

Children constitute about 40% of the population of our country. Some of the more serious and fatal manifestations of tuberculosis also occur mostly in children. Furthermore, the late post-primary reinfection type of pulmonary tuberculosis seen most often in older age groups is usually the culmination of a primary infection which still takes place, by and large, in childhood in countries like ours with high prevalence of disease.

Authentic information about the extent and magnitude of tuberculosis in children is rather scanty, notwithstanding its importance. There are considerable differences between pediatricians, tuberculosis specialists and those working in other disciplines of medicine in this respect. And this is because none of them sees the problem in its entirety. A pediatrician mostly sees children with acute and serious manifestations such as miliary, meningeal and progressive primary disease. Their impressions are based mainly on hospital admissions of tuberculous children vis-à-vis hospital admissions of which they constitute a substantial percentage. Most of the cases seen by tuberculosis/chest clinics are either silent cases discovered during about surveillance of household contacts of pulmonary patients or those with minimal symptoms and pertaining to either respiratory system or sometimes involving the lymph-nodes. Many cases of lymphadenitis also report, at the surgical department of general hospitals. Disease of other organs like bones and joints, abdomen etc. again usually report at the particular specialized departments of general hospitals.

There is yet another difficulty in estimating the true extent of disease in this age group. Finding tubercle bacilli and/or histopathological examination are the only authentic criteria of diagnosis but finding of tubercle bacilli in disease amongst children is exceptional. Histopathological examination, too, is not always possible. These difficulties, thus, further complicate the efforts to assess the extent of disease with a reasonable degree

Paucity of epidemiological studies and the difficulties in organising such studies in this particular age group have been amply brought out in a paper published in this issue. Available information shows that respiratory tuberculosis in children between the ages of 5 and 14 years is very small indeed as compared to older age groups. Although information for children below the age of 5 years is even more scanty (because children in this age group are usually not included in mass photo fluorographic surveys), yet it can be indirectly inferred that respiratory tuberculosis even in this age group must be minimal because infection rates are known to be very low in this age group even in high prevalence countries. Moreover, global epidemiology has shown that whenever tuberculosis starts declining, it first declines in younger age

diagnosis in those persons who present with symptoms pertaining to the various extra-pulmonary systems, the extent of unidentified cases who do not report at the medical facilities cannot even be guessed and yet it could be significant if the analogy of respiratory tuberculosis holds for extra-pulmonary disease also.

The problem of tuberculosis in children was discussed in depth at the 41st National Conference on Tuberculosis and Chest Diseases held in Hyderabad in October 1986 by a panel consisting of tuberculosis specialists and paediatricians. The panel agreed that the prevalence of tuberculosis, both pulmonary and extra-pulmonary, in this age group could not be high, though some of the manifestations resulting from haematogenous dissemination like miliary and meningeal tuberculosis still carry a poor prognosis. Hospital admissions do not reflect the exact prevalence in the community and any difference in the impressions and approach to the problem by the two categories of workers arose because cases seen by both of them are of different types.

It will not be out of place to refer to prevention of disease in this age group. Reduction in the pool of infection, viz., sputum positive cases of pulmonary tuberculosis in the community, is the sine qua non of prevention of tuberculosis in children. Since case-finding and case-holding, on which reduction in the pool of infection depends, are still considerably deficient in our country, one has to depend also on adjuvant preventive measures viz. chemoprophylaxis, BCG vaccination and a good nutritional status.

While chemoprophylaxis is feasible in the case of children in contact with infectious persons in the family, it is not so on a mass scale. Many studies in the world have shown that BCG does confer protection against disease and there is no study carried out anywhere in the world which may have proved that BCG does not offer any protection against any manifestation of tuberculosis in children. Case control studies now being carried out in many parts of the world have confirmed that BCG does confer a certain amount of protection against the disease, whatever be the quantum of protection. In another study, the incidence of tuberculous meningitis during the first 5 years of life after systematic BCG vaccination soon after birth in some West European countries was compared with the results in German Federal Republic where no vaccinations were carried out. The study has shown that BCG vaccination at birth protects the children from the risk of meningitis. This study further corroborates the findings of the BMRC study. On the basis of available information, thus, it is desirable that children should not be denied the protection that is available from BCG vaccination, even though the protection is not absolute.

commemoration of the Centenary of the discovery of the tubercle BACILLUS. It is also a great pleasure for me to be in a country where a good deal of research concerning tuberculosis and its control, particularly in developing countries, was made during the last three decades, and I am delighted to meet here a number of good friends. I hope that you will find the topic of today's contribution relevant and that your research field workers will be encouraged to bridge the gaps to optimize control programmes in developing countries.

While tuberculosis will virtually be eliminated in developed countries in a few decades, it continues to be a major problem in developing countries. Firstly, I will try to sum up several topics concerning more recent discoveries in tuberculosis epidemiology relevant to tuberculosis programmes in developing and developed countries, and secondly, to discuss relevant items of IUAT-assisted National Tuberculosis Programmes in developing countries.

A- SOME ASPECTS OF TUBERCULOSIS EPIDEMIOLOGY RELEVANT TO TUBERCULOSIS CONTROL

1. *Interactions between the tubercle bacillus and man in his environment under "natural conditions"*

It is important to study the interactions between the tubercle bacillus and man in his environment (in a community) under *natural* conditions, i.e. free from any interference, particularly by case-finding and chemotherapy. A considerable amount of information has been collected on that matter over the last two decades, which gives us a better understanding of the way in which tuberculosis behaves and maintains itself in the community (Styblo, 1984). This helps us to estimate the impact of current control measures on the tuberculosis problem.

It is evident that the outcome of interactions between the tubercle bacillus and a po-

*Ranbaxy-Robert Koch Oration delivered at the 41st National Conference on Tuberculosis and Chest Diseases, Hyderabad, in October 1986.

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thousands of years.

Here are three different outcomes of interaction under "natural conditions":

- (a) In some developed countries the tuberculosis problem probably started to decrease in the 19th century or even earlier. Figure 1 shows tuberculosis mortality rates in children aged 0-4 years in England and Wales between 1551 and 1940. Nearly 600 per 100,000 children of that age died annually from tuberculosis in the 1850s. It took some 55 years to reduce this mortality by 50%. The decrease was much steeper between 1905 and 1940, in spite of World War I and the serious economic depression in the late 1920s and early 1930s.

At this point, we would stress that improved socio-economic conditions and hygiene are not the only factors which accelerated the decrease in tuberculosis mortality during the first four decades of this century. Another factor in the more distinct decrease in tuberculosis mortality during the 1920s and 1930s must be related to the *isolation* in sanatoria of an increasing number of patients with infectious tuberculosis. Since a larger proportion of these highly infectious cases was isolated and treated for many months in sanatoria, the risk of infection in the community must have been curtailed to some extent.

There is reliable evidence that, irrespective of its magnitude, the tuberculosis problem in Europe and other developed countries has been decreasing since at least the turn of this century. Between the two World Wars, tuberculosis mortality in most developed countries, showed an annual decrease ranging from 3 to 5%. It is, therefore, evident that tuberculosis would have been eliminated in Europe even without the introduction of antituberculosis chemotherapy provided that

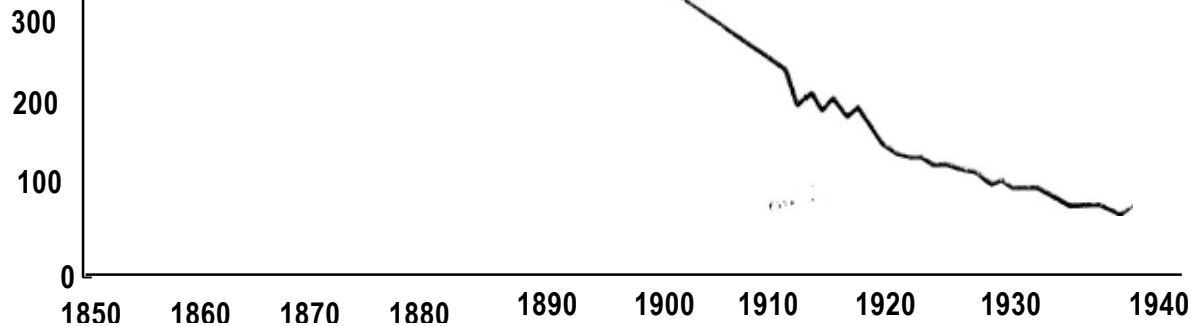


Fig. 1

Rates (per 100,000) of mortality from tuberculosis in England and Wales in children aged 0-4 years, 1851-1940

control measures applied at that time would have continued and that socio-economic conditions would have not deteriorated. The elimination of tuberculosis would have, however, taken approximately 2 1/2 to 3 times longer than after the introduction and maintenance of adequate chemotherapy.

(b) Figure 2 shows that in Eskimos, the death rate among children (and at all ages) was substantially higher between the 1930s and 1950s (among young children, about 1 % died annually from tuberculosis) than in England in the 1850s, and there was no decrease in mortality rates until the introduction of case-finding and treatment in the early 1950s. Also, prevalence rates of tuberculous infection which were found in the early 1950s in Eskimos were extremely high (Figure 3). The figure shows that in children born in 1950, the prevalence of tuberculous infection at the age of 5 years was approximately 90%. The average annual risk of tuberculous infection was then about 25 % the highest ever observed in the annals of medical history, with no tendency to decrease over several decades.

(c) Figure 4 shows the annual risk of tuberculous infection in the Netherlands and Uganda from 1950 to 1970. In Uganda, the risk of infection in 1950 was "only" about 2.5%, thus 10 times lower

annual rate
100,000 population

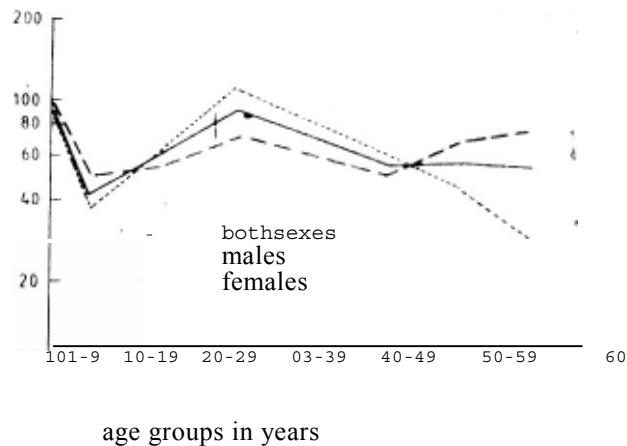


Fig. 2
Age-specific rates of mortality from tuberculosis among Eskimos, 1930-50.

than that observed in Eskimos at the same time. For comparison, Figure 5 shows that in the Netherlands, the risk of infection before World War II was much higher than in Uganda in 1950-1970: 4 % in 1930, nearly 7 % in 1920 and more than 11 % in 1910.

These observations suggest that the balance between the bacillus and a given population can be shifted in favour of the population. This may be brought about by improved socio-

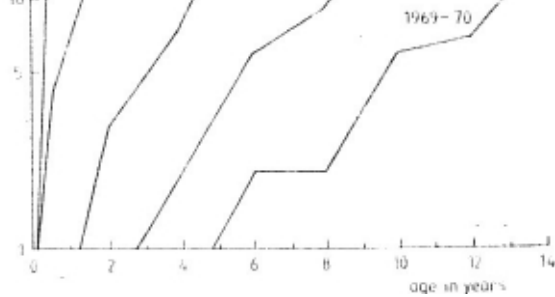


Fig. 3

Age-specific prevalence rates of tuberculous among Eskimos children, 1949-70

Lesotho

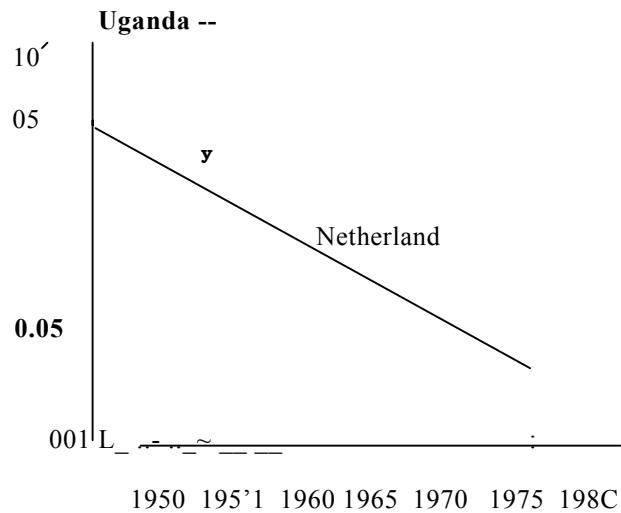


Fig. 4

Annual risk of tuberculous infection in Netherlands, Uganda & Lesotho, 1950-80

economic conditions, identification of sources of infection and their isolation, or their cure by chemotherapy: a combination of improved socio-economic conditions and adequate chemotherapy of diagnosed sources of infection considerably accelerates the defeat of the tubercle bacillus in the community.

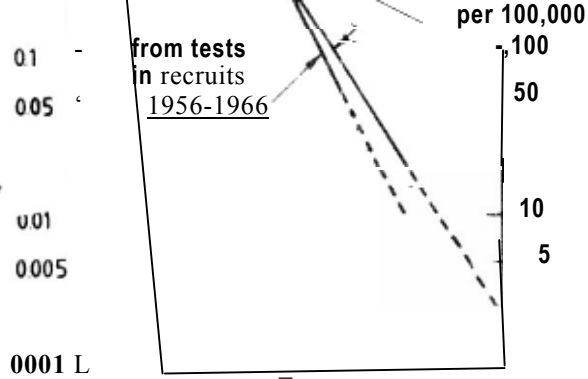


Fig. 5

Annual risk of tuberculous infection the Netherlands, 1910-2000

2. Impact of present control measures on the overall tuberculosis situation

Impact of case finding/treatment

It must be emphatically stressed that the most powerful weapons for the improvement of the epidemiological situation of tuberculosis are chemotherapy and case-finding. The effect of the case-finding/treatment complex can be measured in countries with no mass BCG programme and in which we have been able to assess the tuberculosis situation and its trend over several decades. Two other conditions are required to estimate the impact of the case-finding/treatment complex: (i) the implementation of intensive case-finding for many years, and (ii) a near-100% cure rate in the whole population studied.

It was shown that, in the Netherlands, where all the above conditions could have been fulfilled, decrease in the infection rate due to intensive case-finding and adequate chemotherapy of all diagnosed bacillary cases was 8%, in addition to the 5% due to the "natural" trend (Styblo and Meijer, 1980).

The impact of mass BCG on the overall epidemiological situation is low because most of the prevented cases of primary tuberculosis

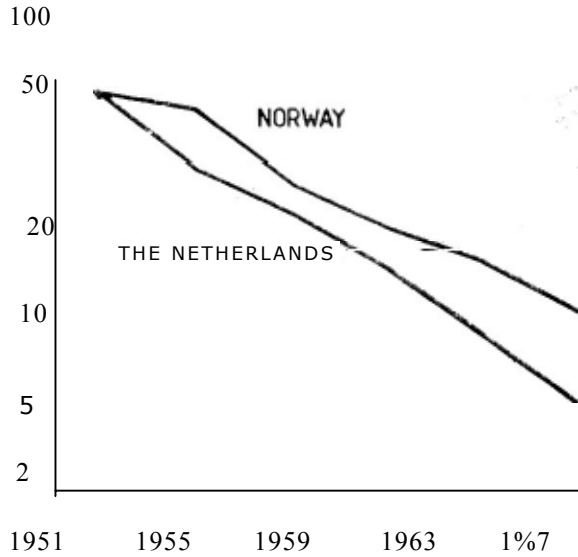


Fig. 6

Notification of tuberculosis (all forms) in children

0-4 years. Norway and the Netherlands, 1951-1968.

It must be stressed, however, that BCG vaccination was introduced for its *direct* effect, i.e. prevention of tuberculosis among the vaccinated individuals and should be applied whenever its use is justified for this effect.

only one table which is quite informative (Table 1).

Table 1 shows that in developed countries, in the pre-chemotherapy era, the ratio between deaths from tuberculosis and reported cases of tuberculosis in the same year was approximately 1 : 2.

Based on the above and other studies not mentioned because of lack of time, the following rationale was put forward by us:

Tuberculosis is one of the few major killing infectious diseases decreasing steadily in developed countries, but still largely uncontrolled in many developing countries. And yet, progress is possible, since:

- (1) Unlike many other infectious diseases in developing countries, tuberculosis can be controlled, with the tools available nowadays, under any socio-economic conditions because *the infectious agent is nearly exclusively in the diseased man whose sputum can be quickly rendered non-infectious.*
- (2) Since a balance also exists in developing countries between the tubercle ba

TABLE

Ratio of deaths from tuberculosis to reported cases of tuberculosis (all forms) in four developed countries in the pre-chemotherapy era, 1925-1944

Author	Country	Period	No. of deaths from TB	No. of reported cases of TB	Ratio deaths cases to
Drolet	USA (Massachusetts)	1933-1935	5,775	10,720	1 : 1.9
	England and Wales	1933-1935	78,139	143,181	1 : 1.8
Lindhardt	Denmark	1925-1934	20,173	39,379	1 : 2.0
Galling	Norway	1925-1944	1,913	3,777	1 : 2.0
From (1)					

annually) and, consequently, the absolute number of smear-positive cases will fall as well.

- (3) *Case-finding of infectious (particularly smear-positive) cases of pulmonary tuberculosis and their cure* are the key to any effective control of the disease, both in developed and developing countries. In addition, they reduce suffering and if adequately applied, considerably lower the death rate of tuberculosis.
- (4) *Reliable diagnostic tools* enabling diagnosis of the great majority of all cases of smear-positive pulmonary tuberculosis and *highly efficient chemotherapy* regimens which can cure nearly all discovered cases of tuberculosis *are available*.

Although the tools for tuberculosis control are the same for both developed and developing countries, their quality and the extent of their application differ tremendously. The use of X-ray and culture examination as case-finding measure is limited in developing countries, so that many cases fail to be diagnosed. Chemotherapy regimens, both for new and retreatment cases, differ substantially, thus producing unequal results. Transport is an enormous problem in most developing countries. Medical care and the social and cultural background determining attitudes towards illness and treatment differ profoundly from those in developed countries. The breakdown rate from infection to disease is affected by malnutrition and many associated diseases in developing countries.

Enumerating other hardships would be of little interest but the reason for mentioning some of these facts is to examine whether the following statement in the 9th Report of the WHO Expert Committee on Tuberculosis (World Health Organization, 1974; p. 22, Styblo and Meijer, 1980) can be challenged:

recommended measures in developing countries were say, only half as effective (or a little less) as those applied in developed countries one would observe a decline in the tuberculosis problem in poor developing countries. However, this is not the case.

The principal reason for failure of tuberculosis control programmes in developing countries is obvious: we are unable to diagnose a sufficient number of sources of infection-smear positive cases of pulmonary tuberculosis and more important, we are unable to cure those who are diagnosed. Although a case-finding and treatment programme must be developed as a whole, as case-finding is preliminary to treatment and cure, the first step to be taken in any efficient tuberculosis control programme is to ensure that the cure rate under routine conditions of all diagnosed cases is raised in order to reach, say, 75% or more. This rate, with some 7-10% deaths from tuberculosis during the first weeks of treatment (because of late diagnosis), will result in elimination of sources of infection in diagnosed cases by more than 80%. The remaining 15-18% of failure cases will not substantially increase the pool of infection. If the success rate is low, say 50% or less, a high number of chronic excretors with drug-resistant bacilli will ensue, with all the consequences known.

Unfortunately, the success rate of standard regimens in many developing countries under routine conditions is very low, i.e. 30-45%. Evidently, the recommended chemotherapy for developing countries is at present, and probably will be for many years to come, beyond the organizational and financial resources of many developing countries. It was hoped that intermittent, fully supervised chemotherapy would improve the results of treatment in developing countries. However, organizational shortcomings, lack of transport facilities, financial problems, a poor network of general health services and many other difficulties are the main reasons for the limited effectiveness of intermittent, fully supervised treatment in chemotherapy programmes under routine conditions in developing countries.

