Review Article
Indian J Med Res 120, October 2004, pp 248-276

Epidemiology of tuberculosis : Current status in India

A.K. Chakraborty

Epidemiology Analyst, Bangalore, India

Received January 10, 2003

India is classified along with the sub-Saharan African countries to be among those with a high burden and the least prospects of a favourable time trend of the disease as of now (Group IV countries). The average prevalence of all forms of tuberculosis in India is estimated to be 5.05 per thousand, prevalence of smear-positive cases 2.27 per thousand and average annual incidence of smear-positive cases at 84 per 1,00,000 annually.

The credibility and use of the estimates are discussed in detail. Reports on recent studies on the time trend of the disease from some areas in India, *e.g.*, Chingleput in Tamil Nadu are discussed. They confirm the slow downward trend over a fairly long period of observation, as in the rural areas around Bangalore. It also outlines the serious escalation of disease burden in a tribal population group in Car Nicobar over a period 1986-2002, and highlights the nature and extent of the emerging threats. Some epidemiologists forecast a rise of 20 per cent in incidence in the next 20 yr, for India, with a cumulative rise of 46 million cases of tuberculosis during that period, largely as a consequence of HIV epidemic.

The Governmental efforts at intervention through Revised National Tuberculosis Control Programme (RNTCP) and at monitoring the epidemiology of intervention through organising routine reporting are highlighted, and data are presented and evaluated on these. RNTCP needs to be used as an effective instrument to bring a change in epidemiological situation, through fast expansion and achievement of global target.

The present review describes the global tuberculosis situation, and views it in the context of the goal of the antituberculosis intervention activities. It presents the epidemiological situation in India, comments on the current trend and discusses the efforts taken towards making projections on the likely burden of disease in India over time.

Key words Annual risk of infection - epidemiology - incidence - infection - mathematical modeling - monitoring - prevalence - survey - time trend - tuberculosis

An increasing morbidity and mortality from tuberculosis (TB) in the near future is forecast for the world at large, with the number of newly occurring cases predicted to increase from 7.5 million a year in 1990 to 8.8, 10.2 and 11.9 million in the years 1995, 2002 and 2005 respectively; an increase amounting to 58.6 per cent over a 15-yr period[1]. The estimates were subsequently found to be appropriate for the year 2000 using a new method[2]. The proportion of tuberculosis cases co-infected with human immuno deficiency virus (HIV) was also found to be rising, being 2-10 times greater for the 1997 estimates, than for1990[2]. The association with HIV and increasing multi drug resistant tuberculosis (MDRTB) appears to be a serious issue, especially for the developing nations.

Zaki in 1968[3], had commented that "The international tuberculosis situation is complicated by the growing impression that tuberculosis is no longer a major public health problem". He had also shortlisted the following factors: chronicity, ability of bacilli to stay alive in body for years, increase in life expectancy, high level of endemicity in ethnic groups even in the midst of affluence in the western world, the frequent occurrences of isolated epidemics in certain parts of the world and the emergence of MDRTB. In the course of a few decades and more, Zaki's extensive analysis[3,4] and forecasting of situation has proved near-prophetic. Apathy of public policy makers, all over the world, including in the affluent countries, had complicated the issue.

India had a National Tuberculosis Programme (NTP) in place from the sixties, following epidemiological assessment of the situation during 1955-1958[5]. However, less than optimal service delivery under the Government controlled antituberculosis programme did not allow it to make much progress in terms of achieving substantially high cure rates. There were serious limitations in the diagnostic paradigm and treatment regimens followed. Besides, there remained considerable leeway to be made in ensuring support of the general health services network, supposed to be running the programme.

On top of that, the question of involving the private service providers had remained an uncharted field. Population size along with most of the maladies of socio-economic nature, as listed by Zaki, are operational in India, infact, more so here, than elsewhere in the developing countries. However, following WHO initiative, there is today a heightened sense of urgency and global awareness to the problem and the impending escalation in it. In 1993, the NTP in India was strengthened in the form of Revised National Tuberculosis Control Programme (RNTCP).

Following a decade of efforts to test-run the RNTCP and then implement it in the field conditions in India, the programme entered into the phase of substantial expansion, under which more than 700 million people are planned to be covered by the year 2004[6]. More than 450 million people are already reported to be under the directly observed treatment short course (DOTS) strategy under the RNTCP by the end of 2001[7]. In the wake of RNTCP, some selected epidemiological data are in use to create awareness, carry out advocacy exercises, and for calculating the resource–allocation needed for the programme. A few epidemiological indices are currently used under the RNTCP for monitoring the efficiency of the given activities under it. They need to be refined for the purpose of setting programme development indicators. A baseline epidemiological situation also needs to be constructed for its periodic evaluation, following intervention. It is in this context that the present article seeks to review the epidemiological scenario with respect to tuberculosis in India.

INDICES USED AND DEFINITIONS

Tuberculosis situation in an area is conveniently measured in terms of (*i*) Death among the known cases of tuberculosis, case fatality; or, that attributable to tuberculosis among total population in the community, mortality; (*ii*) Prevalence and incidence of infection - persons in the community infected with tubercle bacilli at a point of time is prevalence of infection; persons infected between two points of time among those not infected or, BCG vaccinated initially is incidence of infection; (*iii*) Prevalence of disease refers to persons diseased at a point of time in the given community; and (*iv*) Incidence of disease refers to occurrence of disease between two points of time in the community among those not initially affected.

Prevalence and incidence of disease are considered in terms of culture with or without smear positivity (C+), smear positive cases (S+) or, X- ray positive culture/smear negative cases (X+).

Death: Death from tuberculosis is the most adverse outcome. Occurrence of death is the first of the indices to decline in the secular curve of a tuberculosis epidemic, followed by morbidity and infection in that order[8,9]. Subsequently however, it is not much informative to trace the course of the epidemic and to classify countries on the basis of their progress in the epidemiological situation. For example, tuberculosis death toll in several European metropolitan areas was nearly 1 per cent annually at the height of the epidemic. It had reduced during the centuries long epidemic process, to be 1 to 2 per

1,00,000 population by the end of 1980s, a 500-1000 fold reduction[10]. Though death has ceased to be a significant epidemiological information for the most advanced countries, it could still possibly be a measure of the extent of the most visible success of at least the antituberculosis programme delivery and its management, in the developing countries. For example, it is reported that nearly 70 per cent of possible deaths between 1991-2000 in Peru[11], and nearly 46 per cent in China between 1991-1997[12], were averted among smear-positive cases of tuberculosis, through a more efficient process of programme delivery. As an immediate and the most visible effect of antituberculosis intervention, the prevention of death appears without doubt, to be an attractive index to the programme planners. For the purpose of this paper, however, death is not included as an index to classify the countries in their progress towards "elimination" goal, in pursuance of the hypothesis of Styblo[13].

Prevalence and incidence:

Infection: Prevalence of infection in the Indian context cannot be estimated accurately in those aged 14 yr or more. Failure to demarcate the infected from the non infected due to high prevalence of intermediate reactors in India in older ages, does not allow prevalence of infection among the unvaccinated subjects, to be a sensitive indicator[14]. In fact incidence of infection as studied in younger age groups is the appropriate index to measure the tuberculosis situation in a community. However, estimating incidence would call for repeat testing of the same children. To avoid repeat tuberculin testing of the same children, a mathematical estimation is carried out, using the figures on the prevalence of infection in younger children (0-14 yr) to obtain the incidence of infection. The latter is termed the annual risk of infection (ARI)[15]. The estimated ARI is actually observed to be the same as the incidence of infection, when worked out by repeat testing of the same population under Indian conditions[16].

It is understood that ARI is studied among the unvaccinated subjects only[15]. However, in situations where mass BCG vaccination at birth or soon after is the national policy, it is not a convenient to use these children as study subject, as most of them will already be vaccinated. The alternative could be to study the incidence of infection in the vaccinated, for identifying the newly infected subjects by the differences of reactions method[17]. Chadha *et al*[18] have shown the infection estimates in the vaccinated and unvaccinated as not materially different. The same does not stand corroborated from some Indian experiences (Regional Medical Research Centre, Port Blair, 2002, personal communication).

It should be noted that for developing the information base on infection both for prevalence and incidence, periodic community surveys have necessarily to be carried out as these serve as the only data source.

Disease: In most of the western European countries and others in the industrially advanced world, the data on disease and death are obtained mainly from national statistical reports, provided by the Ministry of Health and National TB Organisation[1-4,8-11,19]. No such data are available for vast population groups elsewhere in countries like India and China. Tuberculosis is not considered to be a notifiable disease in India and hence routine health data have not served as the source of information for estimating the disease state in the community. Periodic community surveys, sporadic and in different areas, dependent solely on investigator's convenience, are therefore relied upon, and extrapolated to observe and assess the tuberculosis disease situation in India[14,20].

Data source and indices for observing trend: Information on disease trend is available from repeat tuberculosis surveys carried out from 1961 onwards, in various areas namely, Delhi (urban), Madanapalli, Bangalore, Car Nicobar and Tamil Nadu[19]. The Tuberculosis Research Centre (TRC), Chennai has brought out a comprehensive report on the disease situation in the area during 1968-1986, along with that from a subset for the area till 1996[21], as a follow up to their original report[22]. The isolated tribal community in Car Nicobar is also further followed up in 2002, following the first two surveys in 1986 and 1988[23].

Of the repeat surveys, Delhi and Madanpalli had efficient treatment services for tuberculosis, provided in the study areas. The two areas, namely Car Nicobar and Chingleput in Tamil Nadu, also had provision for treatment for every identified case, through the NTP operating with its given efficiency[22]. The Bangalore area survey, on the other hand, was planned to study the natural dynamics, without a programme in the area for the initial period of five surveys. It was intended to study the baseline problem making it possible to assess intervention effects with the programme introduced at a later date.

At the time these surveys were originally planned, it had appeared logical to expect tuberculosis case prevalence rate to be reduced over a period of time, following intervention. However, it is now understood that prevalence and incidence of cases are not affected over relatively short periods of time, unless of course very intensive and effective treatment of smear-positive cases are carried out[24]. This is especially true for the countries with a high infection transmission. Moreover, small rates of change neither in the case prevalence rates nor in incidence, which are already small, could be appreciated in sample sizes, not specifically decided upon to be sensitive to register very small changes in them[20].

Prevalence of real smear-positive cases is likely to be a good epidemiological index, when the intervention measure is either very effective (close to 100%) or when there is no treatment at all[24]. It is understood that inefficient treatment services would only multiply the prevalence of smear-positive cases, due to pooling of inadequately converted cases. The incidence cases, on the other hand, occur from the breakdown among those previously infected decades back. The incidence rates are therefore constant year to year, representing the aging and progress of the infected cohort of previous decades, with time. In any case, the incidence cases would represent the transmission taking place in the community decades ago, and of course the socio-economic compulsion coupled with the currently obtaining cell mediated immunity (CMI) situation among the infected. Incidence rates of cases are therefore not expected to undergo any change following the best of interventions, in a comparatively short period of 3-4 yr, given the long span of the tuberculosis epidemic. The incidence : prevalence ratio in India is about 1:3[14]. In case an efficient tuberculosis programme, targeting a sufficient number of sputum-positive prevalence cases in the community, is run for a sufficiently long period of time, it could bring down the case prevalence, till probably the point when incidence and prevalence come to be in the same proportions in the community (1:1).

From studies by Styblo and his group in the Netherlands[15], it is now understood that incidence of infection in the younger age group can really be the index representing the current transmission situation. A series of tuberculosis infection surveys, carried out at intervals of 7-10 yr, depending on and related to the intervention efficiency in a given area, could give a trend, following intervention. Styblo[25] had demonstrated about 9 per cent change per year attributed to the intervention measures, over and above about 5 per cent natural decline (*i.e.*, a total of 14% or so annually) in the Netherlands. It is suggested that for developing countries, the natural decline of 0-2 per cent may have to be augmented to be between 5-10 per cent following an intervention, for it to be cost-effective.

It is possible to work out appropriate sample size of population with the hypothesis of decline given above, to measure likely change in India or elsewhere in the developing world, making allowance for the design factor (between 2 and 3), confidence intervals of the proportions in the population studied (95%), years intervening the surveys (7 to 10 yr), relative proportions of annual change designed to be appreciated (upwards of 50% in 7 yr) and relative precision of the estimates. Given the proportion of the BCG vaccinated children in India, this is also a variable to be considered in deciding the sample size.

