GOLDEN JUBILEE LECTURE

Tuberculosis Control in India: Why are we Failing?

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In spite of being the pioneer-leader of research into epidemiology and prevention of tuberculosis among low-income countries, India has the highest population-based burden of tuberculosis among all nations. Children with latent tuberculosis are the pool from which adult pulmonary tuberculosis emerges many years later. In the absence of primary prevention of infection by BCG, sociologic/behavioral interventions must be applied to reduce air-borne transmission. In addition to maximizing passive surveillance of adult disease, pediatric tuberculosis must also be brought under surveillance. Those with latent tuberculosis must be detected and treated to remove them from the pool. Epidemiologically, the realistic monitoring method of tuberculosis control trajectory is documenting progressive reduction of the short incubation period pediatric disease through surveillance, and not the reduction of long incubation period adult pulmonary tuberculosis. Application of scientific tools for the detection and management of pediatric tuberculosis infection – latent and active – holds the key to effective tuberculosis control.

Keywords: *Child, Control, India, Tuberculosis, Strategy.*

THE FAILURE TO CONTROL TUBERCULOSIS IN INDIA: LESSONS TO BE LEARNED

The burden of tuberculosis (TB) in India is the highest in the world and unrelenting in spite of 51 years of control efforts. With 17% of global population, we carry 26% of the global burden of TB [1]. For taking corrective steps, we must know exactly where we went wrong.

In the decade after independence, India's public health pioneers documented high prevalence of adult pulmonary TB (PTB) with mass miniature radiography and high prevalence of latent *Mycobacterium tuberculosis* (MTb) infection with tuberculin skin test (TST) surveys. They knew that latent MTb Infection and PTB mutually feed each other, and both must be addressed simultaneously for TB control. This lesson, the crux of TB control, was lost in subsequent decades.

They designed a National TB Project (NTP) in 1962 with six components established in phases. Mass immunization with Bacille Calmette-Guerin (BCG) was the main plank, believing it would provide 'primary prevention' (protection from infection) plus 'secondary prevention' (preventing latent infection progressing to disease). Three institutions were created: a BCG manufacturing unit, the TB Chemotherapy Center (re-named TB Research Center, now National Institute of Research in TB) in Chennai for epidemiological, microbiological and drug research, and the National TB Institute in Bengaluru for training TB workers and for monitoring time-trend of TB. A BCG vaccine efficacy trial was assigned to TB Research Center. The sixth element was free treatment of PTB, intended for source-reduction of MTb and as humanitarian service for mortality reduction, and for eliciting public cooperation. All components were funded by the Government of India, Ministry of Health (GoIMoH).

State Ministries of Health were to implement PTB treatment, as healthcare is State subject in our Constitution. States never assumed responsibility in spite of GoIMoH establishing TB diagnostic units in over 400 districts covering all States and a demonstration model in Anantapur district, Andhra Pradesh. States continue the same way even now under the Revised National TB Control Project (RNTCP), for two reasons. First, India did not imbibe the political ideology common to socialist and capitalist countries, that the Government is responsible for people's health. So universal healthcare was not designed and private sector was given a free hand to capture as much of the healthcare market as they wanted. Rampant TB is lucrative business for private sector; more disease means more income.

Second, GoIMoH did not design monitoring methods and could not assess how well States were performing, in terms of quality and coverage of PTB treatment. States also erred by not regulating quality, equitable access and cost of healthcare; reporting of diseases by all healthcare functionaries, required legally, was not enforced. Under such near-anarchy, States could not implement universal healthcare.

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Thus, the constitutionally defined division of responsibilities between Center (making policy, writing detailed plans of action and funding disease control) and States (implementing the plans) is dysfunctional and in urgent need of re-engineering. We need not look elsewhere for the suboptimal performance of 'vertical' projects such as Expanded Programme on Immunization and malaria control. Given adequate funding, authority for monitoring and flexibility for midcourse corrections, polio elimination and AIDS control succeeded. So, we do know what it will take to control TB. The segment of population affected determines political will of the ruling elite; polio and AIDS did not spare the rich but TB is a disease of the subaltern.