Experience from the 1960s and 1970s showed that Canetti was right. Whereas in some developing countries, particularly in Latin America and in Arab countries, there was a distinct improvement in the overall epidemiological situation, in many poor developing countries, such as in Africa, in the major part of South East Asia and in some parts of Latin America, signs of improvement in the epidemiological situation of tuberculosis are exceptional despite many efforts aimed at controlling the disease. As Canetti postulated 25 years ago, without a major increase in the cure rate of smear-positive cases of pulmonary tuberculosis, no distinct improvement of the tuberculosis problem can be expected in many developing countries in the foreseeable future.

B. IUAT-ASSISTED NATIONAL TUBERCULOSIS PROGRAMMES IN DEVELOPING COUNTRIES

We have been studying the problem of developing chemotherapeutic methods adapted to the conditions prevailing in developing countries in the Tanzania Tuberculosis/ Leprosy Programme for the last 8 years, and we will refer to it shortly (Chum and Styblo 1987, Styblo and Chum 1987).

1. *Standard chemotherapy*

In Tanzania, the basic regimen of the NTPL for newly diagnosed tuberculosis cases, proposed in 1978, is Thiazina (isoniazid and thiacetazone in combined tablets) for 12 months, supplemented with streptomycin for the first 2 months of chemotherapy. In-patient treatment was indicated at the beginning of the NTPL only for severely ill patients and for those patients who lived too far away from a health unit to attend for daily streptomycin. It soon became obvious, however, that many patients on ambulatory treatment were not

Chemotherapy progress is followed up by sputum examination 6, 9 and 12 months after the start of its application. A patient is declared "cured" when at least two negative smear results were obtained at an interval of 3 months or more. The results of treatment are reported quarterly per district for smear-positive cases of pulmonary tuberculosis registered 15-18 months earlier. Table 2 shows the reported results for 1980-1982.

It is seen that the Programme achieved only about 40% cure on the basis of negative sputum smears. When patients who were discharged without smear results are counted among those cured, the success rate was between 52% and 55%.

Chemotherapy results with the standard regimen, after 4 years of NTPL implementation, were judged too low considering the efforts made and the cost of the Programme. We have come to the conclusion that a substantial improvement in treatment results could not be expected with the standard regimen, in spite of improved drug supplies, supervision of patients, etc. This is because removal of material problems does not automatically result in considerable improvement of the patient's compliance. It is very difficult to explain to ordinary people in developing countries living in hard conditions that they must continue chemotherapy for an entire year after all symptoms of the disease have disappeared. In our opinion, the main disadvantage of standard chemotherapy is that after 60 doses of streptomycin and ThiaAna, around 50% patients remain sputum positive. If they abscond from treatment or are irregular, particularly if this happens soon after completion of the initial intensive phase, they become, in many instances, chronic tuberculous excretors. Inadequate chemotherapy, while not curing the patient, prolongs his life, so that chronic cases increase the number of sources of infection in the community and contributes to perpetuate the transmission of infection.

There is no doubt that the patient complies

1980	5,867	39	16	13	15	10	7
1981	5,527	39	14	12	18	10	7
1982	5,498	37	15	15	14	13	6

best when he is seriously ill. This is the case in most smear-positive patients in developing countries, as the disease is discovered only in those who visit a health centre with complaints. The short-term compliance of the patient, lasting often only a few weeks, must be exploited by giving him a very potent chemotherapy which is able to kill the vast majority of tubercle bacilli in his body as quickly as possible. For this and various other reasons mainly to obtain a greater relief of human suffering and a stronger epidemiological impact on the overall epidemiological situation of tuberculosis in the country-it was decided in 1982 to explore the efficacy of short-course chemotherapy under field conditions (since there was definite evidence that short-course chemotherapy was highly effective in controlled clinical trials).

retreatment cases were on short-course chemotherapy. In 1985, more than 4,500 new and retreatment smear-positive cases from 17 (of 20) regions were enrolled.

By June 1986, short-course chemotherapy was expanded to all 20 regions of Tanzania. A total of 5,781 new smear-positive patients enrolled on short-course chemotherapy completed the 8-month regimen as per June 30, 1986. Table 3 shows that the results of short-course chemotherapy at 8 months under routine conditions continue to be satisfactory : 75% were negative, 3% were positive, 6% died, 12% absconded and 3% were transferred to another district.

TABLE 3

‘) Short-course chemotherapy of new cases

The short-course regimen for new smear-positive cases comprises an initial intensive phase of 4 drugs (isoniazid, rifampicin pyrazinamide and streptomycin) given daily under strict supervision, mostly in a general hospital, and a continuation phase with daily Thiazina (isoniazid and thiacetazone) for a further 6 months on an ambulatory, self-administered basis. When thiacetazone cannot be used because of severe side-effects, isoniazid alone instead of Thiazina is given in the continuation phase, provided that the patient is smear-negative at 2 months. This regimen has a cure rate close to 100% in controlled clinical trials.

The regimen was introduced as a pilot study in the Tanga region in April 1982. A 77% cure rate was achieved in 146 consecutive patients enrolled during 1982. These results were very encouraging and short-course chemotherapy has been extended to other regions since that time. During 1983, 799 patients were enrolled in 7 regions and, in 1984, 2,745 new and 27

Preliminary results of short-course chemotherapy at 8 months in 5,550 new smear-positive cases of tuberculosis Tanzania, April 1982 June 1985

	N	%
Negative	4,186	75
Positive	189	3
Died	320	6
Absconded	666	12
Transferred out	189	3
Total	5,550	100

*a further 231 (4%,-;) patients were “false-positives”.

Negative	4,186	80	Results of short-course chemotherapy at 8 months in		
Positive	189	4	509* smearpositive cases Tanzania, 1984 and the first		
Absconded	666	13	half of 1985		
Transferred out	189	4			
Total	5.230	100			
			Negative	387	76
			Positive	22	4
			Died	21	4
			Absconded	67	13
			Transferred out	12	2
			Total	509	100

If sputum conversion likely to have occurred in a proportion of those from the "transferred out" and "absconded" groups is taken into consideration, the cure rate might be close to 90 %.

Table 5 shows the preliminary results at 5 months in 2,418 patients enrolled during the second half of 1985. Sputum conversion at 5 months was achieved in 76 %; 9 % of patients had no information on smear-examination at 5 months by the end of June 1986.

TABLE 5

Results of short-course chemotherapy at 5 months in 2,418* patients with new smear-positive tuberculosis, Tanzania, July-December, 1985

Negative	1,839	76
Positive	28	1
Smear-examination not (yet) done	214	9
Died	130	5
Absconded	145	6
Transferred out	6:	3
Total	2,418	100

*a further 63(31) patients were "false-

*A further 22(4%) patients were "false-positives". failure cases) are satisfactory: 76% were cured and 13% absconded.

Evaluation of the overall treatment results throughout the country

Table 7 shows that short-course chemotherapy has improved the overall results of treatment since 1983 when the success rate was 58 % (799 new smear-positive patients enrolled on short-course chemotherapy); in 1984, a 67% success rate was reported. (2,745 cases were on short-course chemotherapy).

5. Cost of the tuberculosis part of the NTLF

For the period 1979-1982 the Swiss Government contributed SW F 1.63 million to the tuberculosis part of the NTLF. The estimated overall expenditure for the tuberculosis part of the NTLF for 1986-1989 is slightly higher than US \$ 2 million per year (US \$ 2,070,475). This corresponds to US \$ 172.5 per 1 case reported (all forms; about 12,000 cases annually) or SWF 362. This gives a cost of approximately US \$ 0.1 per capita,

1979	5,418	31	13	10	23	18	5
1980	5,867	39	16	1	15	10	7
1981	5,527	39	14	12	18	11	7
1952	5,498	37	15	15	14	13	6
<i>Standard</i> and short-course chemotherapy							
1983	5,825	43	15	10	15	10	7
1984	7,172	49	18	7	14	5	7

*Results: - "Cured"-see text above;

- "treatment completed chemotherapy of 12 months completed. no clinical signs of tuberculosis but no smear results;
- ___ "Transferred out"--patients who have been transferred to this jurisdiction of another district. -
- "Defaulted"-patients who have not attended for 2 or more consecutive months;
- "Still on treatment"-usually because the patient was smear-positive and continued chemotherapy (standard or retreatment):
- *-treat 1984 onwards "Positive";

6- Predictable evolution of the tuberculosis situation in Tanzania in the 1990s

The present risk of tuberculous infection in Tanzania is about 1.1% (Chum et al, 1987). It is hoped that with the current case-detection rate of smear-positive cases (more than 60% and the results of short-course chemotherapy (not very much "behind" those achieved in developed countries under routine conditions) an annual decrease in the risk of infection by approximately 4 to 5%, will be achieved. This *would* correspond to the decrease in the risk of tuberculous infection (and disease) which existed in developed countries in the pre-chemotherapy era and which accelerated by about 7 to 8% due to chemotherapy. With an annual decrease of 4 to 5% in the risk of infection, the number of persons infected by and persons suffering from tuberculosis would decrease by 50%, in about 15 years.

consequently, the risk would have halved itself by the year 2000, i.e. it would then be of the order of 0.5%, and tuberculosis would cease to be a major public health problem in Tanzania.

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NOTICE

The Asthma Bronchitis and Cancer Lung Foundation has instituted an annual prize of Rs. 750/- to be given to a young doctor under 35 years of age for the best article read at annual medical conference/published in medical journal on any aspect of Chest Diseases. The paper should be based on the work conducted by him/her in India. Six copies of the paper to be sent to the undersigned on or before the 31st of December, 1987. The decision of the panel assessing the papers is binding.

Secretary

The Asthma, Bronchitis and Cancer Lang Foundation

of India

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The subject was chosen mainly to present the STATE OF ART and also some aspects of future developments that could be considered in laboratory aspects of tuberculosis. It will also deal with the attempts made at developing early and rapid diagnosis of tuberculosis using the available technology which could ultimately lead to immunodiagnosis using highly specific antigens and antibodies and simple methods with possibilities of application under field conditions. This may not be possible in the immediate future but should be possible in the light of enormous research work that is being carried out in India and abroad on these lines.

Laboratory Aspects in Tuberculosis

The laboratory investigation for patients suspected of having tuberculosis consists of:

- (1) Bacteriology
- (2) Histopathology and
- (3) Immunology

Bacteriology

Specimens

Sputum: Saliva and nasopharyngeal secretion should be avoided while collecting sputum. Bronchial sputum from the 'depth of the chest' should be collected. Overnight sputum specimens are more likely to contain acid-fast bacilli. In patients presenting with symptoms and having moderately advanced disease, a spot specimen can also be valuable. Production of spot specimen is more acceptable to the patient and requires minimum effort and co-operation. Specimens should not be exposed to direct sunlight, radiation or excessive heat. Table 1 presents the results of the smear and culture examination of various combinations of collection and spot specimens.

Type	Positive by	
	Smear %	Culture %
1 Spot	66	91
1 Collection	77	93
2 Spot	76	94
1 Spot+1 Collection	81	97
2 Collection	83	97
2 Spot+1 Collection	84	98
1 Spot+2 Collection	84	99
2 Spot-1-2 Collection	85	95

are available, a spot specimen can detect almost the same proportion of positive cases as a collection specimen, namely, 91 % and 93 % respectively. (Andrews et al., 1959).

Storage of sputum

A study conducted at Tuberculosis Research Centre (TRC), Madras, on 41 specimens of sputum, showed that smear positivity is not affected by storage of sputum even upto 2'3 days (Paramasivan et al., 1983) (Table 2). Hence, a programme can be organised involving transportation of sputum with very little risk of loss of stainability due to delay in transit. However, if culture examination is required, the transit time should be limited to a maximum of 3 days.

Other specimens

Most specimens sent to the tuberculosis

*Wander-TAI Oration delivered at the 41st National Conference on Tuberculosis and Chest Diseases. Hyderabad, in October, 1986.

“Director, Tuberculosis Research Centre, (Indian Council of Medical Research) Chetput, Madras-

NEG.	17	17	17	18	20	20
POS.	83	83	83	82	80	80

10	1,000	1,00,000
1	10,000	10,00,000

laboratory are sputa, but a wide range of other specimens may also require examination. These include laryngeal swabs, gastric washings, CSF, urine, pleural or peritoneal exudates and tissue biopsies.

Sputum microscopy

Examination of sputum by smear and culture are standard methods for the diagnosis of pulmonary tuberculosis and for the assessment of progress during treatment.

Smear microscopy is the only diagnostic method practicable in most laboratories. In the National Tuberculosis Programme, culture examination has no role at present; case finding is done by means of sputum smear examination at the Peripheral Health Centres. Response to treatment is also assessed by smear examination (usually at 6 months).

Probability of finding *AFB* in Ziehl-Neelsen (ZN) stained smear : The quantity of sputum delivered by a wire loop with an internal diameter of 3mm. is about 0.01 ml., and the area covered by the smear is about 200 square millimeters. An oil immersion objective covers an area of 0.02 sq. mm. per single viewing. This means 10,000 such fields need to be screened to cover the entire area of the smear, which is impracticable. Assuming 100 oil immersion fields are examined per smear, only 1% of each smear will be screened (To-man, 1979).

To find 1 acid-fast bacillus (AFB) per field, it would require 10^6 bacilli per ml. of sputum (Table 3). Hence, if there are 5,000 bacilli per ml., there is only a 50% chance of finding a bacillus even after screening 100 fields.

False positive smears : False positive smears are those positive by smear but negative by culture. False positive smears are caused by

food particles, precipitated stains, saprophytic *AFB*, spores of *B. subtilis*, fibres and pollens, scratches on slides and contamination by transfer of bacilli from one smear to another. False negative smears, on the other hand, are caused by improper or inadequate techniques of sputum collection and storage, smear preparation, storage and examination.

In addition, there are other circumstances when one comes across smear negative culture positive, and smear positive culture negative cases.

Smear negative, culture positive cases
Sputum from patients with minimal lesions, discharging only small amount of bacilli, will almost invariably be negative by smear microscopy even if positive by culture.

In a study, 8 sputum specimens were collected from each of 194 patients with prolonged chest complaints. In 68 of these patients, TB could be ascertained by culture. Of these 68 patients, 22 had all 8 smears negative (Table 4). Further, it may be observed that a third of the patients were sputum smear negative but had confirmed disease as shown by a positive culture (Nagpaul et al., 1979).

Smear positive Culture negative cases : As shown in the Table 5, in all the 4 regimens (three daily 12 month regimens and one 6 month intermittent), a percentage of patients were smear positive but culture negative. Irrespective of the rhythm of administration, this phenomenon was seen more often in rifampicin containing regimens than the others. At the end of 6 months of chemotherapy, 11 % of the patients with rifampicin intermittent therapy were still observed to be smear positive but culture negative (TRC, Madras, Unpublished).

Culture +

Smear - 22 176 62 35.2 114 64.8

Culture +

TABLE 5

Percentage of patients with smear positive culture negative results

Month	Daily 12 months			Rif. intermittent
	P	E	R	
	0	1	0	
3	3	3	16	16
5	8	2	10	9
6	5	6	6	11
12	1	1	2	NA

Additional yield in cases from concurrent smears: About 90% of the cases yield positive result in the first two samples. Another important finding of the investigation was that the same number of new cases (45) were detected by the first two smears as by the first culture examination (44) (Table 6). Thus, it may be concluded that in new untreated patients with prolonged chest symptoms and abnormal X-ray shadows, two consecutive smear examinations (e.g. one spot and one overnight sputum) are practically equivalent to culture examination (Chandrasekhar et al., 1970).

Fluorescent microscopy (FM): The main advantage of FM is that a low power objective is used, which enables a larger area to be scanned. It is also estimated that each technician will be able to read 100 to 200 smears per day by the FM method as against 30 to 40 per

TABLE 6

Additional yield in cases from concurrent smears

Category	Cases No.	No. of specimens			
		1	2	3-8	
Smear Positive	Sm + Cult +	46	34	7	5
	Sm + Cult -	7	2	2	3
		36	9	8	
		41(89%)			
Culture Poositive	Cult + Sm +	46	34	7	5
	Cult + Sm -	19	10	5	4
		65	44	12	9
		100%			
		56(86%)			

Exam by		Specimens	
FM	ZN	No.	%
+	+	405	62
+	-	36	6
-	+	28	4
-	-	186	28
Total culture positive		655	100

CULTURE

The probability of finding bacilli is greater by culture than by smear microscopy when specimens contain only small number of AFB. Reliable culture techniques are essential for isolation, identification and characterisation of mycobacteria to species level, and for performing drug susceptibility tests.

Culture methods

Decontamination and Concentration : Three aspects need to be considered before specimens are processed for culture of mycobacteria: (1) The laboratory specimen should be homogenised to free the bacilli from mucus or cells or tissue in which they might be embedded. (2) The contaminating non-acid fast bacteria and saprophytic fast growing acid fast bacilli must be rendered non-viable since they grow more rapidly than tubercle bacilli and may adversely affect the media. (3) Homogenisation and decontamination procedures should not adversely affect the viability of the tubercle bacilli.

Many different methods are described for decontamination and homogenisation of sputum samples for culturing tubercle bacilli

1915	Petroff's NaOH method
1946	Trisodium phosphate method
1955	Pancreatin-desogen method
1958	Pancreatin+1 % cetrinide
1962	Zephiran trisodium phosphate
1963	N-acetyl L-cysteine+2% NaOH
1969	Swab culture technique+1 % cetrinide
1975	Cetyl pyridinium chloride (CPC NaCl ₂) Method

Specimens other than sputum: Bronchial and gastric lavage specimens, urine, contaminated pus and other fluids are treated with the Petroff's or any other suitable decontaminating procedure.

Laryngeal swabs are processed for culture by decontaminating with 4 % sulphuric acid and neutralising with sodium hydroxide (Darzins, 1958).

Membrane filter concentration method can be used to advantage for the culture of urine and other body fluids. no pretreatment methods are required for material collected with stringent aseptic measures. Fluid specimens can be centrifuged for concentration, If membrane filtration is not used, and the deposits could be inoculated directly onto culture media for handling contaminated material, the membrane filtration method can be used

Uncontaminated specimens such as bone marrow aspirates and pus from cold abscess can be inoculated directly onto the culture medium without decontamination. In case of doubt, an overnight test for contamination on ordinary bacteriological media will be help ful.

Clotting of specimens such as ascitic fluid and pleural fluid can be avoided by the addition of sodium citrate or any other anticoagulant. When clots are present, they can be

minutes and neutralised before inoculating in appropriate media.

Culture of faeces is done after processing the sample by shaking up with 5% saline followed by ether. The supernatant layer is discarded and the gelatinous layer is taken up for culture after treatment with suitable decontamination method.

CSF is concentrated for culture by one of the following three methods: (a) High speed centrifugation, (b) membrane filtration. and (c) precipitation method using sterile 20, solution of sulpho salicylic acid.

Specimen removed aseptically, such as CSF, pleural fluid, synovial fluid and bits of biopsied tissue may be inoculated directly into a fluid medium in a volume to volume ratio of 1 : 5 and incubated at 36°C in a CO₂ incubator followed by weekly examination of smears prepared from the inoculated medium.

Culture media

Solid media: Various solid media used in the cultivation of mycobacteria are given in the Table 9. The IUAT version of LJ medium is recommended for use.