A word of caution on following epidemiological trend through repeat surveys including infection surveys, may not be out of the place. In order to follow the intervention effects over a long time, large scale ARI surveys need to be organized in a valid sample of unvaccinated children, from time to time. In view of the paucity of countrywide data on ARI at present and widespread use of BCG in India, collection of exclusive data and their appropriate interpretation at repeated intervals, on a countrywide basis could be a difficult proposition. Moreover, to estimate the disease incidence/prevalence from ARI, is an exercise in modeling[26]. The recommended rule of the thumb by which figures on ARI are converted into smear-positive case incidence rates is not a phenomenon universally valid[14,22]. Whereas the conversion could be put to use in planning for resources, its reliability in measurement of changes could be untenable. Notification data, on the other hand, on disease were considered reliable when provided by programmes with an established surveillance system[10,19]. In most developing nations, it could be unreliable to interpret it as community prevalence. Huge costs involved in obtaining incidence rates by conducting population surveys could be avoided if the routine data could be interpreted after necessary adjustments. However, for information derived from monitoring data to transcend itself into indices of trend measurement, from mere indicators of programme efficiency, at their best, as at the present times, could require considerable efforts in this direction. The situation and the opportunity need to be understood before such use.

EPIDEMIOLOGY OF TUBERCULOSIS – THE GLOBAL CONTEXT

In line with the hypothesis made by Frost in 1937[27], the countries of the world seem to conveniently align themselves in two broad groups, namely those in whom the "tubercle bacillus is losing ground", so that a given number of sputum-positive transmitters "do not succeed in establishing an equivalent number to carry on the succession", and the others, in whom "no such prospect is in sight" in the conceivable future. It is not a mere coincidence that the above alignment happens to be across the socio-economic divide, between the highly industrialised nations of the world and the so-called developing nations. There is an additional dimension *i.e.*, the huge population size in the latter, in absolute numbers, as well as in its escalation with time. Apart form the above two groups, there are of course others, in whom the tuberculosis situation may not be at either extreme of the divide.

Following this broad posturing, countries of the world could be grouped in four major categories (Table I) as adapted after Styblo[13,28]. In arriving at the pragmatic definition on "goal" to be pursued by the countries of the world, data on incidence of smear-positive cases and prevalence of tuberculous infections, likely to be attained by 2050, among the countries with the most favourable tuberculosis situation, are used (Table II).

While the term control is used by policy makers and programme managers in designating the long-term objective of antituberculosis programme

Table I. Global tuberculosis situation (Grouping of countries)

Annual risk of infection (ARI) (%)	Annual decline (%)	Group
0.1 - 0.01	≥ 10	Group I Industrialised countries (Netherlands, Norway, *etc*.)
0.5 - 1.5	5-10	Group II Middle income countries (Latin America, West & North Africa, *etc*.)
1 – 2.5	≤ 5	Group III Middle income countries (East & South East Asia, *etc*.)
1 - 2.5	0 – 3	Group IV (Sub-Saharan Africa and Indian Sub-continent, *etc*.)

Source : Refs 13, 14

Table II. Global tuberculosis situation - I (Suggested definition of goal)

Eradication (E)
↑
Elimination (EL)
↑
Virtually identical with EL
Incidence of smear positive cases :
Below 1 per 10 million
(Prevalence of infection:
general population 0.1%)
↑
Close to EL
Incidence of smear positive cases :
1 per million population
(Prevalence of Infection below 1%)

Source : Refs 13, 14

(RNTCP) in India, it should be understood that the parameters of control remain yet to be defined. This is for understandable reasons, in the context of the developing countries, where the specific 'goals' of antituberculosis programme, as shown in Table II are rather distant and remote, as is in the case of India, as compared to a group I country, such as the Netherlands (Table III). Even then, it should be understood that the 'goals' of human endeavour, in its fight against tuberculosis, are for the first time defined in concrete terms. These are based on epidemiological situations, attained through the best possible of human efforts, anywhere in the world. Table II defines the stages that the countries could possibly pass through in their journey towards attainment of the final 'goal', *i.e.*, "virtual elimination". Table IV provides the likely time table for the journey.

The long-term epidemiological trend in tuberculosis, unaffected by and secured against short-term spikes or dips through transitory influences, is termed as "secular trend". The best and the worst possible trend scenario anywhere in the world, drawn on the basis of tuberculosis infection rates are projected (Table V). In respect of the ARI[25], there is an exponential decline in the case of countries with the best possible case scenario, such as Netherlands (decline up to about 14% annually: about 5% of it natural and the rest attributed to antituberculosis measures). For the worst case scenario, on the other hand, there could be a rise (Afghanistan) or a state of minimal decline ranging between 1 and 1.4 per cent annually (Lesotho)[2,25,29]. The problem is likely to be halved in five years in countries with the best possible case scenario, without any such prospect in the other[25]. Disease rates, expressed as incidence of smear-positive cases in Group IV vs. Group I countries, as at present, are set against those required to be achieved in case the goal of elimination is addressed (Table III). It could be observed that for the Group I countries (Netherlands) the annual incidence of 12-15 as at present, needs to be reduced to less than one for a million population, to achieve the 'close to elimination' status by 2025[13]. For the

Table III. Task infront of group IV countries set against group I, for pursuing close to elimination status

Country	Epidemiological situation			
	Present		Qualification for 'close to elimination' status	
	Incidence of smear-positive cases per million/year	Prevalence of infection all ages (%)	Incidence of smear-positive cases per million/year	Prevalence of infection all ages (%)
Most advanced†	12 – 15	15		
India	500* (850)**	40	1.0	1.0
China	515**			

†Norway, Netherlands, *etc*.: (ARI 0.1 to 0.01%, 10% annual decline, Close to elimination' status projected to be achieved by 2025 AD)[15,22]
Figures based on *Ref 38, ** Ref 2

Group IV countries on the other hand, this could mean requiring the present incidence of smear-positive cases of about 510 per million, as in China[12], or 840 per million for India[2], to be brought down to 1-2 by that date[13] (Table III).

Styblo[25] had highlighted the challenge before the policy makers, "unless a massive increase in the cure rate for smear-positive pulmonary tuberculosis was achieved, there would be no marked improvement in the tuberculosis problem in many developing countries for the foreseeable future". One might also add here that the intervention effects need to be continuously evaluated in a regular ongoing manner (monitoring). Without an effective monitoring, the improvements or otherwise in disease trend would not be documented. For such ongoing evaluation to take place, the development indicators need to be suitably designed, requiring these to be sensitive and easily obtainable. On sustained monitoring and agglomeration of such indicators, one could derive the course of the disease with time. Surveillance systems are therefore critical to build and sustain, if one has to follow disease trend. Periodic surveys in some selected areas, do give some information, but may not replace a disease surveillance system in the long run.

Table IV. Global situation-time frame of achievement (Best possible)

Group I
Netherlands, *etc.*

Prevalence of infection	Time
15 %	(Present)
(Incidence of smear-positive cases : 12-15 per million)	
9%	(2000 AD)
1%	(2025 AD)
(Incidence of smear-positive cases : < 1 per million)	
0.1%	(2050 AD)

Source: Ref 13, 14, 20

THE INDIAN SITUATION

ARI: ARI from different parts of India till the middle of the last decade (1991-96) was reported to be between 1.0 and 2.0 per cent (Table VI)[14]. There have been fresh estimates available from a few areas in the country since then, the best possible situation being reported from Kerala (ARI, 0.75%)[30]. The high

Table V. Worst and best possible tuberculosis situation in the world

	Group IV countries			Group I countries Netherlands		
	Year	ARI† (%)	Incidence of S+ cases* (per 1,00,000)	Year	ARI† (%)	Incidence rates of S + cases ** (per 1,00,000)
1.	Lesotho (whole country)					
	1956-1957	2.78		1952	0.4	13.9
	1962-1965	2.83		1955	0.265	7.8
	1981-1982	2.03		1958	1.176	5.7
	Current (1999)		173	1961	0.116	4.6
				1964	0.077	3.2
2.	South Sumatra			1967	0.051	2.4
	1975	3.76		1973-76	0.038	1.8
	1980	3.8				
	1985	3.48				
	Current (1999)		128			
3.	Afghanistan					
	1963	2.55 – 4.80				
	1982	3.63				
	Current (1999)	4.0 (2.0 – 3.0)	150			

Source: †Ref. 29; *Ref. 2; **Ref. 26

S+, Sputum smear positive cases
ARI, Annual risk of infection

Table VI. Recent studies: Annual risk of infection (ARI) in various areas in India

	Study by	State	Year	ARI (%)
1.	Kerala TB Association	Kerala[30]	1991	0.75
2.	NTI	Tumkur Dist[14]	1960-72	1.66-1.08
		Bangalore Rural[14]	1962	1.1
		Bangalore Rural[14]	1985	0.61
		Bangalore Urban[32]	1996-99	1.67
		*North India	2000-01	1.9
		North India rural		1.62
		North India urban		2.6
3.	TRC, Chennai	Chingleput (Rural)[21]	1969-84	1.8-1.9
		Chingleput (Rural)[21]	1991-96	2.9-3.2
4.	URMUL Trust	Rajasthan[14]		1.44
5.	DAN TAB (DANIDA)	*Orissa	2002	1.72
		Orissa Rural		1.62
		Orissa Urban		2.48
6.	A & N Govt.	Car Nicobar[14]	1986	1.53
7.	RMRC, Port Blair	Car Nicobar[23]	2002	3.8
8.	MGIMS, Sevagram/ NTI, Bangalore	Maharashtra[31]		
		Nagpur Rural	2001	1.2 (6.34-6.38)
		Nagpur Urban	2001	1.6 (8.44-8.50)
		Thane Rural	2001	1.6 (8.07-8.10)
		Thane Urban	2001	3.3 (15.75-15.80)

95 per cent confidence interval (CI) of prevalence of infection is given in parentheses
*Personal information, unpublished data. NTI
NTI, National Tuberculosis Institute; TRC, Tuberculosis Research Centre;
URMUL, Upper Rajasthan Milk Union Ltd. Lunkaransahr; DAN TAB DANIDA-DANIDA TUBERCULOSIS
A & N, Andaman & Nicobar; RMRC, Regional Medical Research Centre, Port Blair;
MGIMS, Mahatma Gandhi Institute of Medical Sciences, Sevagram

rates of ARI observed in Thane in the outskirts of Mumbai (3.3%) as reported in a study by MGIMS Sevagram/NTI, Bangalore[31] and in Nicobar district (3.8%)[23] merit mention, being among the worst case scenario on record. The rate in Thane urban area is interpreted to be due to HIV seroprevalence and to the increasing component of slum dwellers in the fast expanding population group inhabiting the area[31]. The ARI from Car Nicabor is the only documented instance of ARI in India, escalating with time.

The recent data on ARI (Table VI) confirm the author's earlier suggestions of differences in tuberculosis situation between areas in India[20]. It

Table VII. Problem of tuberculosis in India (average for the country)
(Estimated for 1000 million population)

Population : 1000 million (850 million in 5+ age group, 85%)	Number
Prevalence of infection *	
Rate : (a) 38% all ages (b) 44% all ages	(b) 380 Million (b_1) 440 Million
Prevalence of radiologically active abacillary pulmonary TB (X + cases)	
Rate : (a) 16 per thousand (3.0, 2.6-4.7)	(b) 13.6 million (2.6 million)
Prevalence of all forms of tuberculous disease	
Rate : (a_1) 5.05 per thousand	(b_1) 5.05 million
Prevalence of culture-positive cases (C+ cases)	
Rate : (a) 4.0 per thousand (6.0, 3.0-11.0)	(b) 3.4 million (5.1 million)
Prevalence of smear-positive cases (S+ cases)	
Rate : (a_1) 2.27 per thousand	(b_1) 1.93 million
Prevalence of total pulmonary TB cases	
Rate : (a) 20.0 per thousand (9.0, 5.6-15.7)	(b) 17.0 million (7.7 million)
New culture positive (C+cases) arising annually	
Rate : (a) 1.3 per thousand	(b) 1.1 million
New smear positive (S+cases) arising annually	
Rate : (a_1) 0.84 per thousand	(b_1) 0.71 million
Mortality rate (annual)	
Rate : (a) 50-80/1,00,000	(b) 0.43 – 0.68 million
(a_1) 46, 28-71/1,00,000	(b_1) 0.39, 0.24 – 0.60 million
Case fatality rate (annual)	
Rate : (a) 14 per cent of untreated C+cases	(a_1) 0.48 million
(a_1) 24 per cent of all TB	(b_1) 1.21 million

* Infected : > 50 per cent in age group 40 yr and more

Disease rates applicable to population in 5 + age for rows 3, 5 and 6-9.