TB CONTROL LOST BCG AND COULD NOT RUN ON ONE LEG

In 1979, preliminary results of BCG trial showed no vaccine efficacy for primary or secondary prevention; alternate means to decelerate transmission and inhibit latent infection progressing to disease were urgently needed and NTP was in need of revision [2,3]. Vertical projects have work cut out for functionaries at every level; identifying flaws was not assigned to anyone. The lack of help by BCG vaccination for TB control made no impact on NTP under this cultivated conspiracy of silence.

In mid-1980s, human immunodeficiency virus (HIV) began spreading in India [4]. Concurrently, multi-drug resistance (MDR) of MTb was recognized [5]. These ominous developments also made no impact on NTP with no one in charge of internal program auditing; external auditing was also not designed. In 1990-91, nearly three decades after launch, NTP was evaluated under international pressure and found to have failed to reduce TB burden. By then India had lost three precious decades. The lesson is clear: disease control projects must have inbuilt ongoing regular monitoring mechanisms and periodic evaluations. Spending Government funds but flying blind is irresponsible.

Eventually NTP was revised and RNTCP launched in 1993, but revision was confined to one element – directly observed treatment, short course (DOTS) [6]. The failure to control TB continues to be attributed to poor implementation by the States, but the basic problem is the flawed design. The void left by BCG for prevention remains. The World Health Organization (WHO) had declared TB a global public health emergency in 1993; instead of rapidly expanding national coverage of DOTS, 13 years (1993-2006) were taken to reach all districts as if there was no hurry to control TB.

India, the pioneer-leader of TB control among low income countries, with much research in TB epidemiology, transmission dynamics, natural history, drug regimens, vaccinology and bacteriology, chose not to make autonomous decisions. Instead, the simplistic WHO prescriptions of 85% microbiological cure and 70% case detection of PTB were accepted as the project goals instead of epidemiologic TB control. RNTCP became process-obsessed instead of result-oriented; protocols were inflexibly fixed, without provision for ongoing course-correction. There was no monitoring of TB burden time trends, or of incidence of primary TB [7].

EPIDEMIOLOGY IS THE FOUNDATION OF PUBLIC HEALTH

In epidemiology, control has a specific meaning and definition, which is essentially the reduction of disease burden to a desired level within a stipulated interval, by interventions [8]. Diagnosis, cure and case-fatality reduction, the purposes of DOTS, are excellent objectives of healthcare. Control requires incidence reduction, achievable by reduced transmission frequency (reduction of infection-incidence) or by shrinking the pool of latent MTb infection (reduction of disease-incidence)– ideally by both.

In RNTCP, baseline incidence of infection and disease are not measured, the levels to which they should be brought down not declared and the time frame not defined. The first steps in any disease control are establishing surveillance, declaring control targets and designing instruments to monitor progress. In the eyes of epidemiology, RNTCP is not a TB control program.

A working definition of TB control has been proposed: 5% annual reduction of the incidence of MTb infection [9]. If successful and sustained, in 20 years the incidence of infection can be at par with industrialized countries. As the incubation period to PTB is two decades or more, measurable reduction in incidence of PTB will begin only then. Incidence of infection in children and incidence of childhood TB with short incubation period will decline rapidly if control interventions are effective – these two parameters yield themselves for relatively easy monitoring. Pediatric TB consists of both.

DOTS IS NOT THE SAME AS TB CONTROL

With mass application, disease treatment does not become disease control. That 85% cure of 70% cases (59.5% effective cure) will not control TB in India where prevalence is high [9]. Our health management leadership made technical experts managers of DOTS without mandate or freedom to monitor control

trajectory, make mid-course corrections and modify the design if incidence decline did not meet the target. Retrospectively, it is easy to blame WHO, but it is only an advisory body; policy, design, implementation and evaluation belong to GoIMoH.