TABLE 9

Culture *media* : *Solid*

- 01. LJ medium
- 02. LJ with N₂ pyruvate
- 03. LJ without
- 04. Synthetic Middlebrook's 7H10, - Hit oleic acid albumin agar
- 05. Selective 7H10 medium
- 06. Tarshi's s fresh blood agar medium
- 07. Ogawa medium

- 01. Kirchner-Herman medium
- 02. Dubo's medium
- 03. Sula's medium
- 04. Yournan and Karlson's
- 05. Proskauer and Reel: medium
- 06. 7H9 synthetic medium

In paucibacillary extra-pulmonary manifestations of tuberculosis, the procedures used for processing specimens could often be detrimental to the viability of tubercle bacilli. Also, specimens collected during surgery often cannot be repeated and hence maximum efforts to isolate the few organisms present in these specimens should be made to confirm tin; diagnosis. The Tuberculosis Research Centre, Madras, carried out an investigation of the isolation of tubercle bacilli using multiple media on 3,807 extra-pulmonary specimens of different kinds during the period 1980-1984 (Paramasivan et :d _ 1987). The culture media used were 71111 oleic :acid albumin slopes with malachite green (7H11), Lowenstein Jensen medium containing 0 5% sodium pyruvate (UP), Lowenstein Jensen medium (LJ) and Kirchner's liquid medium (KL). The 71111 and KL media were made selective by the addition of polymyxin 13 sulfate carbenicillin, trimethoprim and amphotericin. Each specimen was inoculated into one set of media consisting of two slopes each of I J, LJP and 7111, and two bottles of KL. Oh the 550 positive cultures. considering the media one by one, KL and LJ gave u high proportion of positive culture (62) % and 60% respectively). Considering the media two by two, LJ+KL gave 93% positives, while LJP+KL was almost as good (88`4). When LJ+LJP+KL were considered together, 546 (99'1,) of the 550 positives were detected. Considering specimen wise, and the media individually, KL yielded the maximum number of positive cultures in urine. CSL and other specimens. In lymph gland, pus and operated specimens, LJ yielded the highest proportion

available for mycobacteria. In a routine peripheral laboratory it is important to do a group of screening tests which will differentiate *M. tuberculosis* from other mycobacteria (NTM). In a central specialised laboratory, all strains of mycobacterial isolates should be identified fully to the species level. Correct identification of these organisms is critical because the management of the patient may be determined by the laboratory identification as well as the clinical significance of the isolate.

Screening tests

The most useful tests in a screening system are those that may be carried out with minimum reagents and in a reasonably short period. The screening tests that are suitably are: 1) Colonial morphology on LJ medium, 2) Microscopy, 3) Niacin test, 4) Susceptibility to para-nitrobenzoic acid (PNB) sodium salt, 5) Pigment production, 6) Growth rate, 7) Catalase 68°C stability test and 8) Growth at 25°C. The colonial morphology depends on the type of organism. *M. tuberculosis* generally produces a rough colony; NTM strains a rough or smooth type; and bovine strains a dysgonic growth. Pigmentation is not produced by *M. tuberculosis* even when exposed to light and typically their colonies are buff in colour. *M. tuberculosis* and *M. bovis* do not grow at 25°C unlike most of the NTM. The qualitative niacin test is positive with *M. tuberculosis* and negative for all other mycobacteria except *M. bovis* which can be occasionally weakly positive. In the 68°C catalase stability test, all strains of *M. tuberculosis* are negative.

Laboratories vary in the techniques used to identify mycobacteria. For instance, Marks (1976) classifies mycobacteria into 15 groups on the basis of growth at 25, 37 and 45°C, pigment production, oxygen preference and Tween 80 hydrolysis. Kubica (1973) has named 12 simple tests which will differentiate the great majority of strains encountered. For detailed taxonomic studies of the mycobacteria, numerous biochemical tests have been developed. These include production of acid from sugars, ammonia

culosis. In the 1950s, when it had become routine to cultivate mycobacteria in vitro from sputum specimens and when the prevalence of tuberculosis began to decrease rapidly, a new concept about mycobacterial infection was evolved. Thereafter, important strides have been made in the taxonomy and identification of non-tuberculous mycobacteria. It is now well established that some of the mycobacteria other than mammalian tubercle bacilli and *M. leprae* are important human pathogens. A summary of NTM diseases of man (Wolinsky, 1979) is given in the Table 11.

With the exception of *M. tuberculosis* and probably *M. leprae*, all species of mycobacteria are virtually environmental saprophytes and, in terms of their total numbers, only a very minute proportion are ever involved in pathogenesis of disease. In contrast to tuberculosis, pulmonary disease associated with NTM is usually not transmitted from person to person, but is acquired somehow from natural sources in the environment. In tuberculosis, recovery of *M. tuberculosis* from the patient is pathognomonic of disease, as no true carrier stage has been demonstrated so far. Hence, criteria for diagnosis of disease due to NTM are rather more stringent than for tuberculosis. The American Thoracic Society has given the following criteria for diagnosis of disease due to NTM (Good, 1979)

A definite diagnosis requires (1) evidence, such as infiltrate, visible on chest x-ray, of disease, the cause of which has been determined by careful clinical and laboratory studies and (2) either (a) isolation of the same strain of mycobacterium repeatedly, usually in the absence of other pathogens or (b) isolation of the same mycobacterium from a closed lesion from which the specimen has been collected and handled under strict aseptic conditions—for example, an abscess or biopsy tissue. However, these organisms, may be isolated from sputum, throat washings and gastric aspirates in the absence of related disease as a result of colonisation in the mucosal surface and environmental habitation of these mycobacteria

Local lymphadenitis in children	M. serofulaceum M. avium complex	M. kansasii M. Fortitum complex
Skin and soft tissue Swimming pool granuloma ¹	M. marinum	
Sporotrichoid	M. marinum	
Local abscess	M. fortuitum complex	
Buruli (Bairnsdale) ulcer	M. ulcerans	
Skeletal (hone, joint,	M. kansasii	M. fortuitum complex IvI. marinum
Disseminated	M. avium complex M. kansasii	M. fortuitum complex M. seofulacium

Most of the information available on NTM infections is from Western Australia, Japan, United States, England and Wales. Reports from developing countries on NTM causing disease are very rare.

In USA, a 1979 survey of 49 public health laboratories showed that *M. tuberculosis* is the most commonly isolated mycobacterial species of clinical significance (65%) followed by *M. avium* complex (21 %). *M. fortuitum* complex accounted for, 6% *M. kansasii* accounted for 3% and *M. serofulacium* accounted for 2%. Among saprophytic species, *M. gordonae* was isolated most often and accounted for 15% or total isolates (Good et al., 1982).

More or less, similar distribution of pathogenic strains was observed in Western Australia, Japan and in many centres in Europe including England.

From India, there is scanty documented evidence available so far. Between the years 1961 and 1979, eight such reports have been published by Indian workers (Ramakrishnan 1981), five from the northern part of the country and three from the South, and this is shown in Table 12.

Excepting for Kaur and Chitkara (1965) and Lal et al., (1972) from Delhi, most of the others have recorded only low figures of non-tuberculous mycobacterial isolates responsible for pulmonary disease. The non-chromogens, especially Battey type (*M. avium intracellulare*) appear to be the predominant type of organism isolated from patients in all these studies.

We have reported recently from our Centre, a retrospective study covering over 2 decades on pulmonary disease due to NTM. Out of a total of 5,435 patients admitted to 12 successive chemotherapy studies 25 (0.45%) patients repeatedly excreted organisms that were not typical human tubercle bacilli. Of the 25 patients, 14 patients yielded repeatedly NTM or the same type (Table 13) after they became bacteriologically quiescent for *M. tuberculosis* (Series A in table) and 11 patients yielded NTM repeatedly in pre-treatment specimens in the absence of *M. tuberculosis* suggesting primary infection with NTM (Series B).

Culture examination is the most conclusive evidence for diagnosis of disease due to NTM. Currently, numerical taxonomy offers excellent guidelines for identification.

Author	Year	Location	Total	Photochromogen	Non chromogen
Thune, s et al.	(1961)	Madras	287	0	--
Kaur & Chitkara	(1964)	Delhi	50	10	Non chromogen
Bhathene et al.	(1970)	Delhi	28	1	Scotochromogen
Kulkarni & Moeller	(1971)	Madanapalle	—	4	Batthey type
La t ci al.	(1972)	Delhi	280	32	Non chromogen
Saran	(1973)	Patna	100	2	Photochromogen
Muhkopadhyaya	(1978)	Madanapalle	43929	5	M. intracellulare

TAME 13

Distribution of NTM cases, TRC study

	Photo-chromogen	Scow-chromogen	Non chromogen
A series (14)	10	-	4
B series (11)	3	1	7
Total (25)	13	1	11

Skin testing and x-ray are of limited diagnostic value (Ramakrishnan. 1981).

Treatment must be considered in terms of the specific mycobacterium and the site of the disease. *M. kansasii* is generally susceptible to most of the antimycobacterial drugs. While not entirely uniform, conversion occurs in 4-6 months in 96% of patients (Paramasivan et al., 1986). Nevertheless, prognosis during treatment in patients with *M. kansasii* infection is comparable to that of patients with *M. tuberculosis*.

The picture is different with infections

caused by *M. avium intracellulare* group. A high proportion of these organisms are resistant in vitro to H, PAS, R, ETH and S. Nevertheless, often the resistance is not total. Susceptibility to Ethionamide and cycloserine is reported frequently. Since medical treatment is so unsatisfactory, surgery could be contemplated in suitable cases. Lester suggests 5 drug combination with capreomycin. Other drugs that may occasionally have a place in combinations are kanamycin, erythromycin and pyrazinamide (Rosenweig, 1980).

Other strains that show multiple drug resistance are *M. marinum*, *M. scrofulaceum*, *M. szulgai*, *M. fortuitum* and *M. chelonae*. In the tubercle bacilli, it is well established that the size of resistant clones does not increase spontaneously from 10^8 - 10^7 to any large value. In NTM, one observes that even in the absence of selective forces imposed upon the population by the drug under study, the bacterial populations are composed of several resistant subclones of large size. The pattern of multiple drug resistance in these mycobacteria may therefore be summarised as follows: The bacterial population usually contains variable proportions of susceptible bacteria, but the size of resistant subclones is large and varies from 10-4 to 1.0 (Meissner et al., 1986).

NTM in Acquired Immuno-deficiency Syndrome (AIDS)

Diseases due to NTM are opportunistic

disseminated *M. avium* complex infection in the five patients studied. The Centres for Disease Control identified mycobacteria isolated from AIDS patients and found that over 80 of the isolates belonged to *M. avium* complex (Good, 1985). Most of the strains were isolated from bone marrow, blood or other non-pulmonary specimens, while some were from sputum specimens. In 30% of patients with AIDS *M. avium intracellulare* were isolated at the National Institute of Health and in these patients, therapy consisting of conventional anti-tuberculous drugs has been almost invariably ineffective (Masur, 1985). Some success has been reported for multiple drug regimens that include third generation cephalosporine or amikacin. Further research in chemotherapy is needed to explore newer antituberculosis drugs for

Sensitivity Testing

Wild strains of *M. tuberculosis* which are not exposed to any drugs consist of only a small proportion of naturally resistant organisms which could be determined by appropriately designed sensitivity tests. Only the most exceptional wild strains would have a degree of resistance likely to reduce the efficacy of standard chemotherapy.

Drug resistance in patients is observed as (1) Primary drug resistance (2) Acquired drug resistance and (3) Transitional resistance (Prabhakar, 1980).

It may be emphasised here that performance of sensitivity tests in patients with a decreasing bacillary population as shown by serial smear or culture examination rarely serves any useful purpose since under these circumstances, only transitional resistance is encountered.

In technically advanced countries, where there is a low level of primary drug resistance, the role of pretreatment sensitivity tests is limited since available resources permit the use of therapy with multiple drug regimens, including first line drugs, in newly diagnosed cases. In developing countries, the existing knowledge of primary or initial drug

BMRC/Hong Kong Tuberculosis Treatment: Services applying 3 policies of Treatment, has evaluated the role of the pretreatment sensitivity tests in organising treatment (HK/ BMRC, 1974). Policy A consisted of treating all patients with a standard regimen of streptomycin, isoniazid and PAS daily for 6 months followed by PAS and isoniazid. In Policy B, standard chemotherapy with streptomycin, PAS and isoniazid was given until pretreatment sensitivity test results became available and changed subsequently, if necessary, with appropriate reserve drugs. In Policy C, treatment was started only after the sensitivity test results were made available by slide culture susceptibility tests. Table 14 shows the response in relation to pretreatment drug resistance in the three policies of treatment. It may be observed from the table that for patients with organisms resistant to one or more drugs initially, the proportions with favourable response was 73 % for Policy A whereas the favourable responses are the same viz. 90% for Policy B & Policy C. In all, 89 of 187 patients in Policy A had a favourable response compared with 93% of 192 patients in Policy B and 94% of 187 patients in Policy C. The differences between the 3 policies were small. Further, in Policy A, it was INH resistance that was associated with unfavourable response whereas resistance to streptomycin had very little influence on the outcome. It was evident from this study that the benefit derived from decision taken to organise chemotherapy on the basis of pretreatment susceptibility test is very small. Further, inaccurate susceptibility testing could lead to a loss in therapeutic terms whereas if no reference is made to pretreatment sensitivity tests, it may benefit in terms of lower toxicity, low operational costs and less expensive regimens. The results of this study indicate that a modified approach with regimens containing more potent and acceptable regimens involving newer drugs like Rifampicin may be tried without resorting to pretreatment drug sensitivity tests in newly diagnosed pulmonary tuberculosis patients. However, this policy may not benefit patients who have drug resistance as a result of long courses of previous irregular chemotherapy. Such patients may benefit from pretreatment sensitivity tests

Susceptible to all 3 drugs	125	98	144	92	125	95
Total resistance to 1 or more drugs	62	73	48	90	62	90
Total resistance to 1 drug only	34	82	29	90	37	92
Total resistance to 2 drugs	18	(72)	9	(89)	9	(89)
Resistance to alt 3 drugs	10	(40)	10	(90)	16	(88)

by slide cultures which have advantage over the standard methods since they would provide information before the start of chemotherapy. Furthermore, the study has shown that even when reliable sensitivity tests are available, for all practical purposes, there is no point in performing sensitivity tests for PAS and very little point in performing them for streptomycin since there was no evidence from the study that initial PAS or streptomycin resistance had influenced the outcome. Most of the unfavourable responses were due to isoniazid resistance. Hence, it may be worthwhile performing, as a routine, isoniazid sensitivity tests before switching over to regimens consisting of reserve drugs.

Strains with natural resistance to thiacetazone have been found in South India, Hong Kong and East Africa which renders the thiacetazone sensitivity test unreliable since a majority of the patients have a favourable response to treatment with thiacetazone and isoniazid. This favourable response is attributed to lower virulence of these strains which offsets the influence of natural resistance to thiacetazone.

Methods of Drug Susceptibility testing

1. Indirect sensitivity tests.
2. Direct sensitivity tests.

Indirect sensitivity tests

Indirect sensitivity tests are set up from positive cultures and the results of the tests are available six to eight weeks after the receipt of the specimen.

Direct sensitivity tests

In this method, the specimen is directly inoculated on to medium with and without drug. This test can also be performed as slide culture technique where the results are available about seven days after receipt of the specimen (Subbammal, 1973). This is early enough to start treatment in the patient. However, this method can be used only when the smear contains moderate or numerous bacilli on direct examination. Sputa containing scanty bacilli may be inoculated onto slopes of solid medium. Results will be available in three to six weeks. But even this method is not suitable for smear negative culture positive specimens and for these specimens indirect tests will have to be set up to avoid waste of medium and labour. Direct sensitivity tests using sputum swabs gave results which were closely similar to those of indirect sensitivity tests for streptomycin and isoniazid. This method could be employed in any laboratory which has facilities for culture of sputum (Table 15).

Measures of sensitivity

Three well-known measures of sensitivity tests are available: (1) The minimal inhibitory concentration or the MIC, (2) the resistance ratio or the RR, and (3) the proportion method. These tests are set up on solid media (L-J without potato starch).

1. Minimal inhibitory concentration (MIC): MIC is defined as the minimal concentration of the drug required to inhibit the growth of the organisms, where growth is defined as

Resistant	Resistant	121		130		134	
Resistant	Sensitive	9	5%	8	4%	6	3%
Sensitive	Resistant	2	1%	5	3%	5	2%
Total specimens		189		198		206	

20 colonies or more. This definition of growth is chosen so that only a small proportion (e.g. 1% of wild strains would be classified as resistant by its use. This method is simple and economical and can be carried out with a single drug containing slope although it is preferable to use more than one slope.

2. *Resistance ratio* : This consists of expressing the resistance as a ratio of the MIC of a test strain to that of control strain. This procedure calls for a rigid standardisation since the inherent technical errors usually make it less efficient than the MIC method in distinguishing sensitive and resistant strains. A further disadvantage of the use of RR is that there may be more variations in sensitivity of the control strain than in wild strains resulting in increase in the error. However, the RR's are more reliable than MIC's when comparisons are made in the same laboratory over a period of years.

3. *Proportion method*: This method of testing sensitivity has a high degree of precision.

The inoculum suspension is standardised by weight of the bacilli and serial ten-fold dilutions of the suspensions are made for seeding onto drug free and drug containing slopes. The proportion of resistant bacilli present in the strain is indicated by the ratio of number of colonies obtained on drug free and drug containing slopes. A strain is classified as sensitive or resistant depending on the proportion. Two variants, a simplified variant and standard variant, are available for this method.

Definition of criteria of resistance

The simplest and most reliable method of

defining the criteria of resistance is obtained by the measure that discriminates most efficiently between a group of predominantly sensitive strains obtained before treatment and another group of predominantly resistant strains obtained during treatment. This procedure could be used for definition of resistance irrespective of the expression of sensitivity tests as proportion resistant, MIC or RR.

In conclusion, the need to do the sensitivity tests arises when sputum is positive following a course of chemotherapy, which may be due to development of resistance in organisms. However, patients may be sputum positive because of inadequate chemotherapy in which case their organisms are likely to be sensitive. Hence, sensitivity tests are helpful when retreatment or change of treatment is planned on the basis of serial smear examination which may show that the degree of positivity is not diminishing. Further, sensitivity tests could be used in sample surveys, to estimate pretreatment drug resistance and to study the pattern of emergence of drug resistance during routine treatment. Sensitivity tests are also used for surveys to estimate the prevalence of initial drug resistance which includes both primary and acquired drug resistance. An estimate of this kind will be helpful in planning a programme of routine chemotherapy and organising good treatment service. Further, it will be of epidemiological interest to conduct surveys of primary drug resistance which estimate the extent of dissemination of resistant strains from one patient to another.

Histopathology

Histological diagnosis plays an important role in the diagnosis of tuberculosis, especially in extrapulmonary forms; with paucibacillary

subjected to bacteriological and histopathological examination (Prabhakar, 1980). Table 16 shows histopathology related to bacteriology. Twenty six patients had results of histopathological examinations of which 22 i.e., 88% had histological evidence of tuberculosis. Of the 4 who were classified as having non-specific histopathological lesions, one was culture positive. Thus, evidence of tuberculosis, either bacteriological or histopathological, was obtained in 23 i.e., 92% of the patients in the surgery group.

TABLE 16

Histopathology related to bacteriology

Histopathology	Total	Culture positive
Typical TB (Zn+vet)	2	2
Typical TB (Zn--ve)	15	8
Probably TB	5	3
Nonspecific	4	1
Total patients	26	14

Immunodiagnosis of Tuberculosis

Though the diagnosis of tuberculosis is best confirmed by the demonstration of tubercle bacillus, it may not be possible under the following circumstances:

- A. Extra pulmonary tuberculosis
 - TB meningitis
 - TB of genito urinary tract
 - TB of gastro intestinal tract
 - TB of skeleton
- B. Smear negative pulmonary tuberculosis
- C. Follow-up during chemotherapy
- D. Case-finding surveys

followed by a complement fixation test, haemagglutination test, agglutination of inert particle coated with antibody, precipitation and gel diffusion and fluorescent antibody test (Affronti et al., 1973; Kaplan et al., 1980).

However, none of the proposed tests went without criticism. All these tests, inspite of several modifications, faced the problem of overlap between diseased patients and skin test positive healthy subjects. The antigenic profile of mycobacteria are very complex. They consist of purified protein derivative, protein A, B and C, arabinogalactans, arabinomannans and glycolipids like wax D, phosphatidyl inositol mannosides, sulphatides and mycosides (Daniel and Janicki, 1978). Many of these antigens are shared by various mycobacterial species and to a lesser extent by other genera. This has been one of the important factors contributing to the non-specificity of the immunologic detection system.