For rows 1,4 & 10 : calculated for persons in all ages

Data given under a & b : worked out by the author[14] from Indian survey data

Data given under a_1 & b_1 : worked out by Dye *et al*[2] by aligning several kinds of data

Rates and numbers in bracket : as per revision suggested by the author on the basis of correctional surveys[14]

For average absolute numbers for revised rates in bracket : Range not presented

Source : Refs. 2, 14

C+, Culture positive; S+, Smear positive could be recalled that the urban rural difference in ARI was also evident in the Bangalore area, Bangalore rural; ARI 1.1 per cent declining to 0.61 per cent in 23 yr up to 1985[16]; urban Bangalore: ARI 1.67 per cent (CI: 1.40-1.93)[32].

Prevalence of pulmonary tuberculosis: The data presented in Table VII are the outcome of several surveys, conducted from time to time in different areas of the country, since 1955-58. An average rate for the country as a whole, is presented in this table, along with the range, to represent the best and the worst possible case scenario. Necessary corrections and refinement to the existing rates of disease are also suggested[14]. For the latter, specific survey results, devised to study and correct the observed inaccuracies and inconsistencies in the previous estimates are relied upon[14]. This method for computation of average rate with the range is adopted, since a representative sample for the country as a whole, has so far eluded the researchers, as also the sample, sensitive enough to discriminate prevalence or incidence rates between one area and the other[20]. As already explained, notification of sputum-positive or other diagnosed cases of tuberculosis is not yet the source of data on incidence and prevalence in India.

A more detailed and extensive exercise was conducted by Dye *et al*[2] directed towards providing an average estimate for the country. The average rates of disease and infection (both prevalence and incidence), as well as death were computed. Data from (*i*) survey results; (*ii*) incidence of cases, calculated out of the ARI based on an empirical model suggested by Styblo[15] and (*iii*) the likely disease rates computed from notification of cases made to the WHO Geneva, were mutually compared and assessed for reliability and internal consistency. The average rates for countries were then worked out, being the "most uptodate" and the "fullest" statement of the burden.

In Table VII, the problem is expressed in terms of rates and absolute numbers, based on a population of 1000 million, both for prevalence as well as for

Table VIII. Culture positive case (C+) prevalence of tuberculosis by geographical areas

Zone	Area	Average C+case prevalence (per 1000)	Confidence limits (95%)*	
			Lower	Upper
Calcutta (Kolkata)	City	6.39	5.16	7.62
Delhi	City	4.06	3.23	4.89
	Towns	2.45	1.54	3.36
	Villages	2.49	1.87	3.11
Hyderabad	City	4.18	3.44	4.92
	Towns	3.44	2.32	4.56
	Villages	2.29	1.70	2.88
Madanapalle	City	2.40	1.64	3.16
	Towns	8.13	6.58	9.68
	Villages	6.11	5.02	7.20
Patna	City	6.38	5.10	7.66
	Towns	5.25	3.83	6.67
	Villages	5.85	4.58	7.12
Trivandrum (Thiruvananthapuram)	City	2.96	2.14	3.78
	Towns	3.20	1.93	4.47
	Villages	2.59	2.08	3.10

*Calculated from C+ cases found and population examined in sample survey ICMR[5]

Table IX. Age distribution of smear-positive prevalence cases in a survey area,1984-1986 (for 100,000 population)

Age (yr)	1968-70	1973-75	1979-81	1984-86
10-14	35 (0.88)	14 (0.30)	8 (0.20)	3 (0.07)
15-24	108 (2.73)	111 (2.40)	105 (2.61)	62 (1.54)
25-34	425 (10.74)	461 (9.96)	404 (10.06)	292 (7.25)
35-44	729 (18.42)	691 (14.93)	570 (14.19)	693 (17.20)
45-54	899 (22.71)	1,127 (24.36)	1,050 (26.14)	921 (22.86)
55-64	994 (25.11)	1,218 (26.32)	966 (24.05)	1,144 (28.40)
65+	768 (19.40)	1,005 (21.72)	914 (22.75)	913 (22.67)
All	3,958 (457)*	4,627 (511)*	4,017 (444)*	4,028 (428) *

Figures in parentheses are proportion of cases of total (%)

*Standardised prevalence rates for 1,00,000 population

Source: Ref. 21

Table X. Age distribution of smear positive cases in TB programme in India (year 2000)

Age(yr)	Total	Non-DOTS	DOTS
0-14	3,838 (2.02)	2,041 (2.08)	1,797 (1.95)
15-24	35,458 (18.65)	14,055 (14.32)	21,403 (23.26)
25-34	45,377 (23.86)	23,911 (24.36)	21,466 (23.33)
35-44	42,597 (22.40)	22,750 (23.18)	19,847 (21.57)
45-54	31,746 (16.69)	17,450 (17.78)	14,296 (15.54)
55-64	11,902 (10.47)	11,205 (11.42)	8,697 (9.457)
65+	11,231 (5.91)	6,735 (6.86)	4,496 (4.89)
All	1,90,149	98,147	92,002

Figures in parentheses are percentage of total cases in all ages
DOTS, directly observed treatment-short course
Source: Ref. 7

new cases arising (incidence). Thus the earlier presentation[14] has been revised to take care of population escalation during the past decade. The hypothesis in computing the numbers diseased for the present population, is that the disease rates in India remain static, but absolute numbers increase owing to demographic reasons. It also needs to be pointed out that the prevalence and incidence rates are applied to 1000 million population, across the board, in the manner it was applied to 850.00 million in the previous estimate[14], without making allowances for changes in age sex wise composition of the population between the two, taking place during the decade. The issue of lack of standardisation in calculating the burden from time to time, by applying prevalence rates of earlier surveys to later populations, has been appreciated in recent times and needs to be addressed for computing the absolute numbers[33]. It has not been attempted here.

Area-wise distribution: From the results or the countrywide sample survey conducted by the Indian Council of Medical Research (ICMR) in 1955-58[5], it was observed that the prevalence rates for this country as a whole were by and large similar in six zones studied and across the urban-rural divide. On a careful review of the above data, it could be observed that the prevalence rates throughout the country were

Table XI. Prevalence of culture-positive pulmonary tuberculosis by occupation in Wardha (per 1,00,000 population)

Occupation	Urban & Rural: Population (Proportion %)	Urban & Rural: Sex ratio of (M/F) cases	Urban & Rural: Proportion of total cases (C+) (%)	Sex ratio of cases (M/F): Urban	Sex ratio of cases (M/F): Rural
Non worker	26.8	0.34	24.9	2.30	1.41
Student	29.0	1.25	6.6	1.17	1.56
Service	5.3	—	—	1.40	0.53
Professional	2.0	12.19	4.4	0.40	—
Cultivator	15.0	2.45	24.8	0.48	1.73
Agriculture-labour	16.4	0.85	21.4	2.25	1.94
Non agriculture labour	3.9	—	—	4.22	2.05
Others	1.5	—	—	1.53	2.87
Total	100.0	1.08	100.0	1.77	1.84

C+, Culture positive cases
Source: Ref. 14

Table XII. Notified new S+ cases : India (1993-2000)[†]against expected S+ incidence cases*

Year	Diagnosed new S+ cases (No. in 1000)	Rate (per 1,00,000)
1993	2,25,256	25
1994	2,26,543	25
1995	2,64,515	29
1996	2,90,953	31
1997	2,74,877	29
1998	2,78,275	29
1999	3,45,150	35
2000	3,49,374	35
TOTAL	22,54,943	25 – 35

*Expectation at 8,40,000 per year : 67,20,000 (cumulative 1993-2000)
S+, smear-positive
[†]Ref. 7

Table XIII. Tuberculosis situation in Car Nicobar (1986-2002)

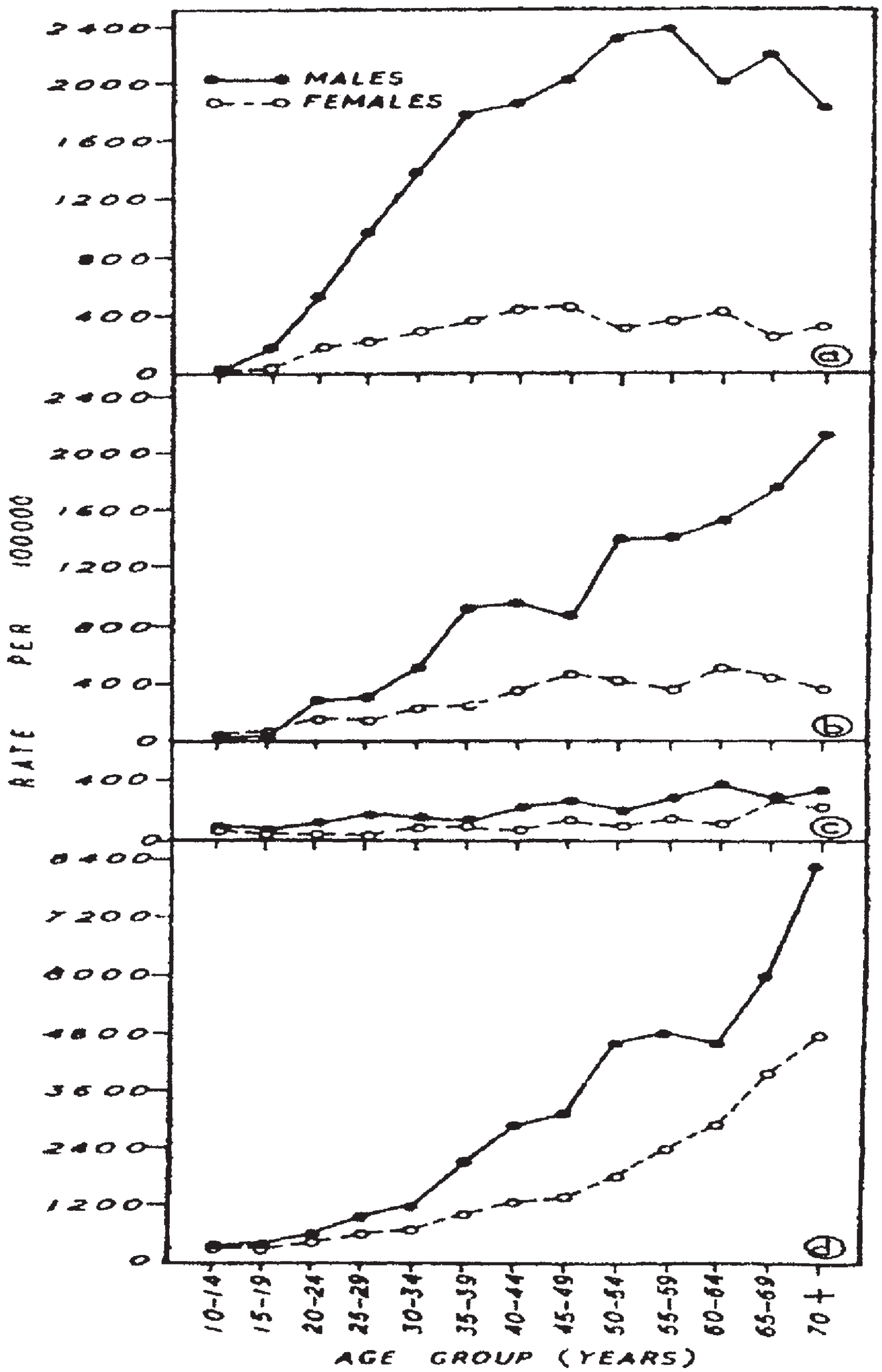
Year	Prevalence of infected (per cent) among 0-14 yr old children without BCG	ARI, per cent/year	Prevalence of S+cases (per 1000)
1986	10.1	1.53	4.1
2001-02	25.1	3.80(3.50)	7.30 (*7.10)[†]

ARI based on standardised prevalence rate of infection is shown in parentheses; [†]Prevalence of disease significantly higher in 2002.

*Standardised prevalence rate

Source: Ref. 23

really not similar[20]. In the first place, the sampling framework did not allow testing of the hypothesis of difference between the areas and zones, if any. In addition, the prevalence rates, on further assessment with the help of 95 per cent confidence limits, do not support the hypothesis of lack of difference between the geographical areas (Table VIII). For example, for the city areas under the Madanapalle zone, the C+ case prevalence rates (2.40 per 1000) were between 1.64 and 3.16 (range for 95% confidence limits), and were significantly lower than those in towns (average, 8.13 per 1000, range for 95% confidence limit, between 6.58 and 9.68), or in the villages (average, 6. 11: range for 95% confidence limits: between 5.02 and 7.20). It would not be out of place to mention here, that from the data shown in Table VIII, as also from information available from surveys elsewhere in India over the years, Bangalore area, falling within the Madanapalle zone in the country wide ICMR survey, appears to have the best possible tuberculosis case scenario anywhere in India. Further, the bacteriological case prevalence rates (C +) for Trivandrum city (average, 2.96 per thousand range between 2.14 and 3.78) were different from Patna city (average, 6.38: range between 5.10 and



Categories of cases :
a) Culture positive on 2 sputum specimens
b) Culture positive on one specimen only
c) Culture negative smear-postive [3 or more acid fast bacilli (AFB)]
d) Abacillary mass miniature radiography (MMR)/ active (by 2 readers)

Fig.1. Prevalence of disease by age, sex and method of diagnosis.

