, Ganesh A, Saraswathi NK, *et al*. Clinical and laboratory profile of AIDS in India. J AIDS. 1992;5:883-9.
27. Chandrasekar S, Jagota P, Choudhuri K. Initial drug resistance to antitubercular drugs in urban and rural district tuberculosis. Indian J Tuberc. 1992;39:171-5.
28. Jain RF. Faulty prescription, an avoidable cause of multidrug resistance in tuberculosis. J Indian Med Assoc. 1996;94:385-8.
29. http://www.tbcindia.nic.in/pdfs/RNTCP%20TB%20India%202011.pdf. Accessed on September 30, 2012.
30. http://planningcommission.nic.in/reports/genrep/health/RNTCP_2011.pdf. Accessed on September 30, 2012.
31. Tuberculosis Research Centre (ICMR), Chennai. Fifteen-year follow up of trial of BCG vaccine in south India for tuberculosis prevention. Indian J Med Res. 1999;110:56-69.
32. Chauhan LS, Arora VK. Management of pediatric tuberculosis under Revised National Tuberculosis Control Programme (RNTCP). Indian Pediatr. 2004;41: 901-5.
33. Sareen D, Sareen N, Singh D, Ohja A, Agarwal KK. Prevalence of tuberculous infection and disease among children under five years in contact with an open case of tuberculosis. Presented at the National Conference of Indian Academy of Pediatrics, 2008, Abstract No. ID/(01) P.
34. John TJ. Tuberculosis control: detect and treat infection in children. Indian Pediatr. 2008;45:261-4.
35. Kamath SR, Dawson SJY, Devadatta SA. A controlled study of segregation of tuberculosis patients for one year on the attack rate of tuberculosis in close family contacts in south India. Bull WHO. 1966;34:577-632.
36. Pothukuchi M, Nagaraja SB, Kelamane S, Satyanarayana S, Shashidhar, Babu S, *et al.* Tuberculosis contact screening and isoniazid preventive therapy in a South Indian District: operational issues for programmatic consideration. PLoS ONE 2011 6(7) e:2250.
37. Nelson LJ, Wells CD. Global epidemiology of childhood tuberculosis. Int J Tuberc Lung Dis. 2004;8:636-47.
38. Kabra SK, Lodha R, Seth V. Tuberculosis in children—what has changed in last 20 years? Indian J Pediatr. 2002;69:S5-10.
39. Singh M, Saini AG, Anil N, Aggarwal A. Latent tuberculosis in children: diagnosis and management. Indian J Pediatr. 2011;78:464-8.
40. GoI Notification of TB as notifiable disease. http://www.tbcindia.nic.in/pdfs/TB%20Notification%20Govt%20%20Order%20dated%2007%2005%202012.pdf Accessed on October 2, 2012.
41. Annual risk of tuberculosis infection in different zones of India. Available from: http://ntiindia.kar.nic.in/docs/ari2000-03/index.html. Accessed on October 2, 2012.
42. John TJ, Samuel R, Balraj V, John R. Disease surveillance at the district level: a model for developing countries. Lancet. 1998:352:58-61.
43. Thacker SB, Berkleman RL. Public health surveillance in the United States. Epidemiol Rev. 1988;10:164-90.