With the introduction of ELISA and RIA techniques, the sensitivity of the assay system has been well taken care of; i.e., the antigen or antibody can be detected at nanogram or even picogram levels. What we lack today is a mono-specific antibody or antigen.

Monoclonal antibodies produced by hybridoma technology can detect a single antigenic determinant in an antigen molecule and are, thus, extremely useful for antigen purification and, hence, Immunodiagnosis. Coates et al., (1981) have reported on 4 monoclonal antibodies against M. tuberculosis (Table-17).

Using antibody-antibody competition radio immune assay, Ivanyi et al. (1983) have shown that these monoclonal antibodies can be used directly in the serodiagnosis of tuberculosis, though the results obtained so far are no better than when using other methods.

The protein antigens that bind to the monoclonal antibodies have been isolated by affinity chromatography. They have been studied in skin tests in guinea pigs sensitized with M. tuberculosis, Al. bovis BCG, and other my-

H37Ry	82	30	19	26	43
SI	99	10	21	18	19
6061	64	30	22	24	30
7219	68	50	21	23	21
M. Bovis _s					
Vallee	65	46	<10	<10	22
13CG	16	<10	<10	<10	<10
M. Kansasii	<10	23	<10	<10	<10
Others	<10	<10	<10	< 10	<10

cobacteria. Human T-cell clones have also been developed against them. The results of these studies have indicated that the antigen molecules carry epitopes that are very specific and also other epitopes of lesser specificity. It is hoped that this approach may lead to the identification of epitopes that are specific for tubercle bacilli. Besides, with the recent advances in genetic engineering, the possibility of obtaining species specific antigens in large quantities is not far away.

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rather than on community surveys and, therefore, may not reflect the actual situation in the community. Tuberculosis in children is seldom infectious and does not constitute a major public health hazard. Both morbidity and mortality from respiratory diseases is high in the pediatric age but it is much less due to Tuberculosis than other non-tuberculosis respiratory diseases, mostly upper respiratory infection and mild tracheo-bronchial catarrh.

Introduction

Tuberculosis still continues to be one of the major health problems in developing countries and India is no exception. The size and extent of the problem in children is directly linked to the problem of pulmonary tuberculosis among adults in the community.

Not enough attention is paid to the problem of tuberculosis in children since no precise data are available. Children are often excluded from large scale community surveys which mainly focus on pulmonary tuberculosis only. Children below 5 years are excluded because:

- (a) MMR of the chest is not possible and sputum examination is not feasible since children can hardly produce any sputum.
- (b) Non-pulmonary tuberculosis which is more common in children has been excluded from such surveys because of the absence of objective methods of diagnosis.

Much of the available information is, therefore, based on hospital figures rather than on community surveys and may not reflect the actual situation in the community.

The extent of tuberculosis in the pediatric age group (0-14 years) is difficult to estimate.

Diagnosis based on radiological examination of the chest is often imprecise and bacteriological confirmation is not usually possible in children aged 0-4 years. Tuberculin reaction, at best, can only indicate infection and is of little help in confirming diagnosis. Thus, the diagnosis of tuberculosis in children, to begin with is usually presumptive rather than confirmed. The information based on the number of children diagnosed as suffering from tuberculosis among those reporting at Clinics/hospitals or pediatric wards could most often be misleading and exaggerated. The main reason for this is that, unlike in adults, the most prevalent form of tuberculosis among children is primary disease; leading often to extra-pulmonary disease. Symptoms of primary disease are neither specific nor alarming enough, with the result that large number of children do not report to any health facility. Since the availability of these facilities varies from place to place and from time to time, very little reliance can be placed on the data obtained from them.

The Pediatric Age Group

In India, the pediatric age group of 0-14 years constitutes about 41% of the population and hence it is important to study what happens to them in terms of general mortality, specific mortality and morbidity with particular reference to tuberculosis.

General Mortality

Registration of births and deaths is compulsory in India under the Registration

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community as a whole. The available information on causes of death is, however, presented in this paper, so that some rough ideas may be formed and conclusions drawn.

TABLE I

Distribution of Deaths by major cause groups-India (Rural), 1979 to 1981

Code No.	Major Cause Group Prominent Symptoms	Total Deaths					
		1979		1980		1981	
		No.	%	No.	%	No.	%
1	Accidents and Injuries	780	4.6	887	5.0	878	5.1
2	Natural Death-Child-birth and Pregnancy	180	1.1	209	1.2	175	1.0
3	Fevers	1501	8.9	1505	8.5	1461	8.4
4	Digestive Disorders	1637	9.7	1634	9.3	1395	8.0
5	Cough (Disorders of Respiratory System)	3415	20.3	3540	20.0	3600	20.7
6	Disorders of CMS	600	3.6	678	3.8	603	3.5
7	Disorders of Circulatory System	1561	9.3	1517	8.6	1538	8.8
8	Other Clear Symptoms	1400	8.3	1325	7.5	1411	8.1
9	Causes Peculiar to Infancy	2280	13.5	2409	13.6	2112	12.1
10	Senility	3120	18.5	3650	20.7	3896	22.4
II	The Rest	374	2.2	318	1.8	325	1.9
	All Causes	16848	100	17672	100	17394	100

SOURCE: Health Statistics of India 1984

system). In higher pediatric age group namely, '5-14 years', fevers come first and cough second. Thus, in all the three pediatric age groups, disorders of the respiratory system form the second most important cause and account for 15% to 25% of the total deaths in these age groups.

Distribution of Medically Certified Deaths by Causes

Medically certified deaths are tabulated according to an abbreviated version of the standard international classification of deaths. Distribution of medically certified deaths by such abbreviated causes in pediatric age groups is shown in Table 3. In "below one year" age group, "certain causes of perinatal morbidity

diseases (54.6%), accidents, poisoning and violence (13.1%), diseases of the nervous system and sense organs (12.1%) and symptoms of ill-defined conditions (11.5%)'. It is significant that these data with reliable causes of death confirm the important position of diseases of the respiratory system as a major cause of death shown in Table 2 and account for 12%, 16.9% and 7.3% the deaths in the three pediatric age groups of 'below one year', '1-4 years' and '5-14 years' respectively.

Percentage of Deaths Due to 10 Selected Diseases by Age Group

Diseases of the respiratory system, however, include not only TB but a number of other

TABLE 2

Distribution of Deaths by major cause groups in pediatric age groups-India (Rural), 1981

Major Cause Group	Below 1 Year		1--4 Years		5-14 Years	
	No	%	No	%	No	%
Accidents and injuries	19	0.6	43	2.8	353	16.8
Fevers	143	4.5	323	21.4	215	23.6
Digestive Disorders	109	3.4	414	27.4	132	14.5
Cough (Disorders of Respiratory System)	475	14.9	382	25.3	158	17.3
Disorders of CNS	23	0.7	42	2.8	42	4.6
Disorders Or Circulatory System	32	1.0	78	5.2	77	8.5
Other Clear Symptoms	258	8.1	154	10.2	92	10.0
Causes peculiar to Infancy	2112	66.4	-	-	-	-
The Rest	11	0.3	74	4.9	42	4.6
	3182	100.0	1510	100.0	911	100.0

Infective and Parasitic Diseases	7533	19.0	6653	41.8	4139	34.6
Neoplasms	15	0.0	89	0.6	247	2.1
Endocrine, Nutritional and Metabolic Diseases	887	2.2	1019	6.4	268	2.2
Diseases of Blood and Blood forming Organs	170	0.4	303	1.9	428	3.6
Mental Disorders	2	*0.0	1	*0.0	7	0.1
Diseases of the Nervous System and Sense Organs	1508	3.8	1816	11.4	1444	12.1
Diseases of the Circulatory System	264	0.7	205	1.3	600	5.0
Diseases of the Respiratory System	4754	12.0	2696	16.9	870	7.3
Diseases of the Digestive System	663	1.7	685	4.3	642	5.4
Diseases of Genito-Urinary System	65	0.2	123	0.8	194	1.6
Congenital Anomalies	1648	4.2	171	1.1	147	1.2
Certain Causes of Perinatal Morbidity and Mortality	19700	49.7				
Others	2446	6.2	2149	13.5	2984	24.9
TOTAL	39655	100.0	15910	100.0	11070	100.0

*Correct to first decimal-percentage negligible

diseases as well. Hence, it is important to consider what proportion of the total deaths is accounted for by TB alone. Table 4 shows very interesting trends in different pediatric age groups: < 1 year, 1-4 years and 5-14 years. This is based on lay reporting-as reported by different health agencies (Health Statistics, 1984). The 10 selected diseases account for only 38.5% of the total deaths in 0-14 years. This proportion varied from 25.6% in 'below 1 year' age group to 60.7% in 1-4 years' age group. The 10 selected diseases have been ranked in Table 4 according to the proportion of total deaths in each age group which they have accounted for. Below 1 year, the major cause of death appears to be pneumonia, followed by tetanus and gastroenteritis.

'1-4 years', pneumonia forms the leading cause followed by gastroenteritis, debility and mal-nutrition. In '5-14 years', pneumonia comes first, typhoid next and gastroenteritis third. If '0-14 years' s taken as a whole, pneumonia is first, gastroenteritis second and tetanus third. It is interesting to note that in all these age groups, tuberculosis of the lungs comes much lower down in ranking. Thus, the very high contribution of diseases of the respiratory system shown by the earlier tables, appears to be mainly due to pneumonia and TB seems to play only an insignificant part.

Reporting from Health Institutions

It would be interesting to compare the above findings from community data with

TABLE 4

Deaths due to 10 selected diseases in pediatric age groups-India (rural)--1981
Age Groups in Years

Sl. No.	Diseases	Below 1 Year			1--4 Years			5-14 Years		
		Number of Deaths	% to Total	Rank	Number of Deaths	% to Total	Rank	Number of Deaths	% to Total	Rank
1	Asthma and Bronchitis	19	2.3	VI	53	5.8	VI	28	6.6	V
2	TB of Lungs	3	0.4	IX	13	1.4	VIII	27	6.4	VI
3	Pneumonia	447	54.8	1	307	33.4	1	97	22.9	1
4	Heart Attack	5	0.6	VIII	5	0.5	X	17	4.0	VIII
5	Anaemia	21	2.6	V	72	7.8	V	53	12.5	IV
6	Typhoid	33	4.0	IV	122	13.3	IV	87	20.6	11
7	Gastro-enteritis	58	7.1	111	165	18.0	II	55	13.0	III
8	Cancer	1	0.1	X	8	0.9	IX	11	2.6	IX
9	Debility and Malnutrition	11	1.3	VII	156	17.0	111	24	5.7	VI
10	Tetanus	217	26.6	II	18	2.0	VII	24	5.7	VII
	TOTAL	15	100.0		919	100.0		423	100.0	
		(25.6)			(60.7)			(46.7)		
	All Causes	3183			1513			904		

SOURCE: Health Statistics of India 1984-Table No. 11.3 (Page 216).
Figures in brackets are percentage to deaths from all cause

Total Deaths	1,479
Mortality Rate	8.19%

	Percent of TotalDeaths
1. Acute Gastrocneritis	20.96%
<u>2. C.N.S. Disorders</u>	20.62%
3. Respiratory Disorders	11.29%
4. TB including TB Meningitis	8.32
5. Nutritional Disorders	6.69%
6. Diseases of Infective Origin	5.07
7. Liver Disorders	3.44%
8. Cardiovascular Disorders	3.38
9. Renal Disorders	1.82%
10. Hetnatological Disorders	1.55%

Commonest Causes of Morbidity in the Hospital

	Percent of Total Deaths
1. Gastroenteritis	39.62%
2. Neurological Disorders	11.61%
3. Respiratory Disorders	10.91%
4. Diseases of Infective Origin	10.36V
5. All forms of TB	4.66;
6. Nutritional Disorders	3.8%
7. Cardiovascular Disorders	2.81
8. Renal Disorders	2.49%
9. Hematological Disorders	2.31

mortality rate in children in India. An indirect method of computing such rate in children is based on one of the earlier papers from NTI (Gothi et al, 1971). Briefly, the survey involved examining a population of 66,000 from 133 villages of Bangalore District, which was repeatedly examined by tuberculin test, X-ray examination of those 5 years and above, followed by sputum examination. The entire population was examined four times at an interval of 1.1/2years. The following epidemiological aspects of tuberculosis among children are presented

1. Prevalence of infection and disease

2. Incidence rates of infection and disease 3. The crude mortality in relation to tuberculin sensitivity.

Persons with tuberculin test induration of size 10 mm or more were regarded as infected. Bacteriologically culture negative patients whose chest X-rays were considered to indicate active or probably active disease including primary complex and pleurisy were labelled as 'Suspects.' Patients with positive sputum on culture examination were termed 'cases'.

Prevalence of Infection

Table 5 shows that of the total population tested, about 30% were infected. The prevalence of infection increased with age from 2.1 % to 16.5% in pediatric age group. In 0-14 year age group, about 9% were tuberculin positive.

Morbidity Prevalence

The morbidity prevalence rates at different surveys during the five years of operation were almost similar. Table 6 shows that the prevalence of disease in 15+ was considerably higher than in 5-14 years.

In 0-4 year age group, since no X-ray is possible and the prevalence of infection in this age group is the lowest (2.1 %), it can be safely presumed that the disease rates would also be low, unless majority of infected children go on to primary disease which is unlikely.

0-4	7981	2.1
5-9	7471	7.9
10-14	7259	16.5
0-14	22711	8.6
15+	27436	46.9
All Ages	50147	29.5

0-4	5685	253	0.9
5-9	4892	342	1.4
10-14	3451	360	2.1
0-14	14028	955	1.4
15+	8418	1188	2.8
All Ages	22446	2143	1.9

TABLE 6

Prevalence of TB Cases and Suspects by Age at Initial Survey

Age in years	No. X-rayed	% Cases Culture Positive	% Suspects only X-ray	% Cases and Suspects
1	2	3	4	5
5-9	4851	0.1	0.3	0.4
10-14	3880	0.1	0.4	0.5
5-14	8731	0.1	0.3	0.4
15+	18941	0.8	1.6	2.3

Incidence of Infection

It is an important index of risk of tuberculous infection to which a community is exposed. Incidence of infection increases with age as shown in Table 7, from 0.9% per year in 0-4 years to 2.8% in 15+. In 0-14 years, it is 1.4% per year. This shows that children have lower risk of new infection as compared to adults,

*Estimated on the basis of observed incidence for 1½ years.

Incidence of Disease

Annual incidence of disease (cases and suspects) increased with age as shown in Table. 8

TABLE 8

Annual Incidence (Attack) rate of Cases (Sputum Positive) and Suspects (Sputum Negative) by Age

Age	No. not classified Cases & Susp. at 1st Round	Per Thousands of Population		
		Cases (1 Yr.)	Susp. (1 Yr.)	Susp. & Cases (1 Yr.)
1	2	3	4	5
5-9	4833	0.2	0.3	0.5
10-14	3860	0.4	0.7	1.0
5-14	8693	0.2	0.5	1.0
15+	18496	2.4	1.6	4.0
Total (5+)	27189	1.6	1.4	3.0

Distribution of Deaths by Age and Tuberculin Reaction Size at Survey Prior to Death

Table 9 shows that in 0-14 years, 91 of the children who died were tuberculin negative (0-9 mm) and only 9% were tuberculin positive prior to death which again shows that death in children may be mostly due to causes other than tuberculosis.

Table. 9

Distribution of Deaths Age & Tuberculin Reaction Size of survey prior to death

Age Groups	No. Dead	0-9	10+
		% Deaths	% Deaths
1	2	3	4
0-4	355	95.5	4.5
5-9	86	81.4	18.6
10-14	66	77.3	22.7
0-14	507	90.7	9.3
15+	1319	46.9	53.1

Tuberculosis in Children in a Slum Community

In another study conducted by NTI (Gothi et al, 1977), an attempt was made to obtain information from a slum area where tuberculosis morbidity is expected to be high. The entire population of a slum area under the comprehensive medical care of CSI Hospital, Bangalore, constituted the study population. The population registered was 3,313. All the persons registered were examined radiologically by a mobile X-ray unit and tuberculin test. Two specimens of sputum were collected from:

- a) Those with abnormal chest X-ray shadows

The proportion of sick children was significantly more in 0-4 years compared to those of 5-9 and 10-14 year age groups.

Symptoms pertaining to respiratory system were the commonest among children in the age groups 0-4 and 5-9, followed by malnutrition.

TABLE 10

Sickness by Age

Age group	persons	Sick	
		Number	Percent
0 - 4	571	309	54.1
5 - 9	502	220	43.8
10 - 14	335	139	41.5
0 - 14	1408	668	47.4

Children showing Respiratory System Abnormality in Different age Groups

Children who had clinical and or radiological evidence of respiratory disease have been diagnosed to have "Respiratory Abnormality" irrespective of presence or absence of symptoms. Of the 1,408 children, 71 were found to have respiratory abnormalities. Further details are given in Table 11.

It would be seen that out of 71 children, 60 were below 10 years and only 5 of these were diagnosed to have primary tuberculosis, and the diagnosis in none of these was established bacteriologically. Passive follow-up two years later revealed that none died and 2 became a symptomatic.

During the two year period, there were 34 deaths in 0-14 years, of whom 31 were in 0-4 year age group, 2 in 5-9 years and 1 in 10-14 years (Table 12). It would be seen that out of a total of 34 deaths in the pediatric age group, cause of death in 14 could be

0 - 4	3	2	23	-	4	12
5 - 9	2	1	21	3	1	28
10 - 14	0	0	8	1	2	11
0 - 14	5	3	52	4	7	71

TABLE 12

Reasons for Death in 0-14 Years Age Group over a *period of 2 years* as given by the Households

Age Group	Viral Fever (Exanthematous)	GIT	Respiratory	Other and Not Stated	Total
0-4	14	6	3	8	31
5-9	-	-	-	2	2
10-14	-	-	-	1*	1
0-14	14	6	3	11	34

* Reason for death not known.

attributed to exanthematous viral fever, 6 due to gastrointestinal disorders, 3 due to respiratory diseases, and for 8, the cause could not be ascertained. There were 3 deaths in 5-14 year age group; none of these were reported to have (lied with respiratory disease.

This investigation showed that in the pediatric age group, tuberculosis does not seem to be a serious health problem. The most common sickness in this age group pertains to respiratory system (28%) and malnutrition accounted for 21 %. Large number of children with sickness rotating to respiratory system were diagnosed to be suffering from

Either upper respiratory infection or mild tracheobronchial catarrh.

Conclusion

1. It would thus be seen from the above data that the low infection and morbidity rate in children indicate that tuberculosis is not a major public health hazard in the pediatric age group namely, 0-14 years.
2. Tuberculosis in children is seldom infectious and almost all infection comes from adult infectious patients of pulmonary

4. From the clinical/hospital practice, tuberculosis among children would continue to remain an important problem because 6.6%, of the total admissions in the hospitals among children were reported to be due to tuberculosis (Udani 1968).

5. The problem of tuberculosis in clinical practice becomes very difficult because the tools of diagnosis are not very precise. The usual clinical signs and symptoms and X-ray examination have serious limitations. Sputum examination has also some limitations but it is the most reliable method.

6. The prevalence and incidence rates of infection and disease in pediatric age group are low and large percentage of children (91%) in the age group 0-14 years remain tuberculin negative and are susceptible to natural infection and hence these children have to be protected with BCG vaccination.

for granting permission to present this paper, to the Statistical Section of NTI for the compilation of data and to Miss Padmalatha Krishnan for the secretarial assistance.

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groups not much evidence can be placed on corresponding figures for these groups. Comparison with data collected during other studies suggests that prevalence of diabetes among pulmonary tuberculosis patients is considerably higher than in the general population. As expected, the rate is higher in persons above the age of 40 years. No evidence was found to suggest that prevalence of diabetes may be related to the extent and severity of pulmonary disease.