Table XIV. Expansion of TB programme and HIV influence on TB incidence

(A) Hypothetical levels of efficiency of TB programme (RNTCP)

		Targets of TB Programme for achievement* (%)			TB incidence (%)
		Current	Year		
			2004	2007	Rate of decline
Most Optimistic	a) Case detection	60			
	b) Cure rate	40	60	80	10% per year
Most Pessimistic	Cure rate	40	45	55	5% per year

* Global Target of WHO - 70% case detection and 85% cure

(B) Rate of programme expansion/rate of HIV spread

1.	Low HIV/Fast expansion of DOTS (say entire country covered by 2005-2006)	Incidence of total and SS + cases reduced	82% likely fall due to Programme could be only 59% by 2020 (due to HIV)
·	Cumulative number of case (in 20 yr)		21 million
2.	High HIV/Slow expansion of DOTS	Incidence increases by 20%	cumulative number of cases (in 20 yr) 46 million

3. Losses due to HIV effect are much greater than the gains made from programme expansion (DOT-S). Even low HIV epidemic affects programme expansion gains.

Source: Ref. 52

7.66). This shows that tuberculosis prevalence rates could not be similar between areas in India. This is understandably so, given the regional diversities in terms of ethnic, economic, cultural complexities and variables, pervading the vast land masses and the population size of near continental dimensions.

With this background information, one could now argue that the average prevalence rate (and incidence rate also) as worked out by Dye *et al* [2](Table VII), may not be used indiscriminately for all areas of the country, as a sort of target, with the ostensible purpose of evaluating supposedly epidemiological gains, through a set of programme activities, as currently being practised under the RNTCP. This could be used for resource mobilisation and advocacy purposes. Measurement of change on a time series or of geographical differences would require statistically sensitive indices of disease (and infection) in order to test a given hypothesis of change/difference (or, otherwise) by examining an appropriate population sample, calculated for the purpose[20]. The grossly average and well rounded rates may not lend themselves to a measurement of change in them with the required degree of precision.

Prevalence/incidence by age: Both prevalence and incidence rise with age, in both sexes, in surveys conducted so far in the country. The rise is seen in all categories of case, namely X+, C+, and S+ in the community[22] (Fig.1). The latest information on the proportional distribution of smear positive prevalence cases in the community by age (1984-1986) in the Chennai area[21], is given in Table IX. It could be observed that, of the prevalent cases in the community, the age-wise proportion of cases were substantially higher 35-44 yr onwards, to be at the peak for the age group 55- 64 yr (28.40%). Moreover, it remains as high as 22.67 per cent in 65 + age group, being similar to that in 45-54 yr. This could be contrasted to the distribution proportions of 0.7, 1.54 and 7.25 per cent in age groups, 10-14, 15-24 and 25-34 yr, respectively.

Table X shows the age-wise proportional distribution of smear-positive cases for India, diagnosed both under the NTP and RNTCP, combined for the year 2000[7]. The peak concentration is seen to be at 25-34 yr age group, reducing thereafter. In 55-64 and 65+ year age groups, only 10.47 and 5.91 per cent of all the cases are respectively distributed. The relative concentration of diagnosed S+ cases to be in the younger age group, peak in 25-34 yr, is a phenomenon also seen in some of the African countries, who are similarly placed with India with respect to tuberculosis situation as group IV countries, *e.g.*, Tanzania (1985-87), Mozambique (1989), Malawai (1989) and Nicaragua (1989)[34].

The situation of less than expected detection of cases in older age groups, as observed under the NTP/RNTCP in India, could be attributed to deficient attendance of the symptomatics in older age groups at the general health service facilities, *i.e.*, not commensurate with the likely prevalence of tuberculosis among them, as was highlighted by Chakraborty in 1981[35], based on data in the Bangalore area. The situation in India appears not to have altered, since. It appears to be a problem of access owing possibly to a degree of discrimination by the society. The latter seems, in a way, to decide on the attendance pattern of the sick persons to the health delivery outlets, younger people being possibly encouraged and preferred to take action and seek relief. The programme thus seems to benefit the younger and socio-economically the more important group within the population, as against the older population group. The latter is much smaller in size and marginalised due to age, and yet positioning itself as a significant epidemiological group, with a higher concentration of the source of infection transmission.

The above discriminatory situation seems to have an epidemiologic significance of no mean consequence. The large majority of the infecters and most of the uninfected and susceptible population at risk of being infected, seem to distribute themselves at the two extremes of the age groups, the former being in the older age groups and the latter in the younger age groups and children. The former remain comparatively unattended to, under the programme, and keep on accumulating in number and proportion in comparison to the middle age groups. Thus a relative concentration of cases seems to be occurring by age. Due to their position in the society and restricted movement, the persons in the older age groups seem to be in close proximity to the susceptible young children within the family, increasing chances of transmission.

The situation in the western countries, on the other hand, (*i.e.*, Group I countries), appears to be quite different in this regard. In 1970, for example, 70 per cent of the cases in Sweden, diagnosed among the Swedish born, were in the age group 65+ yr. In England and Wales also the situation was similar[10]. The difference in this regard may not only be among the countries, depending on their grouping (I to IV). Even within the most developed countries of the world, the age distribution of tuberculosis cases has a direct relationship with the socio-economic/ethnic variable. For example, the relatively unfavouable epidemiological scenario, obtaining among the American minorities is distinctly different from that among the non Hispanic whites, as also the proportional age distribution of cases occurring in them[36,37].

It is possible that apart from the social and programme driven discrimination, the concentration of cases in older age could take place as a secular trend of disease[8,9], as also due to demographic situation, related to higher population size in the elderly with time. It would thus be logical to conclude that the situation in India is a symptom of its socio-economic milieu, interacting with the disease situation. It also remains a moot point fit for investigation, whether the intervention programme, as it is in India, could result in further concentration of cases among the elderly, through a system of a preferential intervention dynamics.

Distribution of prevalence and incidence by gender: The prevalence of disease by sex and age in the BCG trial area in Chingleput[22] is depicted in Fig.1. Prevalence and incidence (the latter not presented) in all categories of diagnosis had increased with age in males. For female, up to 45-49 yr age, the rates had increased, to be at a plateau thereafter. At all ages the prevalence was considerably higher in males than in females (Fig.1). Of all culture positive case, 79 per cent were found to be in males. In the later TRC follow up study 1968-1986, the average male/ female ratio was 3.7 for C+ cases and 4.5 for S+ cases [21]. Of all pulmonary tuberculosis cases in males, 70 per cent were in the age group 20-54 yr (constituting 39% of male population). Among females on the other hand, 56 per cent of these cases were in age group 20-44 yr, *i.e*., in the reproductive age (constituting 40% of female population).

In the longitudinal epidemiological study in Bangalore rural area carried out between 1961-68[38], the annual incidence rate of C+ cases in males increased during the five year observation period from 200 to 300 per 100,000. It however remained stable among females at 100 per 100,000. The incidence among males aged 55+ yr, in successive surveys for the five years period, ranged from 400-700 per 100,000. In females it had increased only from 150 to 200 per 100,000. An unexplained observation in these surveys was the annual incidence of about 100 per 100,000 in both sexes in the 15-34 yr age group. Aside from the above exceptional parity in incidence between the sexes in this age group, the observations are similar in most Indian epidemiological studies[21,22,38]. In general the disease occurrence rates are about similar in both sexes, till the puberty in females. This is followed by a continuing widening of the gap between the sexes in favour of the females, the differences acutely accentuated past the 35-40 yr age mark.

In the European countries during the earlier part of the last century, the case rates among females between the ages 15-35 yr were generally 10-35 per cent higher than in males. Prompted by this, the postulate of a higher case rate in females in India as well, has been the recurrent theme of many an investigation carried out in India in recent times. It appears that, in so far as general distribution of prevalence and incidence of tuberculosis cases in India is concerned, the epidemiological observation from industrialised countries of the West is a poor guide (Jochem Klaus, personal communication). Instead of investigating the anticipated but unsubstantiated gender bias against women reflected in the occurrence of disease in the community, the reasons for apparent protection enjoyed by the women across the age groups, could rather be a theme of immunobiological and sociological investigations in the Indian context.

Tuberculosis by socio-economic criteria: The survey carried out in Wardha District (Maharashtra) is the only source of survey data (unpublished) linking tuberculosis in the community to socio-economic criteria[14]. The prevalence rates in the survey had depended on literacy (lowest in the graduates and highest among the illiterates), employment held (highest among the professionals, followed by cultivators and agricultural labour) (Table XI). These had also depended on income, living standard (those living in "*Kutcha*" houses had a higher prevalence than "*pucca*" house dwellers). Of the total cases in women, 48 per cent were among those unemployed (include housewives). For all demographic variables, rates in female were less than those in males.

As per Dholakia[39], evidence is lacking to assume a differential prevalence rate of tuberculosis among workers than among non-workers. Of the 'workers' group, estimated to be suffering from tuberculosis in India, about 52 per cent were in the age group 15-44 yr. In this age group, about 40 per cent of the workers with tuberculosis were women in the urban areas. The proportion was only 17.9 per cent in rural areas. There was much lower proportion of women among workers with tuberculosis in higher ages, especially in the urban areas. In the Wardha survey[14], the urban professionals and rural service workers, who had a higher prevalence, had a low proportion of the female population in them, and had consequently accounted for a small proportion of the total cases among females.

The extent of tuberculosis morbidity in the males in the economically active age and in females in the reproductive age, marks it out as a priority among the public health problems in India.

Disease burden-diagnosis of tuberculosis assessed from "Notification" against "Expectation" of incidence: As already stated, the RNTCP in India is due to be expanded fast as per a plan. Currently, there

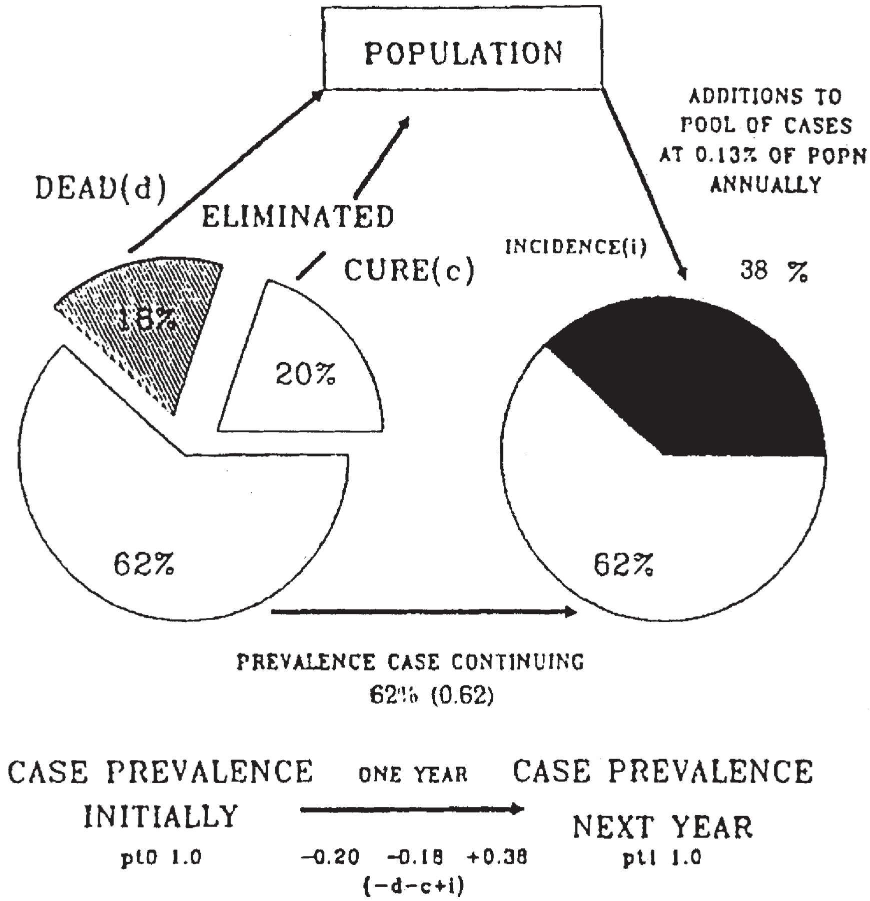


Fig.2. Pool of tuberculosis cases in the community (natural dynamics).
Source: Ref. 14.

is a mixed coverage in the country by NTP and RNTCP. Matching the notifications of the new smear-positive cases, as per WHO Report 2002[7], pertaining to the performance of both NTP and RNTCP areas, for 1993 through 2000, with the expected figures for incidence of S+ cases computed for the period, one could observe a huge short fall (Table XII). Detection rates ranged annually between 25-35 per 1,00,000, against an expectation of 84 per 1,00,000 per year, (annual incidence of S+ cases, as calculated vide Dye *et al*[2], see Table VII). In absolute numbers, whereas a total of 67,20,000 cases for an average population size of 1 billion, could have occurred between 1993-2000 (cumulative likely load; age sex not standardised in computing, over the proportion parameters used in Dye's estimate[2]), the programme had diagnosed only between 2,25,256 and 3,49,374 new S+ cases per year (cumulative: 22,54,943. between 1993-2000). This could be taken as an illustration, in essence, of a part of the epidemiological dynamics, contributing to creating 'left overs" in the community, which is represented by the prevalence. The incidence is the same as prevalence in the Western World. In India, the incidence : prevalence ratio is 1:3[14], for C+ cases, owing to what Grzybowski had aptly termed "left overs"[40].