The WHO tends to apply two principles when recommending public health interventions in low income countries: 'choose one critical tool' (for practicality) and 'one size fits all' (for ease of drafting protocols). Socio-culturally, demographically and by health management system design, India differs from all other countries. DOTS and the benchmarks are good only if they are added to a functionally efficient healthcare platform, which India does not have. By the time a person with PTB is diagnosed and rendered non-infectious, all children in close contact have already been infected [10]. DOTS alone will never control TB in India.

To decelerate MTb infection, airborne transmission must be reduced. Preventive chemotherapy of recently infected children is necessary for shrinking the pool of latent infection from which evolves PTB. Monitoring of incidence of infection by tuberculin skin testing is essential for diagnosing latent TB and for documenting TB control trajectory [9].

SECULAR TREND, SOCIAL DETERMINANTS AND SURVEILLANCE

All industrialized countries registered remarkable decline of incidence of all forms of TB during late 19th and early 20th centuries, even before anti-TB drugs were available. Britain and Singapore are reputed to have banned spitting in public places to reduce air-borne MTb transmission. No civilized country should condone uncovered sneeze/ cough or open spitting. Decline of TB burden in industrialized countries was 'secular trend', due to behavior change and socio-economic development – both helped mitigation of 'social determinants' of TB. Even without TB-specific biomedical intervention, they practiced surveillance and documented the decline. We have bio-medical interventions but have no surveillance, no reliable documentation and no concern for social determinants.

Surveillance is to understand disease epidemiology and to monitor incidence. It is the first step in disease control. Success of surveillance will depend on its design, taking into account the responsibilities of health management between Center and States. Not enforcing TB surveillance was a major flaw in RNTCP design. For monitoring TB control in the short term, surveillance of short-incubation childhood TB is more practical than that of long-incubation adult TB.

In 2012, the diagnosis of TB has been made reportable by a Government order, underscoring the need for counting all cases [11]. However, RNTCP is neither adequately staffed to take responsive actions on reported cases nor has jurisdiction to enforce surveillance. Surveillance can be enforced only if an empowered department of public health is created and all diseases (under control mode) brought under surveillance.

Social improvements have taken place in the rich and upper middle class, among whom TB must have declined greatly. While taking time to create more national wealth and an egalitarian society, there are practical measures to address secular trend, through public participation in TB control. Health education for inculcating habits of cough etiquette and not spitting in public places will help to reduce transmission. These should be compulsory in hospital environments where sick people aggregate. These should be taught in schools for sustained behavior change. Public education on TB has additional benefits; to ensure early care seeking behavior, family support and removal of stigma.

LESSONS FROM SUCCESSFUL CONTROL OF HIV/AIDS

The success of AIDS control in India is on account of its indigenous design that included multiple interventions applied simultaneously [12]. Public education for gaining their participation was introduced soon after the detection of HIV infection in India in 1986 [12]. Denominator-based annual monitoring (called sentinel surveillance) was launched in 1986 itself [12]. Diagnostic services were designed with quality in mind and well regulated. Private-public mix was actively encouraged [12].

Indeed the private sector had played the lead role in detection of the infection, the design of interventions with multiple elements spanning human behavior modification, blood safety and hospital infection control [12]. The first National Reference Center was in private sector, funded by the Indian Council of Medical Research. Foreign experts and funding agencies got involved only 6 years later (in 1992), after we had demonstrated that the design was robust and that the control trajectory was annually monitored, and was on-track. Drug treatment (for AIDS and preventing mother-to-child transmission) was the last element to be added. For TB, drug treatment as the sole intervention is unscientific.

The lessons are: TB control project must be re-designed to include epidemiological principles and to fit the Indian cultural and socio-political milieu and our unique health management system. As far as TB

treatment is concerned, private sector must be involved but with regulatory controls on quality and cost so that people get diagnosis and treatment that are scientifically correct and free of charge. Healthcare professionals who diagnose and treat TB must be held accountable for quality; fair cost and patient follow up.