Diabetic patients are known to have a higher risk of developing pulmonary tuberculosis than non-diabetics and there are several studies on this subject. However, not much is known about the prevalence of diabetes among patients of pulmonary tuberculosis. Deshmukh et al (1962) reported that 4.25% of about 300 patients of pulmonary tuberculosis had diabetes. In view of the importance of the subject, the Research Committee of the Tuberculosis Association of India organized a cooperative study from seven centres throughout India to determine the prevalence of undetected diabetes among pulmonary tuberculosis patients. A large number of centres were contacted but only seven centres agreed to participate in this cooperative trial carried out with a common protocol drawn up by the Research Committee of the Tuberculosis Association of India.

Material and Methods

Of the seven participating centres, three were Tuberculosis and Chest Diseases Departments of Medical College Hospitals in Bombay, Pune and Raipur. One centre was the Department of General Medicine in the Medical College Hospital in Raipur. Two centres in Amargadh and Delhi were Tuberculosis Hospitals with a chest clinic. One centre in Bombay was a tuberculosis clinic.

The protocol provided that all previously untreated new cases of pulmonary tuberculosis diagnosed on the basis of bacteriological and/or radiological examination.

in the study. Known cases of diabetes, in whom the diagnosis of pulmonary tuberculosis was made after the diagnosis of diabetes, were excluded. Patients on steroids or oral contraceptives and those severely debilitated or having evidence of liver damage were also excluded.

In addition to tuberculous cases mentioned above, an equal number of controls were also to be investigated in the same manner as tuberculous patients. These controls were to be drawn equally from patients suffering from non-tuberculous chest conditions presenting at the various participating centres and apparently healthy individuals.

Apart from chest x-ray, routine sputum examination and other routine urine and blood examinations as indicated, glucose tolerance test (GTT) was carried out in all patients within a week of their diagnosis. For GTT, patients were instructed to take nothing by mouth after 10.00 P.M. the preceding night till the GTT was completed. They were required to avoid smoking and alcohol as well. Blood sugar was estimated according to the standard test recommended by the WHO, using ortho-toluidine method of sugar estimation. The fasting test was followed by administration of 75 gm of glucose by mouth and blood sugar estimations were carried out one hour and two hours after glucose administration. The patients were classified according to the following criteria:

(I) Diabetes Mellitus

Fasting glucose not less than 140 mg

*The Research Committee consists of Dr. S.P. Pamra, Convener and Drs. G.V.J. Baits, S.P. Gupta, Nagpaul and R. Prabhakar. Dr. M.M. Singh and the late Dr. H.B. Dingley were also members of the Research Committee when the study was started.

This report was prepared by Dr. S.P. Pamra and Mr. G.P. Mathur on behalf of the Research Committee of the Tuberculosis Association of India and was presented at the 41st National Tuberculosis & Chest Diseases Workers Conference, Hyderabad by Mr. G.P. Manna.

Fasting glucose level less than 140 mg%, 2 hour glucose level equal to or more than 140 mg but less than 200 mg% but the one hour level may be equal to or more than 200 nags.

Patients showing impaired GTT were to be given steroid primed GTT. For this, 10 mg of prednisolone were administered 8 hours and 2 hours prior to carrying out the standard GTT. Patients with sugar more than 140 mg% at 2 hours whose one hour level was at least 20 mg% more than the earlier level were classified as cases of diabetes mellitus. The remaining cases were to be marked as normal non-diabetics.

Bombay 1	70	16	15
Bombay 2	42	6	2
Delhi	72	12	20
Pune	132	23	..
Raipur	60	66	73
Rohtak	36	36	28
Total	935	169	192

Intake into the study lasted from December 1984 to December 1985.

Results

In all, 1,296 persons were included in the study. Of these, 935 were pulmonary tuberculosis patients, 169 persons suffered from non-tuberculous chest conditions and 192 were healthy controls. The distribution of these cases according to the various participating centres is shown in Table 1.

Although the protocol provided for controls to be almost equal in number to the pulmonary tuberculosis patients, the number of the former is much smaller because of the difficulties experienced by a majority of the centres in getting controls. Only two centres could provide almost equal numbers in pulmonary tuberculosis, non-pulmonary tuberculosis chest conditions and healthy sub-groups. It would also be seen that almost half the cases were contributed by one single centre.

The prevalence of diabetes mellitus in the various groups is shown in table 2. The patients in pulmonary tuberculosis groups were divided into bacteriologically positive and bacteriologically negative sub-groups. There was not much difference between the bacteriologically positive and bacteriologically negative cases in respect of prevalence of diabetes

TABLE 2

Prevalence Of Diabetes in various groups

	Number Examined	Diabetes No.	Cases
Pulmonary Tuberculosis (Bast. Pos. 69/743) (Bact. Neg. 22/192)	935	91	9.7
Non-TB Chest Diseases	169	15	8.9
'Healthy' Controls	192	30	15.6

mellitus. On the whole, 9.7% of the pulmonary tuberculosis patients had unknown diabetes amongst them. The percentage in non-tuberculous chest conditions and in healthy controls was 8.9% and 15.6% respectively.

Although the rates among tuberculous and non-tuberculous patients are similar, the very high rate amongst the so-called healthy controls is remarkable. Apart from small numbers, this may partly be due to the fact that healthy controls were usually drawn from the socio-economically better off members of the staff of the institutions whereas the bulk of the patients, both tuberculous as well as non-

G.T.T. showed 'Impaired Glucose tolerance' in 44 persons. Steroid primed G.T.T. however was not carried out in 18 and all the 26 cases where it was performed were found to be diabetic. The 18 cases where the latter test was not performed have all been counted as 'Normal' for purposes of analysis. If some of these were actually diabetic, prevalence rate of diabetes would have been higher than that shown in this table.

It is well known that the incidence of diabetes varies with age; and the material from the point of view of diabetes is usually divided into two age groups, viz. below 40 years and 40 years and above. The prevalence of diabetes amongst pulmonary tuberculosis patients in these two age groups is shown separately for males and females in Table 3. The table shows that the rate amongst 'more than 40 years' males was 17.8 % as against 5.1 amongst males below the age of 40 years. The rates in females were not very different from those in the males, being 23.4 % and 4.0 %; respectively. The over-all rate in males was 10.0% as against 8.7 %; in females.

TABLE 3
Prevalence of Diabetes Mellitus in relation to age & sex (Pulm. TB Cases only)

No. Exmd.	Males		Females		Total	
	<40Y	≥40Y	<40Y	≥40Y	<40Y	≥40Y
Diabetes Mellitus	23	51	6	11	29	62
Cases	5.1	17.8	4.0	23.4%	4.8%	18.6%

An attempt was also made to find Out whether the extent and severity of pulmonary tuberculosis were in any way associated with the prevalence or diabetes. Data presented in Table 4 suggest that the prevalence of diabetes did not differ significantly in respect

TABLE 4
Prevalence of Diabetes Mellitus related to Extent of Disease
(Pulmonary Tuberculosis patients only)

	Minimal or Mod. Adv.		Far Adv.	
	<40Y	≥40Y	<40Y	≥40Y
Number examined	66	61	536	272
Diabetes mellitus cases	4	13	25	49
	6.1 %	21.3%	4.7%	18.0%

of the extent of disease. Similarly, Table 5 shows that the prevalence of diabetes did not vary significantly in respect of bacteriological status of the tuberculous patients, the rate being 16.9% amongst sputum positive patients above the age of 40 years as against 24.0% amongst sputum negative patients in the same age group. The apparent difference in the rate may well be duo to the smaller number of total cases in the latter group.

TABLE 5
Prevalence of Diabetes Mellitus related to Bacteriological Positivity

	Bact. Pos.		Total	Bact. Neg.		Total
	<40Yrs.	≥40Yrs.		<40Yrs.	≥40Yrs.	
Number examined	489	254	743	113	79	192
Diabetes Mellitus Cases	26	43	69	3	19	22
	5.3%	16.9%	9.3%	2.6%	24.0%	11.4%

being slightly higher in males than females but considerably higher in those over the age of 40 years (10.4%) as against those below 40 years (3.1%).

A few more reports were published when the present study was in progress. Jain et al (1984) reported the prevalence of diabetes to be 7%; Deshmukh & Shaw (1984) as 5.6% in 2434 patients; Tripathy et al (1984) as 1.5% in 1359 patients and Roy et al (1984) reported an overall rate of 1.7%; amongst nearly 5,000 patients of pulmonary tuberculosis. Wide variation in the findings of these studies is obvious. It is parlay due to the number of cases being small in some studies but may also be due to the difference in the technique of GTT as well as the variation in the definition of a case of diabetes mellitus. For example, many studies consider a fasting glucose value of over 120 mg% as evidence of diabetes, whereas in this study the cut-off point has been taken as 140 mg%. In other words, if we had also followed the lower standard, the prevalence rate would have been even higher. Furthermore, in most of the studies, it is not mentioned whether the 'cases' were those freshly detected or known cases i.e. known cases of diabetes who had developed pulmonary tuberculosis were also included. Only one study (Roy et al 1984) mentions that 28 of the cases (reported prevalence 1.7%) were known cases. In the present study known cases were excluded.

Two questions arise:

- (1) Is the prevalence of diabetics among pulmonary tuberculosis patients more than in general population?
- (2) Is the prevalence of diabetics among pulmonary tuberculosis patients the same as in patients of non-tuberculous chest diseases?

As far as non-tuberculous chest diseases are concerned, the rate is very nearly the same as amongst pulmonary tuberculosis patients in this study. But the number of the former is small and the age distribution is very different.

than in the tuberculous patients groups. And thirdly, the controls were all drawn from the staff of the participating centres and were probably of a much higher socioeconomic status. Since incidence of diabetes is known to be influenced by age and the socio-economic status, the comparisons with the controls in this study may not be valid.

Therefore, in order to compare the rates of diabetes amongst pulmonary tuberculosis patients and general population, one has to look to the results of recent diabetes surveys carried out in the latter. Verma et al (1986x) questioned 2826 hotel employees in Delhi and found known diabetics to be 1.8% amongst them. No attempt was made to find out the unknown diabetics in this group. Verma et al (1986b) also surveyed 6878 persons in one locality of Delhi which probably is a suitable sample for comparison and found the overall prevalence of known diabetics as 3.1% in this population. The rate was a little higher in males (3.8%) as against females (2.3%). The prevalence was much higher in older age groups.

The Indian Council of Medical Research organised a diabetes survey in 1975 from six centres in the country (Ahmedabad, Calcutta, Cuttack, Delhi, Poona and Trivandrum). Nearly 35,000 persons, both urban and rural, were examined (Gupta et al 1978). The overall prevalence of diabetes in this study was 2.1%, the range being 1.3% in Delhi to 2.86% in Ahmedabad. The rates in persons above the age of 40 years were considerably higher, 1.56% in Delhi and 8.28% in Ahmedabad. This study also showed that known and unknown cases of diabetes were almost equal. The age distribution of the persons examined in the I.C.M.R. study and the present study was broadly comparable. It is obvious that the prevalence worked out in the present study, both in under 40 years and over 40 years, is considerably higher than in the general population examined in the ICMR survey. If the proportion of known and unknown cases in the ICMR survey holds for the present study also, the difference in the prevalence as compared to the ICMR study will get further enhanced.

compared to those under the age of 40 years.

- (3) There is probably not much difference in the prevalence of diabetes in respect of extent and severity of disease.

And as a corollary, it may be mentioned that it would be desirable to investigate pulmonary tuberculosis patients above the age of 40 years for diabetes as a routine. But if that is not feasible for some reason, investigation for un-identified diabetes should be a 'must' if the response to good chemotherapy in the first month or two in a patient of pulmonary tuberculosis is less satisfactory than expected.

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lymphadenitis. None of the 3 important characteristics viz. caseation, matting and adherence was found to be associated with any of the aetiologies of lymphadenitis with any degree of certainty. Tubercle bacilli could be demonstrated either by direct smear or culture only in about 36% of the tuberculous lymphadenitis cases. It was found that females predominated in the tubercular group.

It is common knowledge that patients with cervical lymphadenitis are often labelled as tuberculous on the basis of clinical findings only. Although at some places facilities for bacteriological and histopathologically examination are not available but very often either the patient does not accept biopsy or the treating physician does not consider it necessary. A cooperative study carried out from 1969 to 1971 under the auspices of the ICMR and reported by Pamra and Mathur (1974) had come to the conclusion that apart from caseation, there was no other clinical feature or tuberculin reaction which could be taken as pathognomonic of tuberculous lymphadenitis. Further, cases diagnosed as tuberculous without histopathological examination of the biopsied gland could lead to considerable overdiagnosis and even under-diagnosis. The present study was organised with a view to determine whether there had been any change in the situation during the last 14 years. It was also the purpose of the study to correlate bacteriological and histopathological findings among such patients once again.

Material and Methods

The study sponsored by the Research Committee of the Tuberculosis Association of India was carried out at five centres in the country. Although a large number of centres were contacted, only these 5 agreed to participate. Tuberculosis and Chest Diseases Departments of Medical College Hospitals were the two centres in Bombay; Tuberculosis and Respiratory Diseases Department of Medical College Hospital in Cuttack was the third centre; one centre in Indore was the surgical department of the medical college hospital and

the fifth centre in Delhi was a Tuberculosis Hospital-cum-Chest Clinic.

Patients reporting in the participating centres with enlarged cervical glands, with or without disease anywhere else in the body, were included in the study. After noting the clinical features of the enlarged glands, viz. caseation, matting and adherence to the surrounding structures, all systems were physically examined. Investigations were carried out to determine as definitely as possible about tuberculous involvement of any other system, if it was suspected on physical examination. Chest x-ray was taken as a routine. Tuberculin test with 1 TU PPD RT 23 was carried out and the in duration noted after 48-72 hours. Total and differential leucocytic count was also done as a routine.

Thereafter, biopsy of one or two glands was carried out. One gland (or half a gland if only one had been excised) was put in a bottle of sterile saline and sent to the bacteriological laboratory immediately for examination by direct smear as well as culture for AFB. The other gland (or the other half of the excised gland) was preserved in formal in solution and was sent for histopathological examination. The protocol provided for staining of the section for AFB also but hardly any centre carried out this examination.

Results of all the findings were entered on a special card provided by the Tuberculosis Association of India for this purpose. After the results of all the examinations were available, patients were finally divided into the following three categories:

*The Research Committee at present consists of Drs. S.P. Pamra, (Convener), G.V.J. Baily, S.P. Gupta, D.R. Nagpaul and R. Prabhakar.

Dr. M. M. Singh and the late Dr. H. B. Dingley were members of the Research Committee when the study was started.

This report was prepared by Dr. S.P. Pamra and Mr. G .P. Mathur on behalf of the Research Committee of the Tuberculosis Association of India and was presented at the 41 st National Tuberculosis and Chest Diseases Workers' Conference, Hyderabad by Mr. G. P. Mathur.

reactive hyperplasia, sinus catarrh, etc. Cases were labelled as NSL if the bacteriological result was negative or bacteriological examination was not carried out and the histopathological findings were in favour of this aetiology.

(3) Malignancy

Glands were marked as malignant on the basis of histopathological examination if tubercle bacilli could not be demonstrated. This group included carcinoma, lymphoma, Hodgkin's disease, leukaemia, etc. Cases with primary involvement and metastasis were both included in this group.

The intake lasted from 1.7.83 to 30.6.85 and in all 357 cases were included in the study. Of these 357 patients, 84 were from the two centres in Bombay, 70 from Cuttack, 78 from Delhi and 125 from Indore.

Results

Table 1 shows that out of 357 cases included in the study 233 (65.1%) were found to be tuberculous, 89 (24.9%) were of non-specific lymphadenitis and 35 (9.8%) were cases of malignancy. The proportion of various aetiologies in the five centres differs considerably and was obviously due to the type of cases included in the study. Twenty five out of the 35 cases of malignancy were from one centre which was the surgical department of a general hospital. There were very few cases of non-specific lymphadenitis from Bombay and Cuttack Centres which could be because of considerable selection being exercised before biopsy was carried out or many persons with N.S.L. may be refused biopsy.

Of the 357 cases, 11 had, in addition, enlarged glands in the axilla and 13 in the groin. Twenty nine had lesions in the lung, about half of which were probably inactive. Eighteen cases gave a history of previously having been treated for tuberculosis, mostly of lymph glands. A noteworthy feature was that the history of another tuberculous case in the family was given by 29 patients.

Bombay	32	8	-	40
II				
Cuttack	61	4	5	70
Delhi	32	41	5	78
Indore	70	30	25	125
	233	89	35	357

Table 2 shows the age distribution of the cases included in the study. The table shows that many more cases of TBL were amongst the patients in older age groups, whereas NSL was seldom seen beyond the age of 30 years. An interesting feature of the table is that 7 cases of malignancy were amongst children below the age of 10 years and of these 7, 6 were cases of Hodgkin's disease and one of Lymphoma. Taking all 35 cases of malignancy together, there were 9 cases of Hodgkin's disease, 12 of lymphoma and 14 of carcinoma metastasis. Of the latter, three cases were among females 30, 40 & 57 years old. One was in a male 35 years old and the remaining were all amongst males more than 50 years old. It would be interesting to point out that whereas in the earlier ICMR study only 16 cases out of 303 were of malignancy, in the present study their number was 35 out of 357.

Table 3 shows the sex distribution of all cases. As in the previous ICMR study, females were significantly more than males in the TBL group whereas males were more than females in the other two aetiological groups.

Table 4 shows the clinical characteristics of the glands in relation to the aetiology. Unfortunately, in some of the cases, information under this head was either missing or was incomplete with the result that the total number of cases for whom this information is available is less than the total number of cases included in the study. Furthermore, this lacuna was much more in respect of the most important criterion, viz., caseation, details

21-30 Y	88	80.0	21	19.1	1	0.9	110	100.0
31-40 Y	32	80.0	5	12.5	3	7.5	40	100.0
41-50 Y	21	72.4	3	10.3	5	17.2	29	100.0
51- Y	10	35.7	5	17.9	13	46.4	28	100.0
	233	65.3	89	24.9	35	9.8	357	100.0

Table 3

Sex-Distribution of Patients included in the study

	TBL	NSL	MALIG.	TOTAL
MALES	100 55.2%	55 30.4%	26 14.4%	181 100.0%
FEMALES	133 75.6%	34 19.3%	9 5.1%	176 100.0%
TOTAL	233 65.3%	89 24.9%	35 9.8%	357 100.0%

Of which are therefore not shown in the table. The findings in respect of matting and adherence were, by and large, in conformity with the earlier ICMR study. A substantial number of TBL glands were discrete and non-adherent whereas some cases in the NSL and malignancy groups did show matting and adherence. This brings out once again the fallibility of depending on clinical features alone in the diagnosis of TBL.

Table 5 shows the results of tuberculin test. It would be seen that the tuberculin test could be completed only in 267 cases out of 257. 7.7% of the TBL cases gave a reaction less than 10mms. But this is nothing unusual. The surprising part of this table

Table 4

Character of glands related to type of lymphadenitis

	TBL		NSL		MALIG		TOTAL	
	No.	%	No.	%	No.	%	No.	%
Matted	81	85.3	12	12.6	2	2.1	95	100.0
Discrete	79	54.1	55	37.7	12	8.2	146	100.0
Adherent	34	79.1	6	14.0	3	7.0	43	100.0
Non-adherent	110	62.1	57	32.2	10	5.6	177	100.0
Solid	116	65.5	55	31.1	6	3.4	177	100.0

Results of Tuberculin Testing

	TBL	NSL	MALIG	TOTAL
Induration <10mm	15 7.7%	16 25.4%	8 80.0%	39
Induration ≥ 10mm	179 92.3%	47 74.6%	2 20.0%	228
Total tests Completed	194	63	10	267

The results of bacteriological examination are shown in Table 6. In 50 cases, the bacteriological examination was not complete in respect of both direct smear and culture. Out of 183 TBL cases, 66 (35.6%) only were positive by smear and/or culture. There was only one case which was positive by smear but. negative by culture.