EPIDEMIOLOGICAL TREND IN INDIA

Tuberculosis in the Bangalore rural area: From the natural dynamics of tuberculosis as studied in the rural area around Bangalore[14], the tuberculosis situation is supposed to be presenting a steady state. (Fig.2). Without active intervention, a third of the existing pool of bacillary cases in a year would get eliminated through death and natural cure. But during the interval, the same proportion gets added to it.

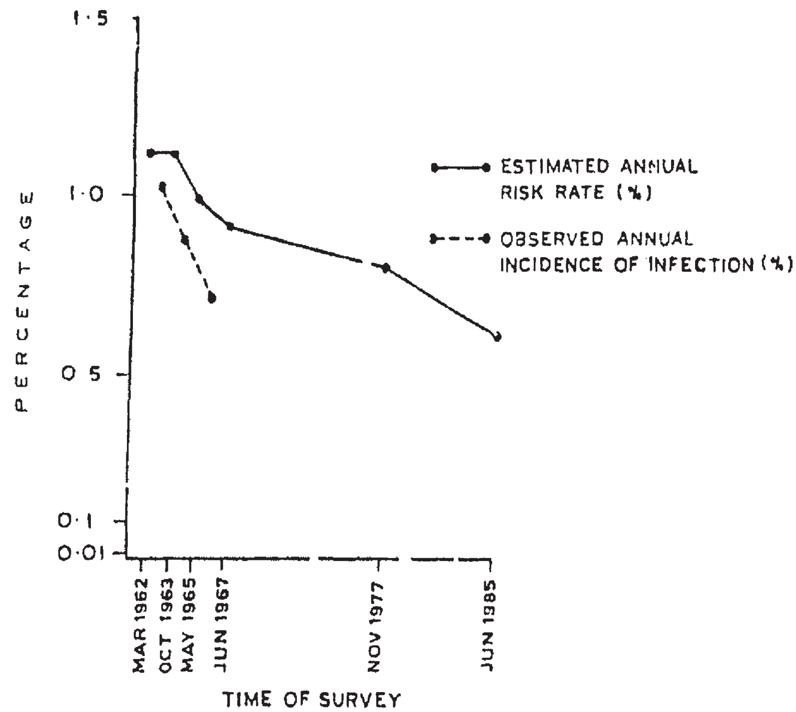


Fig.3. Annual risk of infection (1962-1985) and observed annual incidence of infection (1962-1967). *Source*: Ref. 16.

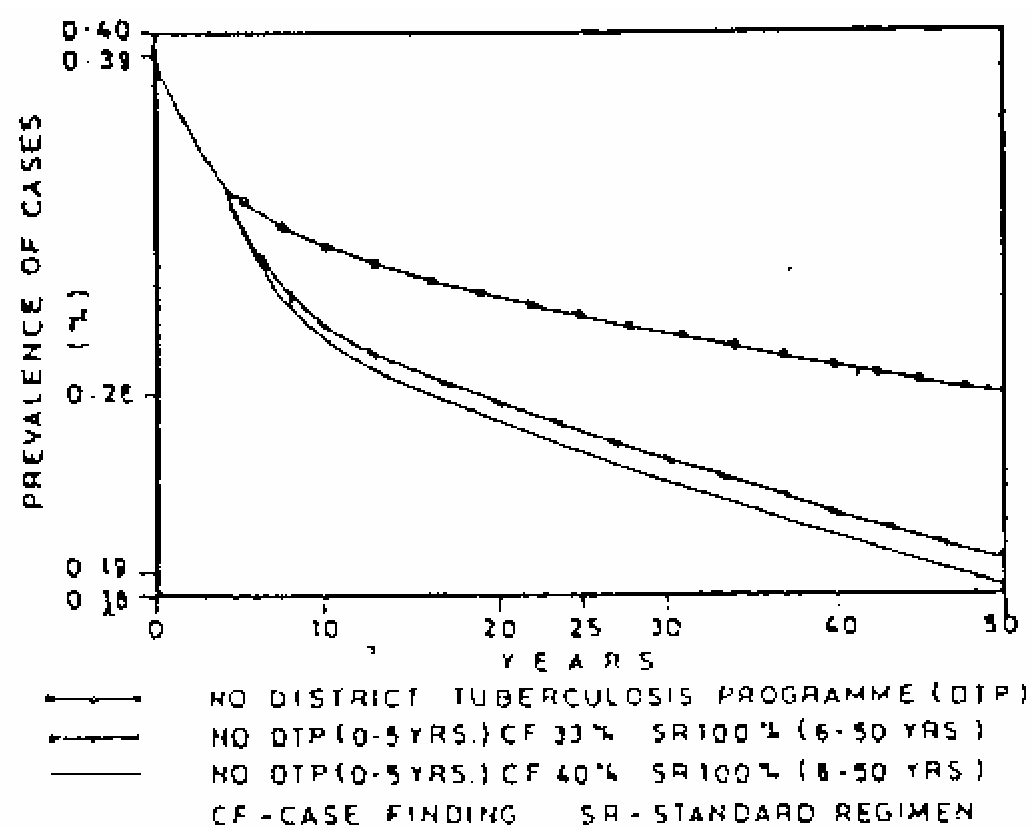


Fig.4. Model depicting hypothetical time-trend of tuberculosis in Bangalore rural area. *Source*: Ref. 14.

The results of the observations from the Bangalore study could be summarised as below, presenting a trend. It is apt to describe the same as natural trend up to the first 5 yr[28]. Thereafter an element of NTP intervention could cloud the interpretations, as it was introduced in the area after the 4th survey (5 yr).

(*i*) Prevalence and incidence rates of C+ cases and X + cases revealed no change in the period of 12 yr (1961-68 to 1977-78), for which information was available[41]. (*ii*) The mean age of cases was higher at later surveys, up to 12 yr period studied[41]. (*iii*) ARI had declined from 1.1 to 0.65 per cent in 23 yr (1962-1985), at around 2.35 per year[16] (Fig.3). (*iv*) Incidence of smear-positive cases had declined for the area from about 65 to 23 per 1,00,000 in the same period[42]. It was observed to the declining in consonance with the fall in ARI.

The observations from the above time series study were extrapolated to the population, taking care of demographic changes in it with time, over a 50 yr period[43]. The observed dynamics of deaths and those due to transfers between the non infected, infected, and several epidemiological classes formed on the basis of the actual study findings over a period of five years, were fed into the mathematical construct for a period of over 50 yr. The natural dynamics were compared with likely disease situations, under various programme effectivity modes, hypothesised for the purpose and fed into the model. The above model showed that even in 50 yr, tuberculosis case rates would come down only minimally. Very large population sizes would be required to be surveyed repeatedly to appreciate a change, if any, which rules out the possibility[14]. Various case finding and treatment levels were imputed into the model, as per the data available from a study on programme dynamics[44]. The model demonstrated that high levels of intervention, however, could result in substantial change in the prevalence rates (Fig.4). The projections could contribute to a decision making process, guiding policy planners to look at likely efficiency modes to be adopted.

Tuberculosis in rural Tamil Nadu: *ARI*: In the study carried out in a rural population of Chingleput in Tamil Nadu by TRC, Chennai[21] (1968-1984, and in a subset of population, again in 1991-1992 and 1994-1996), ARI had remained unchanged for the entire period. It was between 1.8 and 1.9 per cent in the earlier period (1969-84) and 2.9-3.2 per cent (1991-92, 1994-96) (Table VI).

Prevalence of cases: (*i*) The study[21] has shown no change in C+ case prevalence during the period 1968-75 (Fig.5). However, as the resurveys were extended further up to 1984-86, a decline of 2.3 per cent per year was recorded for the later period (overall being 1.4% per annum). Such a decline was not seen in Bangalore rural area (surveyed for first 12 yr)[14,41].

(*ii*) There was a declining trend in C+ cases in all ages, especially in 10-14 yr. This was in line with the agewise trend seen in the 12 yr follow up in the Bangalore rural area[14,41].

(*iii*) There was no change in S+ case prevalence, for all ages (Table IX). However, a declining trend was visible in the younger population, *i.e.*, among those aged upto 35 yr in age. It was statistically significant for 10-14 yr old children.

(iv) There was a strong evidence of decline in both C+ as well as S+ case prevalence in females: 3.8 and 2.8 per cent annually. C+ cases had shown decline at a later period of the follow up in males, (*i.e.*, between 1975-1978 to 1979-1981), without any significant change in the trend of S+ cases.

(v) Because of the above gender related difference, the male : female ratio in C+ case prevalence had increased from 3.5 in 1968-70 to 5.2 in 1984-86 survey (average 4.7). The average for S+ cases for the entire period stood at 1.7 only.

Incidence of cases: (*i*) There was a steady decline in the incidence of C+ cases (at 4.3% per annum) from 352/100,000 between the first two surveys (1968, 1971) to 189 between the last two (1981, 1984). The decline was seen in both sexes and in all age groups. (*ii*) There was only a tendency for decline in incidence of S+ cases. (*iii*) Ratio of prevalence and incidence of S+ cases remained 3.6, at the surveys, probably indicating that new S+ patients would probably continue as S+ cases after occurrence, cumulating