THE WAY FORWARD

There are three compelling reasons why TB must be controlled urgently. TB is essentially the result of public health negligence on the part of GoIMoH; hence, everyone deserves free diagnosis and treatment on humanitarian grounds. Every child has the basic Human Right to grow up in an environment without heavy exposure to MTb in the air they breathe. TB control is thus a moral imperative from which GoIMoH cannot escape.

TB reduces productivity; the Planning Commission has estimated that the loss to national economy on account of TB amounts to 23.7 billion US dollars annually. TB is impoverishing families and the nation. TB control is essential for poverty alleviation and economic development. To plug 23 billion-dollar leak, at least 1 billion dollars must be provided for the application of epidemiology and control. Currently only 200 million dollars are spent on TB control which indicates the lack of political will.

Widespread use of anti-TB drugs while not reducing the incidence of TB results in increasing prevalence of drug resistance; it is thus the unfortunate product of the failed TB control. It was stated in 1992 that "unknowingly we are transforming an eminently treatable disease into one which is life-threatening and exorbitantly expensive to treat" [5] and in 2000, that "each year we delay the control of TB quantitatively the more difficult it will become to achieve control" [7]. TB is indeed a national public health emergency.

RNTCP covers the entire nation and must remain India's backbone for TB control. However, it has major gaps that need bridging. It is unlikely that TB control can be achieved without a public health department that is empowered to respond to data on disease surveillance and to practice epidemiology in health management. The non-application of epidemiological principles, the poor implementation of interventions designed in RNTCP and the lack of public participation have been addressed above. The most critical gap is the neglect of pediatric MTb infection and disease.

Pediatric TB: The Key to Adult TB

"The Child is father of the Man": William Wordsworth.

An important difference between countries with low and high prevalence of TB is the magnitude of annual rate of MTb infection (ARTI). In low prevalence countries, it would take about 14-20 years to cumulatively reach 1% with latent TB as detected by positive TST. The life-time risk of infection remains very low at less than 5%. In India, in each year of life starting from infancy, ARTI is about 1%, cumulating to 15% by 14 years of age. The life time risk of infection is in the range of 40-60%.

Children in households with any adult with PTB are at very high risk of infection. Screening of household members for TB disease and latent infection is included in the RNTCP protocol, but is not implemented for various reasons. Such screening is labor-intensive and RNTCP does not have sufficient medical staff for undertaking the job. The screening by health workers does not assure quality. In the re-design of RNTCP and nesting it within a functional department of public health, sufficient medical staff must be provided to conduct screening of all members of households for adult as well as childhood TB.

All children in the country are at risk of infection. Therefore, TST must be applied on all children as a routine. By age 5, the cross-reaction with BCG response would be minimal /negligible; hence that is the best age for routine TST. All those who are TST negative ought to be re-tested after an interval, arbitrarily suggested here as by age 8 years (earliest) or 10 years (latest). Since school enrolment is very high in India, TST is best included as part of school health program.

Pediatric MTb infection and disease are sentinel events for monitoring of TB transmission dynamics. All children identified with latent MTb infection by TST or diagnosed with symptomatic TB should be treated, according to standard protocol, under supervision. In short, infants and young children are sentinel subjects for monitoring two events – silent infection and childhood TB.

Annual age-based TST will provide data on the incidence of MTb infection, which has been recommended as one parameter for monitoring the trajectory of control of MTb infection. The incidence of symptomatic childhood TB, obtained through maximized passive surveillance will be the second parameter to monitor the trajectory of control of childhood TB.

TB can be Controlled

With political will we can control TB with available tools and within our fragmented health management system. Ideally, TB control must be assigned to public

health departments of GoIMoH and States, but that is no excuse not to fund RNTCP adequately or to give it flexibility for innovation and course-correction.

The battle against TB will be won or lost in population units – the districts and cities – there local leadership must be provided with freedom to experiment. Time trends of MTb infection and pediatric TB must be monitored in all units of population – each district and each city. Pediatric TB, infection and disease, are to be contained and to be monitored. Neglect pediatric TB and we will never control adult TB.

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