TABLE 6
Bacteriological Results among TB
Lymphadenitis Cases

Direct Smear Positive, Culture Positive	10	5.5%
" " Negative " "	55	30.1%
" " Positive " Neg.	1	0.5%
" " Negative " "	117	63.9%
Total	*183	100.0%
Positive by Direct smear and/or Culture.....35.6%		
*Bacteriological examination not completed in 50 cases		

Table 7

Correlation of Bacteriology and Histopathology in 282 cases

	Histopathology		
	TBL	NON-TB	TOTAL
AFB DEMON-Started	66	-	66
Bacteri- Ological Findings not-De-monst-Rated	177	99	216
TOTAL	183	99	282*

*Bacteriological Results not available for 75 cases.

Discussion

The ICMR Cooperative study of Tuberculosis Cervical Lymphadenitis (Pamra and Mathur 1974) had shown that the histopathological examination of the biopsied gland was the only sure diagnostic criterion of tuberculous lymphadenitis and dependence on bacteriological and/or clinical findings, was liable to lead to considerable over-diagnosis/under diagnosis in the absence of histopathological examination. The main objective of this study was to see if the situation had changed at all during the last 14 years. By and large, the results are similar. Of the three clinical features, viz. caseation, matting and adherence, information regarding caseation is incomplete, though many tuberculous cases did not show any evidence of caseation. Although matting and adherence were seen much more frequently in T.B.L. than in the other two groups, the

the diagnosis of TBL.

The findings in respect of age and sex were, by and large, the same as in the earlier study. Females were more than males in the TBL group. Although this finding alone may not validate an epidemiological conclusion about females suffering more than males with TBL, yet this preponderance of females over males in practically all the studies does make this finding significant.

Tuberculous lymphadenitis is supposed to be the result of primary infection through tonsils or immediate post-primary dissemination of the bacilli from the primary pulmonary complex to the glands via lymphatics or blood vessels. Bulk of the infections in our country still take place before the age of 20 years. Had the above hypothesis been correct, most of the cases of TBL should have occurred under 20 years age group. The actual position on the other hand is quite the reverse. Largest number of cases are seen, in this study as well as in the earlier one, in persons above the age of 20 years. It will thus be plausible to assume that TBL also, as diseases of most other extra-pulmonary organs, is the result of re-infection after the primary lesions had healed. The source of bacilli is probably endogenous re-exacerbation of dormant bacilli in aborted foci resulting from lymphatic and/or

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Introduction

Of the several aspects of tuberculosis affecting a people, the sociological aspect has received less than adequate attention. Epidemio-logical method and parameters have for long occupied a pride of place in our understanding of tuberculosis as a disease and dealing with it as a health problem. Progress in chemotherapy also has revolutionized both the management of tuberculosis patients as well as the overall prospect of tuberculosis control in populations. And increasing attention given to operational research has elucidated many a practical aspect of our tuberculosis control programmes. Sociological studies, however, have largely been confined to the understanding of "de fault", both in respect of regularity of drug intake as well as treatment completion. It may be so on account of the complexity of human behaviour and the other related factors. Nonetheless, the problem of tuberculosis in a people is primarily it question of human suffering. And, the aim of national tuberculosis programme (NTP), at least in the developing countries, has been to reach larger numbers of rural as well as urban tuberculosis patients, prevent early death among them and reduce unnecessary suffering. The epidemiological objective no doubt is important but attempts already made to measure the epidemiological impact of NTPs have not been rewarding (1, 2), perhaps because NTPs do not as yet adequately cover the population groups involved in the disease dynamics. Then: therefore, strong justification for monitoring NTPs by means of some sociological parameters which at present need to be carefully considered and developed.

Measuring Suffering

In 1967, the author had presented some ways to measure the suffering caused by tuberculosis in comparison with that by other sicknesses (3)

Among the 2,135 surveyed natal families, 68 having one tuberculosis patient each, information was collected in respect of total 11,315 eligible persons with regard to the

number of sick days experienced by them during two months preceding the interview. Suffering was measured in terms of death, sick man days, absence from work leading to loss of wages and additional expenses incurred on hiring alternate labour, cost of treatment, transportation, etc. Sick mandays were further studied as completely bedridden, partially bedridden and ambulatory days.

In all 4,690 (41.4%) persons had been sick during the two months. There were two deaths (2.94%) among tuberculous compared with 40 deaths (0.16%) in the rest of the population. On an average, a tuberculosis patient had had 39.9 sick manday compared with 28.8 for the other 4,622 sick persons. The proportions of the different kinds of sick mandays were not different in the above two groups perhaps due to diseases like chronic arthritis occurring in the non-tuberculous. The average number of sick mandays were quite similar among sputum positive cases and only radiographically diagnosed patients but the completely bedridden days were significantly more among the confirmed cases.

The overall economic penalty inflicted by tuberculosis was roughly five times that of other illnesses put together

Measuring Tuberculosis by Suggestive Symptoms

Inquiry for the presence of cough on the survey day was a feature of the 1975 Singapore tuberculosis survey (4). Overall, 8.5% of the surveyed population had had cough compared with 17.9% among those having active pulmonary tuberculosis, 31.1% among the with non tuberculous pathology and 7.8% in persons with no radiographic 1111g lesions.

If duration of cough of two weeks or more hereinafter "tuberculous symptomatic", is used as selection criterion then 7.9% of the active tuberculous, 15.2% of the non-tuberculous and the normal population had that duration of cough on the survey day. However, adding bacteriological confirmation to the above criterion showed that

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findings of the mentioned two surveys were somewhat different either because of different quality of symptom questioning or in the levels of tuberculosis prevalence in the two countries: in Korea, 9.5 overall, 46.9% of confirmed cases and 29.7% ; of abacillary cases had cough on the survey day (5).

A valuable contribution from the Korean surveys was the demonstration of concomitant decline in tuberculosis and cough: the prevalence of cough declined from 15.6% in 1965 to 11.8 in 1970 and 9.5 in 1975 compared with that of active pulmonary tuberculosis from 5.1 % to 4.2 % and 3.3 % respectively, suggesting a possible use of cough as sociological parameter.

Actions Taken to Relieve Symptoms

The actions that sufferers might take to relieve their symptoms was an interesting aspect studied in the Philippines survey (1981-1983). In that survey (6), 27.7% of the population had any or all of four suggestive symptoms (mostly cough) while 16.7% could even be categorized as tuberculous symptomatias. The high rates are in line with higher prevalence of tuberculosis in the Philippines: 1.25% bacteriologically confirmed compared with 0.76% in Korea and 0.46% in Singapore in 1975, further supporting the use of cough sociologically.

Of the 1,419 tuberculous symptomatias identified in the Philippines survey, 64.9% had taken some action or other to relieve their suffering. The proportions of tuberculous symptomatias as well as action-takers rose with age but whereas the symptomatias were more among males and rural people, action taking was significantly more in rural females followed by urban males. Thus, epidemiological aspect apart, individual motivation and sociological considerations are bound to influence patient behaviour vis-a-vis NTP.

Suggestive symptoms that occurred alone were commonly ignored or self-medicated, especially in rural areas. For multiple/persistent symptoms, help was more often sought from private medical practitioners, especially in

within two weeks of the start, mostly from private medical practitioners who generally treated fevers non-specifically.

The specific diagnosis of tuberculosis by the health centres/private medical practitioners was mostly established after ten weeks of the onset of symptoms.

On the survey day, there were 75 smear positives, 153 radiographic cases (including 11 culture positives) and 1,191 "non-cases" among the tuberculous symptomatias. Of the smear positives, 36% had either ignored their symptoms or self medicated, 43 % having sought medical assistance had been properly diagnosed (almost equally by governmental and private physicians) while the remaining 21 % were misdiagnosed by such "organised health services". Similarly, Of the 153 radiographic cases, 40% had not contacted the organised health services, 35% were properly diagnosed but in 25% the correct diagnosis had been missed. And, of the non-cases, 66 had not made contact, 26% were correctly declared to be free from the disease and 8% were wrongly labelled to be suffering from tuberculosis. Despite the variable, but most desirable, action-taking on the part of the sufferers, perhaps according to the extent of their suffering resulting from the type of the disease and duration of symptoms, the performance of the organised health services in correctly finding the cases had been less than satisfactory.

Sociological Parameters for Programme Assessment

Based on the foregoing review, development of the following sociological indicators is suggested for assessing NTP:

(a) Mortality

Mortality from tuberculosis could be used even though, epidemiologically, the tuberculosis mortality rate has fallen out of favour after the advent of chemotherapy. Death is the ultimate human suffering; it should not be essential, sociologically, to establish that tuber-

presently observed high mortality under most NTPs, for the expressed reasons that cases are often diagnosed at a very late stage of the disease and routine due regimens under the prevalent field conditions can not prevent early death among them, should not be accepted because NTPs. to be efficient, have to strive to diagnose cases early and deliver treatment with aim to prevent early death and reduce unnecessary suffering.

(h) Suffering Mandays

The duration of symptoms (mostly cough for which action is often taken early) before correct diagnosis is established in a fresh case may be used as an index, despite our incomplete understanding of social perceptions regarding importance of cough and the acceptable way to deal with it. Efficient tuberculosis services and health education should succeed in gradually reducing the period between the onset of symptoms and the contact with a physician health centre (patient delay) as well as time subsequently taken in establishing the correct diagnosis (doctor delay) in a community(7).

Proper elicitation of cough duration in freshly found cases is likely to be difficult in the busy environment of clinics/health centres. Besides, recall of the duration may be time consuming especially in rural/low literacy groups. Therefore, the requisite information must be elicited in the homes of patients. in the presence of other family member-; by trained general health workers- from the area health centre, normally assigned duties connected with delivery of health services in homes.

(c) Numbers on Current Treatment

If an estimate of the prevalence of bacterio

reached which will be determined by local sociological factors such as awareness or symptoms. pattern of action-taking, etc and the case-finding methodology used under NTP. Also, programme efficiency should reduce the margin of errored diagnosis. A more dense network or health centre,, efficient services, rising awareness in flue people and steadily growing confidence in the services should increase the proportion of prevalence cases who are under current treatment of NTP at any given time. which could be a pleasure or the sociological impact of NTP.

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dispensaries, 12% from specialised TB institutions and 6% from practitioners of indigenous medicine. patients reporting after several previous actions were found to have a higher rate of bacteriological positivity even though many of them had had at least some specific anti-tubercular treatment. Proportionately, the greatest financial burden of treatment before reporting at a TB Clinic was borne most by patients least capable of doing so. Economic difficulty was the deciding factor in finally coming to TB Clinic in half the patients.

The basic principle of TB control is to reduce the period of infectivity of tuberculosis patients to the minimum. With a number of efficient chemotherapeutic regimens it has now become possible to reduce the infectivity period after diagnosis to a very great extent. Whether such a reduction has occurred in the period of infectivity before diagnosis is the subject of this paper.

Since several systems of medical and many types of facilities for diagnosis and treatment, of varying degrees of efficiency are available in the country, it is not unusual for patients to go through a series of actions before they finally land up in a specialised TB institution dealing with modern medicine. A large part of our population, even in cities, is still steeped in ignorance and superstition, many patients still waste a lot of time and money before they reach a specialised institution, with proper facilities for diagnosis and free treatment. The present study was intended to determine the behaviour pattern of the patients in this respect and also to quantify the losses in time and money incurred by them. An earlier study carried out at the Centre during 1970 and reported by Pamra et al (1971) would serve as a basis for drawing conclusions regarding any changes that might have occurred in the intervening years.

Material and Methods

The study was carried out on freshly diagnosed cases of pulmonary tuberculosis reporting at the New Delhi TB Centre and residing in the domiciliary treatment area under the Center's jurisdiction. All such patients were personally interviewed by one of the authors (P.S.) and after establishing the necessary rapport, a questionnaire was filled in,

incorporating all necessary information on this subject.

The study covered 256 cases of respiratory tuberculosis newly diagnosed during 1986. Of these, 106 were bacteriologically positive at start, 148 were bacteriologically negative and for 2 patients (both young children) bacteriological examination could not be carried out. With the exception of these 2 cases all others were adults above the age of 15.

Results

Table I shows the time lost by patients before they took the first remedial action ('Patients' Delay'). In other words, this table charts the gap between onset of symptoms and the first action taken by the patient. One can see that 41% of the patients took some remedial action within one month. On the other hand almost 33% delayed such action for even longer than 3 months. The table also shows that long delays were more frequent in the uneducated sector. Unfortunately, the proportion of patients (or their guardians) who had had education is so low that this conclusion, however plausible, can only be regarded as suggestive.

In the first instance, 54% of the patients sought relief from general medical practitioners, 28% from hospitals and dispensaries and 12% from specialised TB institutions (Table 2). Only 6% went to practitioners of indigenous medicine.

How many patients continued running from pillar to post, without adequate relief, before they landed up at the TB Clinic can be seen from Table 3. Nearly 12% came straightaway, 40% after one earlier action, 25% after 2

*New Delhi Tuberculosis Centre, New Delhi.

Paper presented at the 41 st National Conference on TB and Chest Diseases, Hyderabad, 1986.

> 3 "	48	36.4	34	30.9	3	21.4	85	33.2
Total	132	100.0	110.	100.0	14	100.0	256	100.0

TABLE 2

Nature of First Action

	Patients	
	No.	%
General Practitioner	139	54.3
General Hospital or Dispensary	71	27.7
Indigenous Medicine	15	5.9
TB Institution	31	12.1
Total	256	100.0

TABLE 3

Number of actions before reaching Institutions

Actions	Patients	
	No.	%
0	31	12.1
1	103	40.2
2	64	25.0
3	38	14.8
4 or more	20	7.8
Total	256	100.0

Actions, about 15% after 3 actions and nearly 8% after 4 or more actions. It is not unnatural that, in the first instance, a patient having prolonged cough should visit a G. P. or a general dispensary for relief but it is worth nothing that even though the New Delhi TB Centre has been running a fairly efficient domiciliary treatment Programme in the area for over 45 years, almost half the patients visit two or more facilities before reaching the Centre. Interestingly, this is as much true of the educated group as of the uneducated although detailed data are not being presented. What price the patients pay for this delay in terms of clinical deterioration can be seen from Table. 4. charted in this table is the rate of bacteriological positivity among patients who come to the centre after 1, 2, 3, 4 or more actions as also among patients who come there in the first instance. While assessing these

Table 4

Bacillary status related to number of previous actions

No of previous Action	Bact.	Positivity
0	8/31	25.8%
1	45/101*	44.5%
2	25/64	39.1%
3	16/38	42.1%
4 or more	12/20	60.0%
Total	106/254	41.7%

*Two children not examined bacteriologically

financial burden which can be had from Table 6. To begin with, one notices that practically all of them come from the poorest stratum of society, more than half with a declared income of less than Rs. 400/- p.m. The average expenditure incurred per patient on previous treatment varies from Rs. 188/- to Rs. 315/- in the various income groups. Even if one were to take into account the general tendency to declare an income less than the correct one, it is obvious that, proportionately, the greatest financial burden i, borne be those [cast capable of carrying it. Similar finding was recorded by Pamra et al (1971) in the earlier study but due to steep fall in the value of the rupee u more precise comparison is not possible.

Rs. 200-400	97	
R. 400-600	37.9%	216
	62	
	24.2%	213
Rs. 600-1,000	46	
	18.0%	315
> Rs. 1,000	11	
	4.3	227
	256	
	100.0%	

How the patients ultimately reached the TB clinic is brought out in Table 7. In a very large proportion of cases it was the immediately preceding treatment facility, be it the G. P. or the general hospital, which referred them to the specialised clinic. Even so, it is worth nothing that economic motivation was the deciding factor in fully half of the patients.

Table 5
Total time lost before reaching TB Institution

0 – 31 days	91	35.5%
31 – 90 "	63	24.6%
91 – 180 „	44	17.2%
181 – 270 „	10	3.9%
271 – 365 „	5	2.0%
> - 365 „	43	16.8%
	256	100.0%

TABLE 7

Why patients came to TB Clinic

	Patients	
	No.	%
Referred by General Hospital Or Dispensary	90	35.2
„ „ General Practitioner	10	3.9
„ „ Friends/ neighbors	8	3.1
Not satisfied with earlier treatment	4	1.6
Attracted by free treatment facilities	128	50.0
Discovered in case-finding surveys	16	6.2
	256	100.0

Discussion

Before drawing any conclusions from this study one should keep in mind its limitations.

It would appear from this study that in the first instance most patients complaining of chest symptoms report either to a general practitioner or to a general dispensary for relief. This is not unexpected in as much as most chest symptoms are not specific for tuberculosis and patients have no reason to suspect that they may be suffering from tuberculosis. What is alarming is that nearly 1/3rd of the patients wait for longer than 3 months before taking any remedial action.

A point of some importance is that the proportion of patients consulting practitioners of indigenous medicine in the first instance is only 6%. This is a considerable change from the situation about 15 years back when Pamra et al (1971) reported that this figure was of the order of 20%. Whether such a change has occurred only in urban areas or is indicative of a change all over the country can only be surmised.

Almost 114th of the patients seek relief at 3 or more places before they report to a TB institution. How many of them receive anti-TB treatment and whether the treatment prescribed is scientifically correct is not known.

It is clear that much remains to be done by way of health education to reduce the losses in time and money referred to in this paper. It would, obviously, be a great help if general hospitals and dispensaries and general practitioners develop a high suspicion index in respect of patients reporting with chest symptoms. Further, the general practitioners themselves need to be informed about recent advances in chemotherapy. Where patients are not in a position to bear the cost of treatment, private practitioners would be well advised to refer them as early as possible to a specialized TB institution, with free treatment facilities. Only if action is taken along these lines can we expect some improvement in the present situation.

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The objective improvement in control group was 25 per cent as against 95 per cent in treated group.

Introduction

The commonest toxic reaction to daily streptomycin therapy is vestibular damage. The predisposing factors include old age (Smith and Zirk, 1961), renal insufficiency (Line et al., 1970), high dose of the drug (Bignall et al., 1951), otitis media (Miszke, 1972) and concomitant intake of other ototoxic drugs (Manten, 1975). Symptoms of vestibular damage include difficulty in maintaining equilibrium, giddiness, headache, nausea and vomiting. Important objective evidence include difficulty in focusing the eyes, spontaneous nystagmus and positive Romberg's Test. Confirmatory objective tests for vestibular damage are caloric test and craniocorpography. The latter test has been found to be more sensitive and less time consuming than the former.

Penman (1958) observed that the streptomycin induced vestibular damage was reversible on pantothenic acid therapy but Johnston et al. (1964) found that given concomitantly with streptomycin, it was ineffective in preventing the drug induced vestibular dysfunction. Purohit et al. (1976) used furosemide in patients having streptomycin induced vestibular damage and found a favourable response but the study was based on subjective assessment only.

The present study was undertaken at the Hospital for Chest Diseases and Tuberculosis, Jaipur to assess the type of vestibular damage induced by streptomycin as revealed by craniocorpography, and to see whether or not furosemide therapy is effective in reversing the streptomycin induced vestibular damage.

Material And Methods

The study was carried out in 40 cases of

Pulmonary Tuberculosis, who developed vestibular toxicity due to parenteral streptomycin. Cases having concurrent neurological involvement, renal failure, cardiac failure or any gross otolaryngeal problem were excluded from the study. The diagnosis of streptomycin induced vestibular damage was made on the basis of history, neurological and otolaryngeal examination and was substantiated by craniocorpography.

All the patients were investigated thoroughly, General examination and examination of respiratory system and vestibular system were carried out. Routine investigations included blood, urine, sputum, X-ray chest, blood urea, serum creatinine and Alanine Transaminase Level. Vestibular tests like nystagmus, Romberg's sign, straight line walking test. Fukuda's modified method of craniocorpography followed by Bafna A.S. (Personal communication) were carried out to record the vestibular function of the patients.

Requisites for this test were:

1. Sound and light proof room of 10'x12' size.
2. Ordinary box camera.
3. Craniocorpography cap comprising three headlights connected to 6 V battery. With the help of these lights movements of the patient's head was recorded in camera during the process of stepping test which was carried out in a dark room.
4. 400 AST film with a breadth of 120 mm.