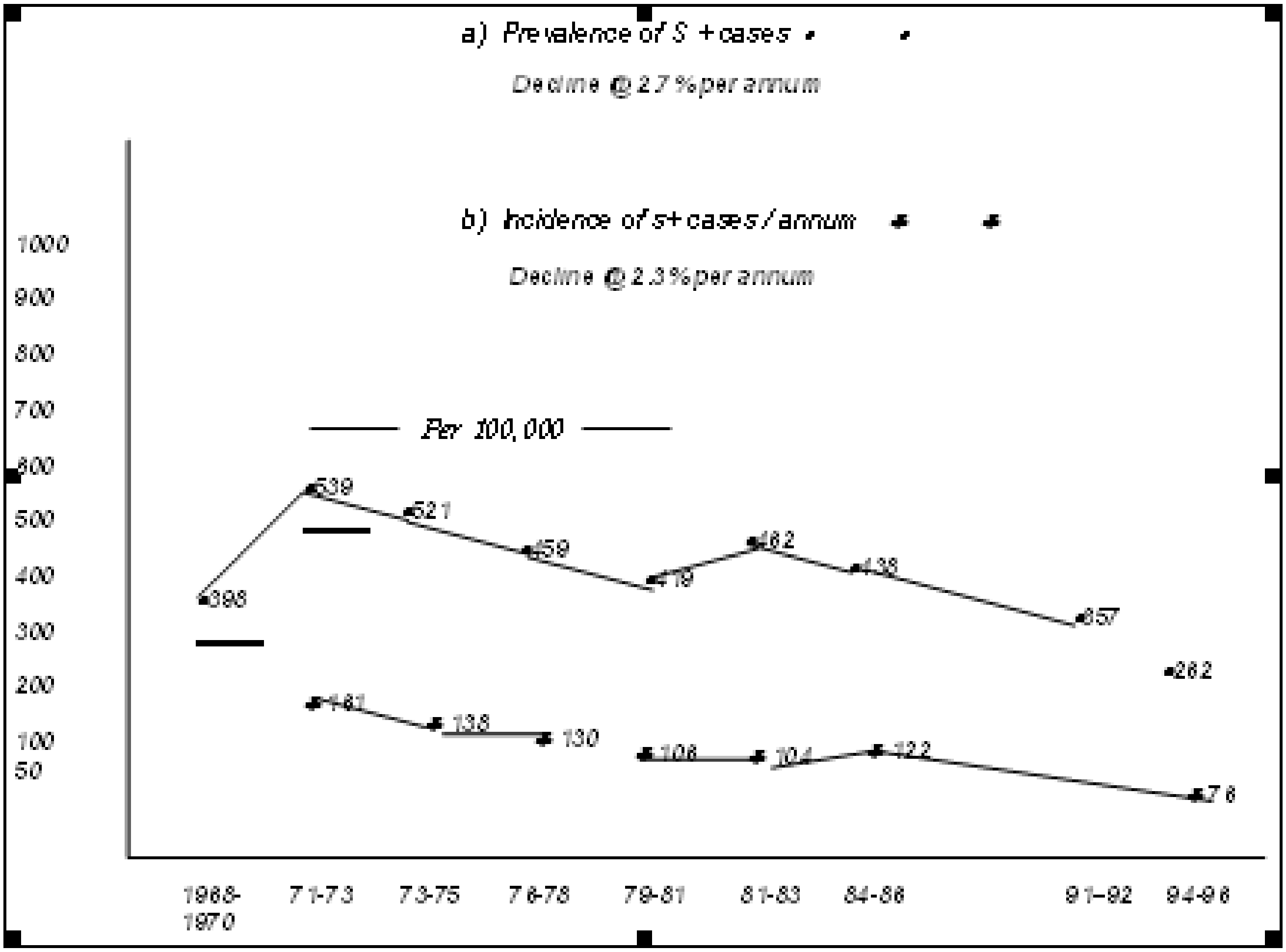


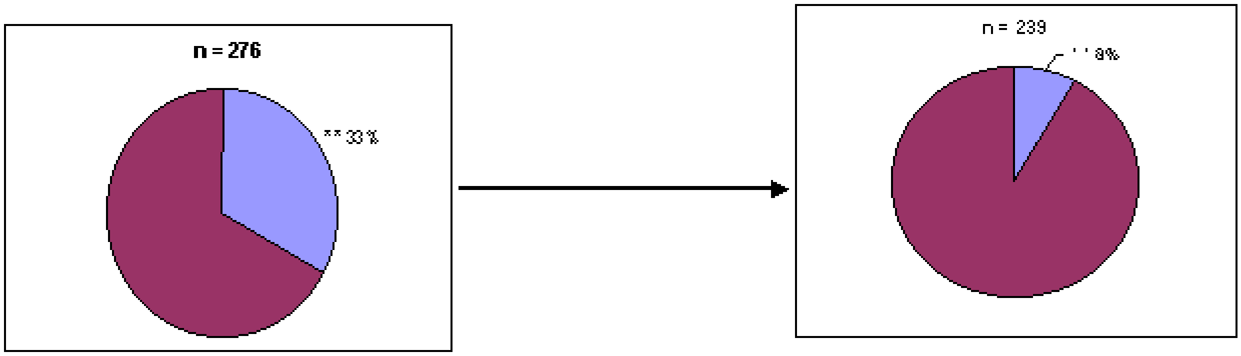
Fig.5. Trend in smear positive cases (incidence and prevalence) in a subset of Chingleput (1968 through 1996)
Source: Ref. 21.

themselves for 3.6 yr in the community, to constitute prevalence. Findings are more or less similar for both rural Bangalore and urban Delhi (between 3.33 and 3.7).

X+ cases: There was significant and substantial decline in X+ case prevalence rate from 1289 / 100,000 to 827/100,000 between 1968 and 1986 (average decline 3.2% per year). The pattern was not gender specific.

Comments on findings: (*i*) It was revealing to observe that incidence of S+ cases, arising at a later survey, from the radiographic class of tuberculous shadows on X ray in an earlier survey, was coming down significantly, with time for the area[21,22]. This was likely to be due to the treatment programme in place for the area, as pursued under NTP, no doubt accentuated due to the presence and interaction with the research field staff of TRC, Chennai. They could act either by motivating patients and probably ensuring drug supply at treatment centres also. Being the long term study area for the TRC evidently had influenced intervention situations and brought long term benefit to the area.

(*ii*) The decline in C+ cases, not initially seen, could also be evidenced on a longer term follow up, as different from the NTI rural area. There was substantial reduction in C+ case prevalence in later surveys (1991/1996 surveys). Whether it had anything to do with reduction of incidence from X + case class, is a point to consider.



n = Incidence of S+case (1971-73)

n = Incidence of S+case (1984-86)

** Having X-ray abnormality consistent with TB at an earlier survey.
Others: Smear+TB incidence from groups other than initial TB on X-ray.

Fig.6. Proportional contribution of the group with tuberculosis abnormality on X-ray at a survey to incidence of smear+tuberculosis at a later survey. *Source*: Ref. 21.

(*iii*) A hypothesis could be considered that when the ARI and S+ case prevalence (and incidence) are relatively high in an area, as it appears to be so in Tamil Nadu rural area, active and intense interventions for a long enough and sustained span of time, are necessary to record change in them. The situation in the subset, for example, in Chingleput area, could record a change in C+ / S+ case situation, only in later surveys. In the subset studied longer (1991, 1994) a significant decline (2.7% per year) had occurred in the prevalence of S+ cases (398 to 262 per 100,000) (Fig.5). However, for reducing breakdown from among the X+ cases into C+ cases, on the other hand, a relatively low key treatment, as followed in the programme, could suffice to achieve the objective early enough.

(*iv*) It is of consequence to programme managers while estimating the S+ case load from ARI data, to observe that the rate of incidence of S+ for 1 per cent of ARI had decreased from 74 to 42 per 100,000 in about 7.5 yr of observation (a decreased by over 40%). The decline in the relationship between S+ incidence and ARI with time, in the Indian context, is reported earlier from the Bangalore rural areas, under long term repeat surveys[42].

(*v*) The findings of the Chingleput area appear to be in line with the overall projections of change made in the 50 yr construct of epidemiological situation with a 2.3 per cent reduction annually, in response to a relatively low key programme dispensation[43].

(*vi*) One of the most significant findings from this study concerned the incidence of C+ and S+ cases, from out of the persons sputum negative but identified as having radiographic abnormality at an earlier survey. There was no decline in incidence from those with a normal X-ray or in those with non tuberculous X-ray abnormality at an earlier survey. However, in those with a TB abnormality initially, the incidence of C+ cases had declined substantially (4.7% annually). It is also true for S+ cases. Of the total C+ S+ cases, arising in 1971-73, about a third had originated from those with an X-ray abnormality interpreted as tuberculosis. This proportion declined consistently from year to year and was only 8 per cent at the 1984-86 survey (Fig.6).

It could be interpreted that the treatment given to the specific epidemiological class of X-ray shadows consistent with tuberculosis disease (X+ cases), had caused a substantially reduced incidence of S+ / C+ cases from this class. The selective decline in incidence by radiological classes moreover indicates a good standard of interpretation and classification of various radiographic abnormalities throughout the survey period. An alternative hypothesis of likely socio-economic change in the area reducing breakdown, may not be tenable, as the same was not reflected in ARI and incidence of S+ cases. The socio-economic improvement, if responsible, could have caused reduction in incidence in all radiographic classes, not confined to X+ cases alone.

It is generally recognised that for appreciation of change with time, culture-positive case prevalence rate of tuberculosis is not the appropriate index to rely on. In the Styblo study[24], the C+ prevalence rate had been observed to register a high only during the survey years. However, it was also a crucial observation in the above study that the S+ cases, detected in a survey, and not confirmed on culture, were mostly found not to be the real cases. It thus stands to reason that in considering trend in the Chingleput studies, S+ cases are considered as cases, only when they are C+. The same was the case in NTI longitudinal surveys also. Thus prevalence of smear-positivity in a survey, unless supported by culture, is not considered representative. At the same time, prevalence of real smear-positive cases, in situations where there is considerable pooling of untreated or inadequately treated cases, is the index which is influenced in an effective control programme. For example, in a situation like as it is in India, where prevalence is about thrice the annual incidence, an effective control programme could possibly work by reducing the smear-positive case prevalence. It is in this context that the reduction in C+ prevalence cases over time, even earlier to that in S+ incidence cases, needs to be understood. It appears to be due to reduced breakdown, and the consequent incidence, specifically from among the X+ cases, through their treatment (a sort of secondary chemoprophylaxis). It appears possible that transmission in the present time did not come down sufficiently largely to be reflected in ARI. It needs to be kept in mind that the treatment of S+ cases was not energetic enough under the routine NTP treatment regimens, as pursued in the study areas. Even though it had salutory effect with regard to the breakdown from X+ class, in the manner of secondary chemoprophylaxis it could not reduce S+ case incidence/prevalence as a whole, and consequently the ARI for the area.

Trend in an urban area: Findings from a study carried out in the New Delhi TB Centre area (NDTBC) are unique in the sense that it gives the only trend for an urban area in the country. The study was conducted for a sufficiently long span of 30 yr, following up the same community seven times after the first survey[45]. The diagnosis in the survey was based only on culture and X-ray result. All the X+ and C+ cases were efficiently treated through the survey period (90% cure rate achieved during 1995-96).

The findings and comments on the trend are summarised as follows:

(*i*) About a tenth (8%) of the bacillary cases had continued as such for about a decade (*i.e.*, between the last two follow up 1982 to 1991). This was despite a good service programme in the area. Of the C+ cases 30 per cent were dead in the period. The proportions remaining as C+ or as X+ cases during the above period were significantly lower than observed between earlier two periods of follow up.

(*ii*) The standardised prevalence rate of C+ cases had not changed over the period, being around 4.0 per thousand (*i.e.*, for 95% confidence level: 2.54-4.84). However, as in Bangalore and Chingleput study areas, there was a higher C+ prevalence at survey VIII among population 55+ yr age group, compared to earlier surveys. The peak of C+ cases at survey VIII in females, had shifted to around 45-54 yr from around 25-34 yr, as seen between survey I through VI.

However, a proportional concentration in the number of cases in higher ages with time, as seen in Bangalore rural area[14], did not occur in the New Delhi area. This was interpreted to be due to a significantly reducing population size in the area, in the age group of 45+, compared to that in survey I, 30 yr back. Influx of wage earners in younger group and exodus of those in higher age (possibly considered to be without ostensible economic worth) from out of city area, was the essential demographic feature in the New Delhi city area[45]. This was not observed to be so in the rural areas of Bangalore, possibly causing the difference in the nature of epidemiological pooling of cases by age with time, between the areas.

(*iii*) There was considerable decline in prevalence of X + cases at later compared to the earlier surveys (Survey I: 13.2, Survey VII, VIII: 6.5 and 5.4 per 1000).

(*iv*) The X+ cases of earlier surveys had the highest rate of breakdown into C+ cases subsequently, this being the highest risk group. The reduction in rate of incidence from among X+ cases with time, as observed in Chingleput study was not observed in New Delhi.

(*v*) Data on sputum smear positive (S+) cases as well as on infection rates (ARI) were not studied in these surveys.

Trend in a tribal area: Car Nicobar is an island in the Bay of Bengal, with a total population of 15,575 residing in 15 villages. An intensified tuberculosis control project was launched there by the Island Administration in 1986[46,47]. All S + as well as C+ prevalence cases were detected on house-to-house survey and treated adequately. Children aged 5+ yr were given chemoprophylaxis for six months after tuberculin testing and those 0-4 yr given BCG vaccination. Infection prevalence was 10 per cent among the 0-14 yr old (Table XIII). The prevalence rate of S+ cases was 4.1 per 1000 and X + case, 7.9 per 1000. At the end of a nine month short course chemotherapy 94 per cent of S+ cases were sputum negative. At a resurvey after a 16 month period, no fresh infected children were detected by the differences of reactions method[17,47]. Number of new S+ cases arising in the area in the period of 16 months was only a third of the previous prevalence (*i.e.*, in conformity with NTI surveys[38]). The intensive programme was then discontinued at a time when there was no observed cumulative prevalence and no fresh infection taking place in 16 months. At this point, the NTP was implemented, leaving the routine district tuberculosis programe (DTP) to operate in the area. The survey in the area has been repeated in 2001-2002[23].