Procedure: The simple box camera was

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*Paper presented at the 41st National Conference on TB and Chest Diseases, Hyderabad, 1986.

patient's eyes were closed with a mask and he/she was advised to stretch his/ her arms straight forward. In the process of stepping test, patient had to alternately Lift his/her legs at (Ire point of initiation and this exercise was continued for one minute During the process of stepping test patient's rotation on his own axis. lateral deviation and sway were recorded in the camera kept at the ceiling. After developing the film Al the three parameters, i.e., rotation. Lateral deviation and sway were compared with the normal values. Normal values were as follows:

Lateral deviation - Right upto 70° -
Left upto 50*

Angle of Rotation - Right 9°.64° --- Left
51.6°

Sway -- within the range of 20 cm.

These 40 patients were randomly allocated to the following 2 groups (alternate patient to each group)

Group A - Inj. Glucose normal saline
(5%) 2 cc intravenously daily
for 7 consecutive flays.

ages ranging from 15 years to 62 years (Table I). Mean age of the patients in two groups was 40.1 ± 12.4 and 37.4±13.0 years, respectively. According to radiological extent of the disease, 17 (42.5 %) patient, had far advanced. Lesions, 16 (40%) moderately advanced and 7 (17.5%), minimal disease. The sputum smear of 13 patients (32.8%) was negative for Acid Fast Bacilli. Vertigo was the commonest symptom found in all the patients. Next in order was tinnitus which was present in 7 and 3 patients respectively. Headache and vomiting were Less common and reported by 5 and 4 and 3 and 4 patients respectively (Table 2).

Tile result of craniocorpography shows that majority of (52.5%) of patients had peripheral lesions. Central and combined defects were seen in 12 (30%) and 1 (17.5%) patients respectively (Table 3). While analyzing the subjective improvement in both the group, it was observed that 15 patients (75%) of Group I showed no improvement or partial improvement compared to only one patient (5%) in Group it (Study group). Good to excellent improvement was seen in 5 (25%) and 19 (95%) patients of Groups I and II respectively (p <0.0(11). The results of the objective craniocorpography assessment are

TABLE 1

Age and Sex Distribution of the patients

age Group ^s (in year.)	<u>Group I</u>		<u>Group II</u>		Total	percentage
	Male	Female	Male	Female		
≤30	4	1	7	3	15	37.5
31 - 40	5	3	3	1	12	30.0
41 - 5(1	1	1	3	-	5	12.5
>50	-	-	3	-	3	20.0
Total:	15	5	16	4	40	100.0

Tinnitus	7	8
Headache	5	4
Vomiting	3	4

In the present study all the patients developed vertigo while on streptomycin therapy and showing obvious abnormalities on craniocorpography were included. Forty such patients could be included between April 1985 to August 1986.

The patients were randomly allocated to one of the two groups of 20 each. The two groups were comparable as regards age and sex distribution, total duration of illness, radiological extent of lesions and bacteriological status.

*Most of the patients had more than one symptom.

shown in Table 3. Craniocorpography reverted to normal in 5 (25%) of the 20 Group I patients, as compared to 19 (95%) in Group II (P<0.001). All patients whose cranio

A feeling of rotation (vertigo) was common

TABLE 3

Streptomycin Induced vestibular Damage Assessed by Craniocorpography (before and after therapy)

Type of defect	Group I			Group II		
	Before therapy	Change in CCG* after therapy		Before therapy	Change in CCG* after therapy	
		CCG* Remained Abnormal	CCG* changed to Normal		CCG* remained abnormal	CCG* changed to normal
Peripheral						
- Left	10	8	2	3	-	3
- Right	3	3	-	5	-	5
Central	5	2	3	7	1	6
Combined	2	2	-	5	-	5
TOTAL	20	15	5	20	1	19

P Value < 0.001

	abnormal	normal	abnormal	normal		
No Improvement (-)	8	8	-	1		
Slight Improvement (+)	7	7	-	-		
Good Improvement (++)	4	-	4	8	-	8
Excellent Improvement (+++)	1	-	1	11	--	11
TOTAL	20	15	5	20	1	19

to all the patients. The other symptoms included tinnitus (15; 37.5%), headache (9; 22.5 %), and vomiting (7; 17.5 %). These symptoms of streptomycin induced vestibular damage were described by Bignall et al. as early as 1951.

Majority of our patients (32 out of 40; 80%) developed vertigo between first and third weeks of streptomycin therapy. Only two patients (10%) developed it after receiving streptomycin for more than 4 weeks. Further, our patients developed vertigo after receiving smaller doses of streptomycin as compared to those of Miszke (1972), where vertigo developed in half of the patients only after receiving more than 30 grits. of the drug.

Results of the craniocorpography revealed peripheral lesions in 21 and combined lesions in 7. In the remaining 12 patients the lesions were purely central. It is, thus, clear that streptomycin not only damages the labyrinth but may also damage the vestibular nerves of the brain.

Purohit et al., (1976) reported that furosemide reverted the streptomycin induced vertigo in 17 out of 20 patients as compared to only 2 out of 20 controls. In the present study also, 19 out of the 20 patients on furosemide therapy showed good to excellent clinical response. Craniocorpography also reverted to normal in these patients. One patient in this group failed to respond as against 5 from among the control.

The objective assessment using the most modern vestibule spinal function test, i.e., craniocorpography in the present study, confirms the results of Purohit et al. (1976).

How furosemide, a drug known to cause ototoxicity by itself (Cooperman and Rubin, 1973), helped in reverting the streptomycin induced vestibular damage is unknown. Possibly, furosemide in smaller doses, as used in this study, helped to flush out streptomycin from the blood and/or the vestibular system and, thus, prevented further damage of the vestibular apparatus or the vestibular neurons of the brain. Although streptomycin levels of the serum could not be estimated in the present study, yet Line et al. (1970), observed a significant correlation between the development of dizziness and the 24 hours' streptomycin serum levels. Purohit et al. (1976) have explained the favourable clinical response with furosemide on this basis.

Furosemide is also known to influence serum electrolytes when given intravenously (Cooperman et al., 1973). Furosemide causes hyponatremia which is known to damage vestibular system (Lloyd et al. 1971 and Gallagher et al., 1979) and, therefore, the probability of getting relief in streptomycin induced giddiness through change in serum electrolyte levels seems improbable.

Furosemide is a potent diuretic and reduces

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The XVth Conference of the Eastern Region of the International Union Against Tuberculosis and Respiratory Diseases will be held in Lahore (Pakistan) from 10th to 13th December, 1987. Those who wish to present papers may obtain copies of proforma for sending the Abstracts from Prof. Abdul Aziz, C/o. T.B. House, 34/F, Gulberg-2, Lahore-11, Pakistan.

2. The National Programme had two objectives, viz. a short-term objective consisting of reduction in the suffering due to tuberculosis and a long-term objective to control tuberculosis. Considerable fall in the mortality from tuberculosis and the much larger number of patients being treated for tuberculosis today and being cured, more so in rural areas, show the success in short-term objective. The Long-term objective, viz. to bring down the prevalence and incidence of disease will certainly take time because of inadequate facilities for diagnosis and treatment and inadequate socio-economic progress.

3. Sputum examination is the only authentic diagnostic test for pulmonary tuberculosis. X-ray examination is, at best, a screening procedure. Usually two sputum examinations are recommended. This may not always be possible because of paucity of staff. It is, therefore, recommended that larger primary health institutions should have two laboratory technicians instead of one with a view to cope with the increase in the number of sputum specimens to be examined. Where only one laboratory technician is available, second sputum examination may not be insisted but one x-ray examination should be carried out properly and diligently.

4. General hospitals with big out-patient attendance should be mobilised for case-finding. Provision of MMR unit and additions to the laboratory will not constitute a big input but will help to diagnose a large number of cases.

5. Age old doctor-patient-community relationship should be developed to improve case-holding. Where motivation by doctors is not feasible because of heavy work load, proper motivation should be insisted upon by para-medical workers.

6. Only robust drug regimens of proven efficiency should be prescribed. Regimens recommended by the Standing Technical Committee of the Tuberculosis Association of India fulfil these criteria.

7. Routine hospitalisation, specialised institutions at all levels and exclusive tuberculosis workers at the peripheral health institutions are neither feasible nor advisable. Integration of tuberculosis services with the general health services of the country should be the ultimate goal.

8. The 20-Point Programme signifies official recognition of the impor-

in anti-tuberculosis work.

10. Health education is a must for improving the performance under the National Programme. No efforts should be spared to mount an intensive health education drive all over the country.

Three short-course regimens are being tried under programme conditions in 18 districts in the country i.e. six districts have been allotted to each one of the three regimens. The regimens are 2 RA_ZZ_Z/4 R₂H₁; 2 RHZ/6TH; 2 RHZ/4 R_ZH₂. If regimens 1 and 3 were not feasible in the case of any patient to the district to which these regimens were allocated, the patient was put on regimen No. 2 as an alternative. The first regimen was fully supervised and the second regimen entirely unsupervised. The third regimen was unsupervised in the first two months and supervised during the subsequent intermittent phase. All patients were sputum positive, 15 years or more in age with previous treatment, if any, less than 2 months. 50% of the eligible patients in the case of regimen 1, 30% in regimen 2 and 50% in regimen 3 accepted the regimen, range being from 19 to 81 %. Patients who did not accept the particular regimen were treated with conventional drug regimens. 49% of the patients in regimen 1 completed >80% of the treatment and 43% were lost cases. The corresponding figures for regimens 2 were 52% and 39% and for regimen 3, 50% and 36%. Interim results of treatment were presented only for the districts of North Arcot and Pondicherry where treatment was started 41 months and 27 months earlier, respectively. In North Arcot, 45% of the patients completed treatment, 47% were lost and death, migration and change of regimen accounted for 8 %. In Pondicherry, the respective figures were 73 %, 16 % and 11 %. In the case of patients put on conventional regimens, only 26 completed treatment. Sputum conversion at the end of treatment was 81 % in North Arcot and 90% in Pondicherry.

MONITORING SHORT-COURSE CHEMOTHERAPY UNDER DTP CONDITIONS - A REVIEW

M.S. KRISHNAMURTHY, *et al.*

Methodology of obtaining data and monitoring were discussed in the light of the short-course chemotherapy study in 18 districts under programme conditions. Punctual and prompt reporting is essential. Data received from the treatment centres should be checked for completion and consistency. Any large deviation from the previous data should be further probed to determine whether the departure is real. And if so, any local cause for that should be investigated. Difficulties and problems encountered in the monitoring were highlighted.

ACCEPTABILITY OF TWO 8-MONTH REGIMENS OF SHORT-COURSE CHEMOTHERAPY UNDER CONDITIONS OF AN URBAN TUBERCULOSIS PROGRAMME

G.V.J. BATLY

(Paper will be published in full)

RIFAMPICIN-INDUCED RELEASE OF HYDRAZINE FROM ISONIAZID : A POSSIBLE CAUSE OF HEPATITIS DURING TREATMENT OF TUBERCULOSIS WITH REGIMENS CONTAINING ISONIAZID AND RIFAMPICIN

G. RAGHUPATI SARMA

Incidence of hepatitis during treatment with INH was studied. The regimen in 885 patients included Rifampicin also and in 2,836 no Rifampicin was included in the regimen. Hepatitis occurred in 7 % in the former as against 1% in the latter. There was no difference in the two regimens amongst rapid inactivators of INH but amongst slow inactivators the percentage was 11 and 2 respectively. Hydrazine, a metabolite of INH, is found oftener in slow than in rapid inactivators. It is stimulated by administration of Rifampicin and appears to be responsible for hepato-toxicity.

ADVERSE REACTIONS OF SHORT-TERM

CHEMOTHERAPY

P.A. DESHMUKH, *et al.*

Adverse reactions seen in 855 patients on short course chemotherapy with various regimens containing HRSZE were reported. Adverse reactions were noticed in 34% of the patients. In half of these, the offending drug/drugs had to be withdrawn. Maximum withdrawals were in EHRZ regimen but were almost equal in all other regimens. Streptomycin had to be withdrawn in the largest number of cases (10%) followed by Rifampicin (7%, Ethambutol and Pyrazinamide (3%. Withdrawals because of INH were found necessary only in 0.6%. Maximum reactions (70% were noticed in the first month of treatment.

PARENTRAL FRUSEMIDE IN THE MANAGEMENT OF STREPTOMYCIN INDUCED VERTIGO-EVALUATION BY CRANIOCORPOGRAPHY

S.D. PUROHIT

(Paper being published in full)

MANAGEMENT OF TREATMENT FAILURE CASES

K. JAGANNATH, *et al.*

Ninety seven patients resistant to at least two anti-tuberculous drugs whose previous treatment had been a failure and who had no other associated illness were hospitalised for one year. 95 % of the patients were in the age group of 21 to 60 years, 64% were males. All patients were given Kanamycin either twice or thrice a week in a dose of 0.75 grams in addition to three or four other drugs. Rifampicin, IN H and Ethambutol were given to all patients. Bacteriological conversion was seen in 40% at the end of the second month, 82% by the end of the fourth month and 98 % at the end of sixth month.

MANAGEMENT OF PRIMARY TREATMENT FAILURES UNDER TB CONTROL PROGRAMME

S. RAJASEKARAN, *et al.*

Patients who had a minimum treatment of 6 months without sputum conversion and without any associated disease and pregnancy were included in the study. Nine hundred and six patients were put on 2 E,R,Z,/10 E2R2 ; 387 patients on 1 E7R7Z7/11 E,R. and 81 patients on 1 K7E7R7Z7/5 E3R3Z3 regimens. 90% of the patients in 6-month regimen completed the treatment as against 66% in the other two regimens. Sputum conversion was 100% in all the three regimens. Relapse rates were 5.1 %, 5.2 % and 3.3 % respectively, after one year's follow-up.

ROLE OF RIFAMPICIN IN THE TREATMENT OF TUBERCULOSIS

P. SENSI

The introduction of rifampicin has had a revolutionary effect on the chemotherapy of tuberculosis. Although high activity of Rifampicin in vitro and in vivo, against a variety of pathogens was recognized early, the major interest has been in respect of its antituberculous activity. This drug possesses properties very near to those required for an ideal antituberculous agent: e.g. quick bactericidal effect at very low concentrations on various bacillary sub-populations, including those scarcely metabolizing; in various situations and inside the macrophages; in various pH conditions, with a low frequency of resistant mutants. All these properties explain the high sterilizing activity of rifampicin on tuberculous infections.

Administration of rifampicin with one or two other drugs in the initial phase results in a complete cure of tuberculosis in 6-9 months. The short course chemotherapy regimens of rifampicin and isoniazid for 6 months with pyrazinamide and another drug for the first 2 months, or for 9 months with only a third drug for the first 2 months have been adopted in almost all developed countries. It would be highly desirable for the developing countries also to adopt the same regimens or some modifications of them, of proved efficacy, which take into account the socio-economic and epidemiological situations and the health care systems of each country. Further research on a triple combination of rifampicin, isoniazid and pyrazinamide, has shown it to be particularly useful for the initial intensive phase. The first results of the clinical trials with this combination in various countries, have demonstrated its efficacy, especially in improving the compliance of the patients. Another development in the field of rifampicin is represented by "rifapentine", a long lasting rifampicin which hopefully can be effective in once-a-week regimens in the continuation phase after the first two months of intensive chemotherapy.

RIFABUTINE-A NEW ANTI-MYCOBACTERIAL DRUG

P.R.J. GANGADHARAM

(Paper not received)

TUBERCULOSIS ASSOCIATION OF INDIA : DIABETES STUDI

(Paper being published in full)

PREVALENCE AND CLINICAL PROFILE OF DIABETES MELLITUS AMONG PULMONARY TUBERCULOSIS PATIENTS

R. RAMAKRISHNA, et al.

Of the 500 sputum positive patients of pulmonary tuberculosis attending the TB Centre, Visakhapatnam, 10.5% were found to be diabetic. The prevalence of diabetes was found to be increasing with age (2.9% in 25-34 years age group as against 27.3 % in those 55 years and above in age). There was no significant difference between males and females. Diabetics had very advanced and cavitory disease and haemoptysis also was more common amongst diabetics.

MORBIDITY AND MORTALITY FROM TUBERCULOSIS IN CHILD POPULATION-A

BRIEF REPORT

P. CHANDRASEKHAR

(Paper being published in full)

ARE SURGICAL PROCEDURES REDUNDANT IN THE PRESENT DAY ANTI-TB REGIMEN”

R. JAYASWAL., et al.

Surgical treatment was carried out in 75 (9%) patients out of 837 pulmonary patients created in 1984. The main indications for surgery were: bronchiectasis 13 cases; persistent cavity 25 cases; destroyed lobe/lung 17 cases; empyema 10 cases; tuberculoma 6 cases and recurrent and massive haemoptysis 4 cases. Seventy out of the 75 patients could be subsequently returned to active military service Which Was the main justification for resort to surgery. Only one patient died due to post-operative empyema/septicaemia.

LATE SEQUELAE IN QUIESCENT CASES OF PULMONARY TUBERCULOSIS

BALDEV RAJ, et al.

Attempt Was made to recall for assessment 1,250 cases treated for pulmonary tuberculosis 10 or more years ago. Of these, 813 patients responded. Twenty-four had died during the period and the others did not respond. Of the 813 Who responded or attended voluntarily because of symptoms, 312 had some complications. The main complications Were cough and sputum in 58%, haemoptysis in 12% and hoarseness in 3.5%. 16% had breathlessness even at rest and 6.7% complained of pain in the chest. Radio logically, 17 cases had open negative syndrome, 36% gave a history of recurrent respiratory infections and 6% showed evidence of relapse.

PROFILE OF GERIATRIC TUBERCULOSIS IN HILLY AREA (HIMACHAL PRADESH)

R.S. BEDI, et al.

One hundred cases of pulmonary tuberculosis over 50 years in age who attended the Tuberculosis Department from 1983 to 1985 Were studied. The clinical presentation Was altered due to associated chronic obstructive airway disease as Well as smoking. Breathlessness Was the main presenting feature. Sixty five cases showed fresh exudative lesions. Drug toxicity Was not a major problem in both conventional and short-course chemotherapy. Both regimens were equally effective. Compliance Was poorer than in the case of younger persons. Only 48 patients completed the stipulated treatment of 6 to 12 months as against 70% of the patients in the younger age groups.

IgA was significantly higher.

HEPATO-PULMONARY AMOEBIASIS: CLINICAL PROFILE AND EFFICACY OF VARIOUS TREATMENT REGIMENS

N.K. JAW, et al.

Thirty three cases of hepato-pulmonary amoebiasis were studied. Majority of the patients were young and middle aged males. Lungs were involved in 55 %, pleura in 15% and both lungs and pleura in 30%. Typical chocolate coloured sputum was seen in 24%;. Pleural fluid was chocolate coloured in 21%, Amoebae were isolated from sputum in 6 %; and in pleural fluids and stools in 15%. A combination of dehydroemetine and Metronidazole give best results.

PULMONARY AMOEBIASIS-A 30 YEARS' STUDY

A.L. ANAND

Fifty cases of pulmonary amoebiasis were treated in K.J. Mehta T13 Hospital from 1955 to 1934. Liver was involved in 8 of these. Pulmonary amoebiasis should be suspected in the case of basal pneumonitis, especially on the right side when sputum is repeatedly negative for AFB and there is no response to commonly used anti-bacterial drugs.

RE-EVALUATION OF DIRECT SENSITIVITY METHOD FOR MYCO. TUBERCULOSIS

N. K. JAIN, et al.

A study was carried out at the New Delhi TB Centre to compare the results of direct and indirect sensitivity tests. One hundred and ninety eight patients (101 previously untreated) were included in the study. Taking the results of indirect sensitivity test as the standard, it was found that the direct sensitivity method missed as many as 49 % of the resistant cases in respect of INH, 40% for Streptomycin, 61 % for Rifampicin and 100%;; for Ethambutol. The percentage of 'false' resistant cases was found to be 33% 37%, 46% and 0% ; respectively for the four drugs. No major differences were found in the previously treated and untreated patients.