It appears from treatment records, available with the local health authorities that over the years, the programme was not maintained in the island. Investigation and follow up of cases diagnosed from year-to-year since 1988 in the area, showed only 66 per cent of the S+ cases on register completing treatment, their sputum results unavailable. Incomplete treatment, if taking place in these cases year-to-year, could have prevented death, not ensuring sputum negativity though (Annual case fatality 3.7% among the cases on record since 1988, as against the likely rate of over 20 per cent among the cases in an area without an organised programme[38], the latter taken to represent the natural dynamics of tuberculosis). In all likelihood this cumulation of cases over the years had returned the tribal community, back to where their epidemiological trend originally was, infact much worse than it was, before 1986. The force of infection of the relatively fresh cases all diagnosed afresh after 1986, must have caused an escalation of ARI as well, the incidence cases being more prone to cause higher transmission of infection in the community.

Similar trend reversal from a tribal community in Greenland[48] has been observed. Obviously, programmes need to be continued with an accepted level of efficiency for a long enough time. Lack of advocacy and priority could be important causes of attenuation of epidemiological trend in a community. Trends of reduction in a community, achieved through care and effort as in Car Nicobar, could be rudely halted or reversed through lack of prioritisation at a later stage. This could be seen even in the most developed countries, as in Japan[49].

RECENT FACTORS THREATENING ESCALATION

Tuberculosis and HIV/AIDS

Disease burden for HIV/AIDS: The first case of AIDS in India was reported in 1986. As per estimates provided by the WHO/UNAIDS[50], together with those developed through the use of data available with the National AIDS Control Organisation (NACO) in India, the current prevalence of HIV infection in India could be as follows: 1998 : 3.50 million; 1999 : 3.70 million; 2000 : 3.86 million; 2001 : 4.00 million.

Currently, the estimated HIV infection rate among general population in 15-49 yr of age is 0.7 per cent[51].

HIV infection has crossed 2 per cent in Mumbai and is more than 1 per cent in Hyderabad, Bangalore and Chennai. This shows that it is not merely the population groups, manifesting special behaviour alone, but the general population at large, which is progressively at the risk of getting infected.

The escalating HIV-TB situation: Tuberculosis is the only AIDS-related opportunistic infection that significantly affects people not infected with HIV. People infected with tubercle bacilli and HIV are 30 times more likely to develop active tuberculosis in a given year, than those infected with tuberculosis alone. The risk of tuberculosis infection progressing to active tuberculosis is estimated to be 8 per cent per year in an HIV positive person, as opposed to 10 per cent life time risk in an immunocompetent person, infected with tuberculosis, (non-HIV). This results in creating a larger pool of infectious tuberculosis patients[51].

Studies in India show that the proportion of HIV seropositivity in tuberculsis patients in hospitals in Chennai and in Mumbai has risen from 2.6 per cent in 1988-89 to 15.28 per cent in 1999[51]. On the other hand, it has risen in Pune from initial level of between 3.25 and 3.6 per cent in 1991 to about 20.1 per cent in 1996. A study from Tanjavur (Tamil Nadu) rural areas reports a rise in HIV seropositivity among tuberculosis patients from 0.59 per cent in 1996 to 8.89 per cent in 1999[51].

HIV-AIDS - TB-interface: epidemiological situation and intervention: From the global model on spread of HIV-AIDS and how it could be affecting tuberculosis epidemic in India, it is derived by Williams[52] that under the hypothetically simulated scenario of even the best possible expansion rate and the most effective implementation of RNTCP in India, together with the best possible situation of a low HIV-spread, there could still be a rising number of tuberculosis cases in the country (Table XIV). The number of tuberculosis cases could still be higher by 59 per cent by 2020 (cumulative no. of incidence 21 million). The above situation could be seen as better than an alternative worst possible case scenario with a likely rise in tuberculosis incidence by 82 per cent during the period, under a favourable HIV situation but without an RNTCP, with the requisite expansion and adequate efficiency. However, with the worst case scenario of high rise of HIV and slow expansion of RNTCP, the cumulative number of cases could be 46 million by 2020, *i.e.*, more than double, with the spectre of a 20 per cent rise in the incidence of fresh cases of tuberculosis(Table XIV).

Tuberculosis and multi drug resistance (MDR TB): Like HIV-AIDS, threat perception due to occurrence of multidrug resistance has assumed considerable gravity in constructing the epidemic situation analysis and appropriate intervention. In a recent review of the Indian situation[53], eminent workers from the TRC, Chennai, have concluded that the magnitude of the drug resistance problem is principally due to acquired resistance (replaced in recent times by the term drug resistance among previously treated cases). In Gujarat, the patients with treatment failure or relapses, had shown an increased rifampicin resistance from 2.8 per cent (1980) to 37.3 per cent in 1986, and isoniazid (INH) resistance from 34.5 to 55.8 per cent. MDR TB was of the order of 30 per cent. In New Delhi, a similar extent of acquired drug resistance was reported. Institute of Thoracic medicine in Chennai had shown acquired resistance of about 63 per cent among patients from District Tuberculosis Centres of Tamil Nadu. Resistance to INH and rifampicin (MDR TB) was of the order of 20.3 per cent. It was considered[53] that initial drug resistance in India (freshly defined as, drug resistance among new cases) could be at a lower order than similarly placed countries globally, as distinct from the acquired drug resistance situation given above. There could be 5-10 per cent resistance to INH, 2-11.45 for streptomycin and nil for rifampicin in Indian children. This could be reflecting the primary drug resistance problem in the Indian context, and there could be no immediate cause for alarm on this score[53].

The situation thus could be interpreted that (*i*) there is inadequate and inappropriate treatment, both in private and public, including the NTP; (*ii*) the situation has caused high levels of widespread drug resistance in previously treated patients; and (*iii*) the acquired drug resistance has not so far caused primary infections to be causing alarm, inspite of the NTP being operative for over four decades and more. It is possible that drug resistance in tuberculosis patients is less prone to cause transmission. This may, to an extent, explain the phenomenon that high levels of acquired drug resistance is a disconnected observation from a situation of no escalation in ARI and the initial resistance being still low in the community.

ASSESSING TUBERCULOSIS THROUGH MATHEMATICAL MODELING:

Tuberculosis across the globe through modeling: In the global context, the process of mathematically estimating the impact of the strategy of DOTS, is possible now. Murray and Solomon[54,55] evaluated a range of extensions to global control strategies in terms of their potential effects on tuberculosis incidence and mortality, by regions of the world, from 1998 to 2030. The impact of each of the likely items of the DOTS strategy are evaluated separately and incrementally. They have concluded, that globally, 171 million new cases and 60 million deaths are expected in the best possible DOTS scenario and 249 million new cases and 90 million deaths in the worst case scenario, by 2028. Uncertainty prevails on outcome estimates for Asia. In the model by Dye *et al*[56], it is shown that the potential effect of chemotherapy delivered as DOTS on tuberculosis is greater in many developing countries now, than it was in developed countries years ago. The potential needs to be realised fully.

It is forecast that without greater effort to control tuberculosis, the annual incidence of tuberculosis disease is expected to increase by 41 per cent, between 1998 and 2020 (from 7.4 to 10.6 million cases per year) in view of the HIV AIDS/TB epidemic. It is envisaged that DOTS would save a greater proportion of deaths than lower the incidence of cases. The proportion of difference is bigger in the presence of HIV- 1.

Tuberculosis modeling in the Indian context: The tuberculosis model developed at the NTI in 1992[43,44], to study the natural trend and that on some hypothetical situational outcomes created through various efficiency variables of programme delivery has already been commented upon. This is the first mathematical model to study disease trend of tuberculosis in India. However, the model was meant for decision making on alternatives rather than on forecasting the disease situation. Further, it also did not make the equations available, in a manner that other set of variables could be used in forecasting. Clearly, with the change in the nature of the programme and in the hypotheses oscillating around it, there is a felt need today for forecasting the situation with the help of model constructs. One needs to construct situational variables owing to introduction of DOTS, the attendant HIV problem, a fast-paced programme expansion along with a changed face of programme delivery with higher private participation *etc*. The recent work to construct a model to address the Indian situation, carried out under the World Bank auspices by the present author and associates, is a progress in that direction (unpublished document).

As stated earlier, the NTP and the RNTCP are simultaneously operating in India since 1993 as state controlled antituberculosis intervention processes. These operate subject to their own dynamics of delivery, along with the attendant variables with their respective ability to place tuberculosis patients in the community, on treatment, and their outcome. This has created, and will be creating in time, several artificially induced epidemiological classes (or groups) in the community by age sex, socio-economic parameters, demographic distributions with time. Such classes will come into reckoning, besides, on the behaviour of the population, their access to the diagnostic and treatment facilities available within and outside the intervention programme and the dynamics of operations within the latter. The number of classes and their interdependence could be much more complex than under the natural dynamics, as identified and estimated by Gothi *et al*[57], from the longitudinal survey data of the NTI, Bangalore[14]. In the final analysis, however, the epidemiological implementation of the national programmes depends on the "Cure", (or, achievement of a durable state of sputum negativity, following antituberculosis treatment) and prevention of death. The latter, along with the freshly occurring cases in a period, would

Table XV. Varying epidemiological observations by areas in India

Areas	Worst case-scenario Chennai slum, Wardha district Nicobar tribal	Best case-scenario Bangalore area (Urban slum and rural)
Urban-rural distribution	High in urban pocket	No difference
ARI (%)	Around 3.0	1.0
Infection prevalence (%)		
Age group 0-4 yr	> 7 (U), 2-3 (R)	2-4
Age group 5-9 yr	22.0 (U), 15.0 (R)	8-12
Disease incidence (Per thousand per year)	3.0 (U)	1.0
Type of disease	i) Disseminating forms (Lymphadenopathy predominant 4-6 per thousand)	
	ii) Pulmonary TB	Pulmonary fibrotic (Remnant of primary)
	iii) Spine TB	
TB mortality in children (Less than 4 yr age)	Very high, more than 230 (per hundred thousand)	About 50

U, urban; R, rural
Source: Ref. 58

tend to increase the load and the cure would dent the load of existing, as well as freshly occurring tuberculosis cases in the community.

The present mathematical model prepares the initial disease state as caused due to programme delivery process and the respective efficiency levels of various components under it with time. The itinerant size of the classes and the fractional changes in them, caused through processes of transfers between classes together with the directional forces responsible for these, are expressed in mathematical denominations, called “Symbols” and “Vectors” respectively. Persuaded by an unavoidably large number of variables, 47 model vector states and 26 mathematical equations are conceived. These are intended to measure the effect of intervention, causing changes in the size of the respective classes, including that of “cure”. The equations await simulation/ validation in due course. It could pave the way for an epidemiological statement of the disease state in India, in an ongoing manner, by regions/states.

Conclusion

The likely estimates on the tuberculosis problem in India, expressed both as average rates (with range for 95% confidence intervals) and the absolute numbers, are discussed based both on rates from Indian survey results, as well as on the basis of global consensus statements. It also presents disease rates, after adjusting for under and over diagnosis made in the surveys, from which the rates are derived, depending on the survey method used. It could be of considerable significance in this context to note that the adjusted rates for culture-positive cases could be as high as 6.0 per thousand and that for radiologically positive cases, about 3.0 per thousand, on the average. The rates are recommended to be used for estimation of the burden for the purposes of resources mobilisation and advocacy. It is also suggested that for ongoing evaluation of programme effectivity, instead of average rates, as in use for the vast country under RNTCP, alternative rates for the given areas corresponding to their identification as having the best and worst possible disease scenario, could be more desirable to use. The hypothetical disease situations, for the best and worst possible case scenarios, as per information available for some areas, is depicted in Table XV[57]. Some economic indices in the nature of physical quality of life indices (literacy rate, life expectancy at birth, maternal mortality rate and infant mortality rate), as developed from census data, could also be used along with ARI, to classify areas for the purpose of applying average indices (virtual targets) for monitoring.

Over comparatively shorter periods of observation of the natural dynamics in the NTI-longitudinal survey[38] or the TRC study in rural Tamil Nadu[22], tuberculosis appears to be having a near steady state in India[14]. Evidences are available to permit one to draw the hypothesis that the epidemic situation in India is probably on a slow downward curve of the epidemic. Such evidences could be as follows: declining mortality and case fatality rates due to TB, decline in meningeal and miliary forms of the disease, relatively high prevalence of cases in higher ages with a low rate of positive cases in children, relative concentration of cases in higher ages, higher prevalence of cases in males, especially adult males and equal prevalence rates across the urban-rural divide. However, even if on a downward curve, the decline at present could only be minimal, as seen from the direct measurement of ARI in some areas in India, and the nature and extent of the recorded decline in the Chennai area. It is apparent that India has the epidemiological trend in common with the countries of sub Saharan region, with an ARI between 1 and 3 per cent, and an annual decline of around 0-3 per cent. Only when high efficiency intervention, both in case finding and treatment is carried out, a decline of between 7-10 per cent would result.