A COLD STAINING METHOD FOR ACID FAST BACILLI

R. VASANTHAKUMARI, et al.

One thousand one hundred sputum samples were studied. Two smears each were prepared from 700 samples. One of these was stained by conventional Ziehl-Neelsen's Method and the other was stained by the new cold staining technique. The other 400 samples were concentrated by Petroff's method and the deposit was stained both by the Ziehl-Neelsen's method and the cold staining method. Out of the first 700 specimens, 216 were positive by both conventional and the cold staining techniques, 13 specimens were positive by cold staining technique but negative by Ziehl-Neelsen's technique and 9 specimens were positive by the conventional method and negative by cold staining method. In the other 400 specimens, the results by Ziehl-Neelsen and Cold staining methods were almost identical. One case was negative by Ziehl-Neelsen but positive by cold staining technique. Two cases were positive by Ziehl-Neelsen technique but negative by cold staining method.

TUBERCULOSIS IN CHILDREN

Moderator : S.P. PAMRA

Panelists : P.A. DESHMUKH, G.D. GOTHI, K. JAGANNATH, R. NARMADA AND M. NAGARAJ RAO

The following are the salient points of the panel discussion:

- (1) Although tuberculosis in children is declining on the whole in our country, it still constitutes a major and important problem. Some of its manifestations in children still carry a poor prognosis.
 - (2) Epidemiological data based on figures of attendance in various hospitals, clinics, etc. cannot per se give a precise idea about the epidemiology of disease in the country since children with different manifestations attend different places. Epidemiological study about extra-pulmonary tuberculosis on the lines of the survey for respiratory diseases has neither been made nor perhaps is it possible. Tuberculosis specialists and paediatricians often see different manifestations in different stages of evolution and hence their approach seems to be somewhat different.
 - (3) Symptoms, physical findings, history of contact have very little relevance in the diagnosis of tuberculosis in children. Mantoux test is of some significance only if it is negative in the case of infants. Scoring systems have many lacunae and at best can be used as a screening procedure and not for clinching the diagnosis. In the usual absence of bacteriological and histological confirmation of diagnosis, diagnosis depends on correlation of all available evidence supplemented by a short period of observation in some cases. Blood sedimentation rate has no diagnostic value.
 - (4) Hospitalisation of every child is not necessary for treatment. Hospitalisation is desirable for children who are acutely ill or are suffering from tuberculous meningitis. The following chemotherapy regimens recommended by the IUAT are acceptable in cases where drugs like Rifampicin and Pyrazinamide are available. If these two drugs are not available, conventional regimens based on Streptomycin, INH and Thiacetazone are fairly effective.

- | | |
|---|--|
| 1. Prophylactic | - H 10 mg/kg for one year. |
| 2. Primary Complex | - -do |
| 3. Progressive Primary Pulmonary Disease | - H 10 mg/kg plus R 10 mg /kg for 9 months or 2HRZ/4 HR |
| 4. Endobronchial Tuberculosis plus Prednisolone 1 mg/kg for | - -do-
6-12 weeks initially. |
| Pleurisy | - -do |
| 6. Miliary Tuberculosis | - 2 HRZS/10 RH plus prednisolone (if child is acutely ill) initially for 6-12 weeks. |

IVP alone is quite adequate for treating uncomplicated primary complex or chemoprophylaxis. Steroids should be used in miliary and meningeal tuberculosis or Pleural, Pericardial effusion. Children who are acutely ill with high toxæmia may also be given steroids for a few days initially till toxæmia abates.

- (6) There is no study in any part of the world which has shown that BCG does not confer any protection against any manifestation of tuberculosis. Under the circumstances, every child in the country should be given BCG vaccination as early in life as possible.

Chemoprophylaxis, as a mass measure, is not recommended. It is recommended in individual cases, such as Mantoux positive infants, children below the age of 5 who are in contact with an open pulmonary case in the family, recent converters and those on prolonged steroids.

TUBERCULOSIS ASSOCIATION OF INDIA : CERVICAL LYMPHADENITIS STUDY

(Paper being published in full)

RENAL INVOLVEMENT IN PULMONARY TUBERCULOSIS

R. N. MANIA et al.

Seventy four consecutive previously untreated bacteriologically confirmed and uncomplicated cases of pulmonary tuberculosis hospitalised in Burla Medical College/ Hospital were studied from January 1985 to February 1986. Renal biopsy could be done only in 50 cases. Majority of the cases belonged to the third and fourth decade of life. Male to female ratio was 4 : 1. Forty two out of the 74 patients had some urinary symptoms; 29 of these 42 had symptoms for less than 3 months. Albuminuria was present in nearly half the cases. All had pyuria. AFB were demonstrated in the urine in 8 cases and in 6 cases urine became negative after 2 months of chemotherapy. Biopsy was successful in 37 out of the 50 cases where it was carried out; in 7, the histopathological findings were within normal limits. Only 2 cases showed definite evidence of tuberculosis. The remaining showed non-specific changes. None showed amyloidosis. Out of the 8 cases of bacilluria, 2 showed typical tuberculosis lesions, 4 showed only fibrosis and one each showed interstitial nephritis and focal lymphocytic infiltration.

A STUDY OF RENAL TUBERCULOSIS AMONG HOSPITALISED PATIENTS OF PULMONARY TUBERCULOSIS

RAJENDRA PRASAD, et al.

Two hundred consecutive bacteriologically proved patients of pulmonary tuberculosis were studied. Morning urine was cultured for AFB and IVP and Isotope Renography were performed in 9% patients whose urine culture was positive. Of the 17 urine culture positive patients, 8 had urinary symptoms, dysuria being the commonest. Ten patients had abnormal urine analysis, 8 had abnormal IVP and 16 had abnormal renogram.

ROLE OF BRONCHOALVEOLAR LAVAGE & TISSUE BIOPSY IN THE DIAGNOSIS OF SMEAR NEGATIVE PULMONARY TUBERCULOSIS

S.C. TEWARI, *et al.*

Bronchoscopy and bronchial lavage was carried out in 179 cases of lung lesions whose sputum was negative by smear and culture. Endobronchial lesions were seen in 36 cases. Lavage was positive for AFB in 5 by smear and 8 by culture. Biopsy of granulation tissue in 8 cases showed tuberculosis in 6. In 103 cases where bronchoscopy did not reveal any endobronchial lesion, bronchial lavage was positive for AFB by smear in 4 cases (including 2 cases of post-bronchoscopy sputum specimen) and culture was positive in 7 cases. Including other adjuvant procedures like lymphnode biopsy, thoracotomy, mediastinoscopy and pleural biopsy, a positive bacteriological or histopathological diagnosis was obtained in 43 cases.

ROLE OF DRILL BIOPSY IN DIAGNOSIS OF LUNG LESIONS

P.V.P. RAU, *et al.*

Lung biopsy was performed with a high speed pneumatic drill in 152 patients from January 1978 to June, 1986. Adequate lung tissue to give a definite diagnosis could be obtained in 138 patients. Seventy one patients developed complications, sub-cutaneous emphysema being the commonest. However, only 7 of these patients required active treatment. There was one death as a result of asphyxia following aspiration of the stomach contents within 24 hours of the biopsy. The procedure is simple and can safely be carried out in an out-patient department and gives satisfactory results.

ULTRASONICALLY GUIDED NEEDLE ASPIRATION BIOPSY OF INTRA-THORACIC LESIONS

M.M. SINGH, *et al.*

Fine needle aspiration biopsy and bronchoscopy were performed in 25 cases under ultrasound guidance. Ninety percent of the lesions could be diagnosed. Diagnostic yield in peripheral chest lesions was 80%, in malignant lesions 91%, and in benign lesions 75 %. None of the patients developed any complication except minor asymptomatic pneumothorax in one case.

NEEDLE BIOPSY OF THE LUNG-ITS DIAGNOSTIC YIELD IN DIFFUSE AND MASS LESIONS

K. VENU, *et al.*

Biopsy was performed with Vim Silverman needle in 29 patients with diffuse nodular lesions and massive lesions near the periphery which could not be diagnosed by radiology, bronchoscopy and sputum cytology. Adequate tissue for diagnosis was obtained in 19 cases. In 14 of these, the diagnosis was bronchogenic carcinoma. Three cases were tuberculosis and one each of lung abscess and pleural effusion. Two cases developed haemoptysis and 2 cases developed minor pneumothorax.

T. SHAW, et al.

Five hundred and eleven symptomatics attended the camp. MMR X-ray examination was followed by sputum examination if radiology showed a lesion. Two hundred and thirty five were new symptomatics and 276 had attended a medical facility earlier also. Three hundred & nine cases were diagnosed as tubercular, 56 out of 235 persons previously unexamined persons and 253 out of 276 previously examined individuals. Sputum was examined in 182 cases and was found to be positive in 75 only. Nearly 80% of the patients were in the age group 15-50 years. At the end of treatment with various regimens, 66% were cured, 25 % dropped out, 4% died and 2% were failures of treatment.

TB CASE-FINDING CAMPS-OUTCOME AND FEEDBACK

M. ABDUL RAHIM

Twenty five case-finding camps were organised in 66 villages; 18,125 symptomatics attended the camps. 15,912 sputum specimens were examined, 6932 MMR examinations and 2213 tuberculin tests were carried out and 40% were found to have a reaction of 10 mm. or more. Three hundred twelve persons were found to be tuberculous, out of whom 66 were known cases and 246 were newly discovered. Out of 312 cases, 27 were found to be sputum positive, 207 abacillary and 78 cases had enlarged hilar and mediastinal glands without a parenchymal lesion.

SOCIOLOGICAL ASPECTS OF TUBERCULOSIS

D.R. NAGPAUL

(Paper being published in full)

TREATMENT TAKEN BEFORE REPORTING AT A TUBERCULOSIS CLINIC

P. SAXENA

(paper being published in full)

University in 1960. He worked with International TB Campaign teams from 1949 to 1956 and served as TB Officer with Government of India, Ministry of Health, in 1957-58. He was appointed Director, TB Demonstration and Training Centre, Agra in 1962 and in 1977 he was designated as Director-Professor, Chest Institute and TB Demonstration and Training Centre, Agra, which post he held till he retired in 1984.



Dr. Mehrotra is one of our senior-most specialists in Tuberculosis and Chest Diseases. He was largely responsible for the development of the Chest Institute and TB Demonstration and Training Centre, Agra into one of the premier diagnostic, treatment and training centres for TB in the country. He received the Wander-TAI Oration Award in 1975 and the Dr. Om Prakash Memorial Oration of the All India Medical Sciences, New Delhi, in 1977. He was Chairman of the *Dr. M. L. Mehrotra* Technical Committee and President of the 24th National Conference on TB and Chest Diseases held at Jaipur in 1979. He is at present a member of the Technical Committee of the Tuberculosis Association of India and Corresponding Member of the International Union Against Tuberculosis's Scientific Committee on 'Treatment'. He has attended almost all our National Conferences and several World Conferences on Tuberculosis and Chest Diseases and has presented more than 80 papers on Tuberculosis and allied diseases at these Conferences.

In recognition of the meritorious services rendered in the field of Tuberculosis, the Tuberculosis Association of India has decided to award its Gold Medal to Dr. Mehrotra.

Road, New Delhi-1. The meeting was presided over by Slut S. Ranganathan. ICS (Read.), President of the Association and it was followed by a meeting of the Central Committee of the Association.

The Conference of Secretaries of Stat+; TB Associations was held at 10.00 A.M. on Tuesday, the 31st April, 1987.

The Research Committee and the Technical Committee of the Association met on Monday, the 20th April, 1987 at 9.00 A.M. and 10.30 A.M. respectively.

CHAIRMAN, TECHNICAL COMMITTEE

Dr. P.A. Deshmukh, Professor of Tuberculosis and Chest Diseases, M.G.M. Medical College, Chest physician, Taut Main Hospital and Superintendent, Ardeshir Dalal Memorial Hospital, Jamshedpur, has been nominated as Chairman of the Standing Technical Committee of the TB Association of India for 1987-88 vice Dr. S.P. Gupta, whose term of office expired with the 41st National Conference held in Hyderabad in October 1986. Dr. Deshmukh will also preside over the 42nd National Conference on TB & Chest Disease, to be held in Lucknow from 2nd to 5th December, 1987.

42nd NATIONAL CONFERENCE

The 42nd National Conference on Tuberculosis and Chest Diseases will be held Lucknow (U.P.) from 2nd to 5th December, 1987. The tentative subjects proposed for discussion at this Conference are

1. Strategy to reduce the TB problem by the year 1995.
2. Influence of environment on Chest Diseases
3. Sequelae of a treated ease of pulmonary tuberculosis
4. Interaction between tuberculosis and properly.

tuberculosis, non-tuberculosis chest diseases/ extra-pulmonary tuberculosis will be eligible for presentation at the Conference. Those who wish to attend the Conference and present papers at its scientific sessions may kindly send two copies of the abstracts of their papers to reach the Secretary-General, TB Association of India, 3, Red Cross Road, New Delhi-110001, by 30th May, 1987.

CHANCHAL SINGH MEMORIAL AWARD -1987.

The Tuberculosis Association of India will award a cash prize of Rs. 1,000/- to a medical graduate (non-medical scientists working as bacteriologists, biochemists, etc. in a Tuberculosis/Chest Diseases Institution will be eligible) below 45 years of age and working in tuberculosis, for an original article not exceeding 30 double-spaced foolscap typed pages (approximately 6,000 words) excluding charts and diagrams on a subject relating to TB. Articles or papers already published' Or based on work of more than one author will not be considered for this award. Papers may be sent, in quadruplicate, to reach the Secretary General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-1 10 001, before 31st July, 1987.

ESSAY COMPETITION-1987

The Tuberculosis Association of India awards every year a cash prize of Rs. 500/to a final year medical student in India for an original essay on Tuberculosis, adjudged best by a special Committee of the Association. The subject selected for the 1987 competition is 'Anti-tuberculosis drugs--their action, dosage, adverse reactions, etc.'. The essay should be written in English typed in foolscap page, double spaced and should not exceed 15 pages (approximately 3,000 words excluding tables, diagrams, etc.). Four copies of the manuscript should be through the Dean of Principal of College University' to reach the Secretary-General. TB Association India 3, Red Cross Road, New Delhi-1 10 001, before 31st July, 1987.

Honorary Technical Adviser, Tuberculosis Association of India.

The Conference was attended by about 300 persons including practically all the DTOs of the State and a large number of para-medical workers. Prof. M.S. Agnihotri delivered the Robert Koch's Discovery of TB Centenary Oration on 'Bronchial Asthma'. A number of scientific papers on short-course chemotherapy, District Tuberculosis Programme and non-tuberculosis chest diseases were presented. A paper was presented on 'Tuberculosis Amongst Animals'.

A special session attended by the Additional Director, Joint Director incharge of Tuberculosis, the District Tuberculosis Officers and Dr. S.P. Pamra was organised in connection with the health education programme in the State.

MAHARASHTRA STATE CONFERENCE

The 23rd Maharashtra State TB and Chest Diseases Workers' Conference was held on 7th and 8th February, 1987 at Nagpur. The conference was inaugurated by Miss Saroj Khaparde, Minister of state for health and family welfare and it was presided over by Dr. H. V. Bahulkar, Hon. Prof. & Head. Deptt. Of TB & Respiratory Disease, B. J. Medical College Pune. The Scientific Sessions which was inaugurated by Dr. B. S. Choube, Deane Medical College, Nagpur, Included the Dr. B. B. Yodh memorial oration by Dr. P. A. Deshmukh and a Guest Lecture by Dr. A. G. Patel on Urban, tuberculosis Programme in Ahmedabad; Present status of chemotherapy Short-course Chemotherapy Trial Extra- Pulmonary Tuberculosis, Continued Medical Education etc. These was also a workshop on National Tuberculosis Programme.

PROJECT OF TUBERCULOSIS CONTROL IN CAR NICOBAR

The Project was inaugurated by the Government of India in September 1986 with financial assistance from WHO and technical

home with newer drugs for 6-9 months. Tuberculin testing of all children from village to village has been undertaken. BCG vaccination to new horns has been introduced as a routine measure. Chemoprophylaxis with INH is being given to all the healthy children by house to house administration.

Every village is divided into 4-5 sectors. Houses in each sector are numbered and placed under surveillance of a tribal volunteer selected by the village captains. The volunteers educate the population, administer INH tablets daily to children for chemoprophylaxis and supervise the treatment of patients. A small TB Hospital and a mini Distt. TB programme will be introduced to continue the activity.

Prior to the implementation of the Project, only 2-3 cases were being diagnosed every month in Car Nicobar. During the three months period after the implementation of the project, in nine out of the 16 villages, 75 new tuberculosis patients have been identified and they are continuing regular treatment.

REFRESHES COURSES

Bihar : The Muzaffarpur branch of the Indian Medical Association organised under the auspices of the Tuberculosis Association of India, a refresher course at Muzaffarpur on 14th December, 1986. The course was attended by 96 doctors and was sponsored by M/s Lupin Laboratories Private Limited, Bombay

Maharashtra : The Maharashtra state Anti-TB Association organised under the auspices of the Tuberculosis Association of India, a refresher course at Khed (District Ratnagiri) on 4th January, 1987. The course was attended by 75 doctors and was sponsored by the National Academy of Medical Sciences.

Tamil Nadu : The Coimbatore District Tuberculosis Association organised under the joint auspices of the Tuberculosis Association of India and the Anti-TB Association of Tamil Nadu, a refresher course at Coimbatore on 18th January, 1987. The course was inaugurated

Magistrate and President, District TB Association, Srirakulam About 75 doctors from private and Government institutions attended this course.

Meghalaya The Tuberculosis Association of Meghalaya organised under the auspices of the Tuberculosis Association of India, a refresher course at Shillong on 14th February, 1987. The course was attended by 135 doctors and it was sponsored by the National Academy of Medical Sciences.

HEALTH CHECK-UP CAMP IN ANDHRA PRADESH

A free General Health Check-up Camp was organised under the auspices of the Cosmopolitan Employees' Cultural Association, Hyderabad, at Saheb Nagar, Vanasthalipuram on 8th November, 1986. Dr. P.L. Sanjeeva Reddy, [AS, Principal Secretary to Govt., Medical & Health Department, Andhra Pradesh, inaugurated the Camp which was presided over by Shri G. Sudhir, IAS, Collector and District Magistrate and President, District TB Association, Ranga Reddy District. A total of 1,100 persons attended the Camp. Out of the 32 sputums examined, 6 were found sputum positive.

TB WEEK -- MAHARASHTRA

The Maharashtra state Anti-TB Association celebrated TB Week from 16th to 23rd February, 1987, in collaboration with the Western Railway Tuberculosis Association and the Lions Club of Tardeo. Lt.-Col. Potdar, Divisional Railway Manager, Western Railway, inaugurated the Week and Lion Suresh Mehta, past District Governor, was the Chief Guest. During the Week, 5 case-finding Camps were organised. 596 persons were examined out of whom 19 were found X-ray positives- Over

The Tuberculosis Association of Pondicherry has now moved into its own building which was inaugurated by the Hon' ble Thiru M.O.11. Farook, Chief Minister of Pondicherry, on 7th February, 1987. Thiru P. Khanna, Health Minister presided over the function. On this occasion the 37th TB Seal Campaign was also inaugurated by Thiru V. Vaithilingam, Public Works Minister, Pondicherry. Thiru L. Joseph Mariadoss, Minister for Cooperation, distributed cloties to poor TB patients. Thiru R. Vaithyanathan, M.L.A., graced this function.

AWARDS FOR OUTSTANDING RESEARCH

The Ranbaxy Research Foundation invites nominations for two annual awards of Rs. 50,000/- each for outstanding research work in medical and pharmaceutical sciences.

Indian nationals resident in India or abroad, who have not already received a major award for a particular research work will be eligible for sponsorship by heads of institutions such as universities, medical and pharmacy colleges, civil and military health services and state level education and research centres, among others. Nominations for the Awards can be sponsored only by the Heads of the institutions and should reach the Trustee, Ranbaxy Research Foundation, 19, Nehru Place, New Delhi-110019 by 31st May, 1987.

There is no special Nomination Form for the purpose. However, nomination papers should include eight copies each of Bio-data List of Publications/Research Papers, Statement of Research, Achievements already rewarded. Details of Research Work for claiming Award and Five sets of relevant **Publications/ research Papers.**

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