Planners need to be cautions on nascent disasters, possible through cursory programme applications and failure of sustenance of activities through lack of advocacy and awareness as well as inadequacy in the priority setting. It cites specific instances of escalation of the tuberculosis situation, especially among two tribal population groups, one being in India (Car Nicobar). It also suggests that baseline ARI studies, as are being currently completed throughout the country, could be repeated in due time to obtain a trend in the tuberculosis situation, subject to various levels of the intervention efficiencies. Small population sizes, as required for infection surveys, make such studies possible to conduct and these could yield valuable information. The role of monitoring of the programme dynamics and its use in assessing the changes in the epidemiological classes in the community, brought about by a successful application of the programme is also discussed. The likely threat perceptions due to HIV-AIDS/TB and MDR TB are reviewed. The possible use of mathematical modeling, as a tool in the hands of epidemiologists to forecast long-term trend is also described.

References

1. Dolin PJ. Raviglione MC, Kochi A. A review of current epidemiological data and estimation of future tuberculosis incidence and mortality. WHO /TB/93.173. Geneva: World Health Organization; 1993.

2. Dye C, Scheele S, Dolin, P, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence and mortality by country. WHO Global Surveillance and Monitoring Project. *JAMA* 1999; *282* : 677-86.

3. Zaki MH. On the epidemiology of tuberculosis in some selected countries: highlights and prospects for control and eradication, Part I. *Am J Public Health* 1968; *58* : 1692-712.

4. Zaki MH. On the epidemiology of tuberculosis in some selected countries: Highlights and prospects for control and eradication, Part II. *Am J Public Health* 1971; *61*: 843-54.

5. Indian Council of Medical Research: *Tuberculosis in India. A sample survey 1955-58*. Special Report Series No. 34. New Delhi: Indian Council of Medical Research; 1-121.

6. Ministry of Health and Family Welfare. *TB India 2002: RNTCP status report*. New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare; 2000.

7. World Health Organization, *Global TB control*. WHO Report 2002. Country Profile India, 2002.WHO/CDS/TB/ 2002. 295 p. 75-6.

8. Grigg ERN. The arcana of tuberculosis. With a brief epidemiologic history of the disease in the USA.Parts I and II. *Am Rev Tuberc Pulm Dis* 1958; *78* : 151-72.

9. Grigg ERN. The arcana of tuberculosis. With a brief epidemiologic history of the disease in the USA. Part III. Epidemiologic history of tuberculosis in the United States. *Am Rev Tuberc Pulm Dis* 1958; *78* : 426-53.

10. Raviglione MC, Sudre P, Rieder HL, Spinaci S, Kochi A. *Secular trends of tuberculosis in Western Europe: epidemiological situation in 14 countries*,. Publication No.WHO/TB/92. Geneva: World Health Organization, Tuberculosis Program, Division of Communicable Diseases, 1992 p. 170.

11. Suarez PG, Watt CJ, Alarcon E, Portocarrero J, Zavala D, Canales R, *et al*. The dynamics of tuberculosis in response to 10 years of intensive control effort in Peru. *J Infect Dis* 2001; *184* : 473-8.

12. Dye C, Fengzeng Z. Scheele S, Williams B. Evaluating the impact of tuberculosis control: number of deaths prevented by short-course chemotherapy in China. *Int J Epidemiol* 2000; *29* : 558-64.

13. Styblo K. The elimination of tuberculosis in the Netherlands. *Bull Int Union Tuberc Lung Dis* 1990; *65* : 49-55.

14. Chakraborty AK. Prevalence and incidence of tuberculosis infection and disease in India: a comprehensive review. 1997, WHO / TB / 97. 231, p 1-26 (+ attachment). Geneva: World Health Organization.

15. Styblo K, Meijer J, Sutherland I. Tuberculosis Surveillance Research Unit Report No.1: the transmission of tubercle bacilli. Its trend in human population. *Bull Int Union Tuberc* 1969; *42* : 1-104.

16. Chakraborty AK, Chaudhuri K, Sreenivas TR, Krishna Murthy MS, Shashidhara AN, Channabasavaiah R. Tuberculous infection in a rural population of south India: 23 year trend. *Tuberc Lung Dis* 1992; *73* : 213-8.

17. Raj Narian, Nair SS, Chandrasekhar P, Ramanatha Rao G. Problems connected with the estimation of the incidence of tuberculosis infection. *Indian J Tuberc* 1965; *13* : 5-23.

18. Chadha VK, Krishna Murthy MS, Shashidhara AN, Jagannath PS, Magesh V. Estimation of annual risk of tuberculosis infection among BCG vaccinated children. *Indian J Tuberc* 1999; *46* : 105-12.

19. Sudre P, ten Dam G, Chan C, Kochi A. *Tuberculosis in the present time: a global overview of the tuberculosis situation*. WHO/TUB/91. 158, Geneva: WHO; 1991.

20. Chakraborty AK. Tuberculosis situation in India : measuring it through time. *Indian J Tuberc* 1993; *40* : 215-25.

21. Tuberculosis Research Centre, Chennai. Trends in the prevalence and incidence of tuberculosis in south India. *Int J Tuberc Lung Dis* 2001; *5* : 142-57.

22. Tuberculosis Prevention Trial. Madras. Trial of BCG vaccines in south India for tuberculosis prevention. *Indian J Med Res* 1980; *72* (*Suppl*) : 1-74.

23. Murhekar MV, Kolappan C, Gopi PG, Chakraborty AK, Sehgal SC. Tuberculosis situation in the isolated tribal community of Car Nicobar India, 15 years after the extensive tuberculosis control programme (in press).

24. Styblo K. Recent advances in epidemiological research in tuberculosis. *Adv Tuberc Res* 1980; *20* : 1-63.

25. Styblo K. Overview and epidemiologic assessment of the current global tuberculosis situation with an emphasis on control in developing countries. Rev *Infect Dis* 1989; *11* (*Suppl 2*) : S339-46.

26. Styblo K. The relationship between the risk of tuberculous infection and the risk of developing infectious tuberculosis. *Bull Int Union Tuberc* 1985; *60* : 117-9.

27. Frost WH. How much control of tuberculosis ? *Am J Public Health* 1937; *27* : 759-66.

28. Styblo K. Tuberculosis control and surveillance. In : Flenley DC, Petty TL, editors. *Recent advances in respiratory medicine*. vol.4. Edinburgh: Churchill Livingstone; 1986 p. 77-108.

29. Cauthen GM, Pio A, ten Dam HG. *Annual risk of tuberculous infection*. WHO/TB/88. 154. Geneva: World Health Organization; 1988 p.1-34.

30. Kumari Indira KS, Sivaraman S, Joshi M, Pillai NS. Annual risk of tuberculosis infection: an estimate from ten year old children in Trivandrum district. *Indian J Tuberc* 2000; *47* : 211-7.

31. Chadha VK, Jagannatha PS, Pratibha Narang, Savanur SJ, Mendiratta DK, Lakshminarayana. Annual risk of tuberculosis infection in three districts of Maharashtra. *Indian J Tuberc* 2003; *50* : 125-32.

32. Chadha VK, Jagannatha PS, Savanur SJ. The annual risk of tuberculosis infection in Bangalore city. *Indian J Tuberc* 2001; *48* : 63-71.

33. Krishna Murthy MS. Problems in estimating the burden of pulmonary tuberculosis in India; a review. *Indian J Tuberc* 2001; *48* : 193-9.

34. Murray C, Styblo K, Rouillon A. Tuberculosis. In: Jamison DT, Mosley WH, Measham AR, Bobadille JL, editors. *Disease control priorities in developing countries*. New York: Oxford Medical Publications; 1993 p. 233-59.

35. Chakraborty AK. Tuberculosis case-finding among symptomatics in the community - a reapprisal. *Indian J Tuberc* 1981; *28 :* 12-7.

36. Zeidberg LD, Gass RS, Dillon A, Hutcheson RH. The Williamson country tuberculosis study - a twenty four year epidemiological study. *Am Rev Respir Dis* 1963; *81* : 1-88.

37. Rieder HL, Cauthen GM, Comstock GW, Snider DE Jr. Epidemiology of tuberculosis in the United States. *Epidemiol Rev* 1989; *11* : 79-98.

38. National Tuberculosis Institute, Bangalore. Tuberculosis in a rural population of south India : a five- year epidemiological study. *Bull World Health Organ* 1974; *51* : 473-88.

39. Dholakia R. The potential economic benefits of the DOTS strategy against TB in India. Geneva: World Health Organization, WHO/TB/96.218.

40. Grzybowski S. Natural history of tuberculosis. Epidemiology. *Bull Int Union Tuberc Lung Dis* 1991; *66* : 193-4.

41. Chakraborty AK, Singh H, Srikantan K, Rangaswamy KR, Krishna Murthy MS, Stephen JA. Tuberculosis in a rural population of south India: Report on five surveys. *Indian J Tuberc* 1982; *29 :* 153-67.

42. Chakraborty AK, Suryanarayana HV, Krishnamurthy VV, Krishna Murthy MS, Shashidhara AN. Prevalence of tuberculosis in a rural area by an alternative survey method without prior radiographic screening of the population. *Tuberc Lung Dis* 1995; *76* : 20-4.

43. Balasangameshwara VH, Chakraborty AK, Chaudhuri K. A mathematical construct of epidemiological time trend in tuberculosis - a fifty year study. *Indian J Tuberc* 1992; *39* : 87-98.

44. Chakraborty AK, Balasangameshwara VH, Jagota P, Sreenivas TR, Chaudhury K. Short-course chemotherapy and efficiency variables in National Tuberculosis Programme: a model. *Indian J Tuberc* 1992; *39* : 9-20.

45. New Delhi Tuberculosis Centre. Study of epidemiology of tuberculosis in an urban population of Delhi : report on 30 year follow up. *Indian J Tuberc* 1999; *46* : 113-24.

46. Directorate of Health Services, A & N Admin. Intensified TB Control Programme in the isolated tribal population of Car Nicobar. WHO-HSR GOI Project No. IND/ HSR/001/ D. 1989. p. 1- 64 (unpublished).

47. Chakraborty AK, Channabasavaiah R, Krishna Murthy MS, Shashidhara AN, Motiram G. Tuberculin skin sensitivity following chemoprophylaxis in an island community. *Indian J Tuberc* 1991; *38* : 201-11.

48. Soborg C, Soborg B, Pouelsen S, Pallisgaard G, Thybo S, Bauer J. Doubling of the tuberculosis incidence in Greenland over an 8-year period (1990-1997). *Int J Tuberc Lung Dis* 2001; *5* : 257-65.

49. Inoue K, Matoba S. Counterattack of re-emerging tuberculosis after 38 years. *Int J Tuberc Lung Dis* 2001; *5* : 873-5.

50. UNAIDS. *AIDS epidemic update*. December 2001, Geneva: UNAIDS.

51. Sahni A, Chakraborty AK. TB-HIV disease burden in India. The Health Administrator, Special issue on Tuberculosis. *15* : 186-9.

52. Williams B. Estimating the impact of the epidemic of HIV on tuberculosis in India; as quoted by Chakraborty AK, in, Expansion of the tuberculosis programme in India: The policy evolution towards decentralization and integration, Feb. 2003. Central for Health Research and Development, Pune p.1-66.

53. Venkataraman P, Paramasivan. Drug resistance in tuberculosis and issues related to multidrug resistance in planning for TB Control in India. The Health Administrator, Special issue on Tuberculosis, 15: 127-36.

54. Murray CJL, Salomon JA. Modeling the impact of global tuberculosis control strategies. *Proc Natl Acad Sci USA* 1998; *95 :* 13881-6.

55. Murray CJL, Salomon JA. Using mathematical models to evaluate global tuberculosis control strategies. Harvard University, Cambridge MA: Center for Population and Developmental Studies; 1998.

56. Dye C, Garnett GP, Sleeman K, Williams BG. Prospects for worldwide tuberculosis control under the WHO DOTS strategy. *Lancet* 1998; *352* : 1886-91.

57. Gothi GD, Chakraborty AK, Jayalakshmi MJ. Incidence of spectum positive tuberculosis in different epidemiological groups during five years follow up of a rural population in south India. *Indian J Tuberc* 1978; *25* : 83-91.

58. Chakraborty AK. Problem of tuberculosis among children in the community: situation analysis in the perspective of tuberculosis in India. *Indian J Tuberc* 1999; *46 :* 91 -104.

Reprint requests: Dr A.K. Chakraborty, “BIKALPA” 557, 4th Block, 8th Main, Koramangla, Bangalore 560034, India
e-mail: akchakraborty@rediffmail.com