

# The Indian Journal of Tuberculosis

---

Vol. XXI

New Delhi, April 1974

No. 2

---

## THE MADRAS CONFERENCE

The Twenty-eighth National Conference on Tuberculosis and Chest Diseases was held at Madras for four days from the 5th of January this year. This was a joint one with the 14th Conference of the Indian Association for Chest Diseases.

Readers will recall that the Association had accepted the invitation of the Madhya Pradesh State TB Association to hold the Conference at Bhopal in November 1973. That Association, however, intimated six weeks before the scheduled dates for the conference that they would not be able to hold the Conference. The Association was reluctant to forego an annual meet of TB workers at the national level and disappoint the hundreds of delegates who were preparing to attend it. Therefore the Tamil Nadu and Maharashtra Associations were requested to come to its rescue. Fortunately, both agreed. However, as Tamil Nadu had hosted a conference fifteen years ago and Maharashtra had one five years ago the Association preferred to have the Conference in Tamil Nadu.

Hosting a National Conference is not an easy undertaking and to do so within a short period of six to eight weeks is definitely difficult. Still, the Hon'ble Health Minister of Tamil Nadu, Prof. K. Anbazhagan, who is Chairman of the State Association undertook to shoulder the responsibility. Under his leadership and with the cooperation of Shri H.M. Singh, the State Health Secretary, Dr. P.R. Balakrishnan, the Director of Health Services, Dr. Sudersan Lal, State TB Officer and others, the official and non-official machinery in Tamil Nadu was set in motion with full speed and the joint conference was successfully held from the 5th to 8th January, 1974 in Madras.

A day prior to the inauguration of the National Conference, the State Government called a Conference of District TB Officers and ancillary workers of Tamil Nadu. Prof. K. Anbazhagan and Dr. P.R. Balakrishnan addressed this meeting. Apart from discussing the working of the control programme this meeting helped TB workers at District and peripheral levels to participate in the National Conference.

The Conference was inaugurated in the Senate House, Madras. Delegates who numbered over 400 from different parts of India were warmly welcomed by Prof. K. Anbazhagan. Shri K.K. Shah, Governor of Tamil Nadu, inaugurated the Conference. The Governor awarded the T.A.I. Gold Medal to Major (Dr.) Khushdeva Singh of Patiala, the T.A.I. Cash Award to Dr. K.G.

Kulkarni and the prize meant for a Medical Student to Shri Ganapathy. The Wander-TAI Oration was given by Dr. R.N. Tandon.

Dr. S.P. Pamra, President of the TB Conference, made a critical appraisal of the National Control Programme and made certain concrete suggestions for improving its performance. Dr. Hans Kumar, President of the Chest Physicians Association, dealt with the development of surgical treatment of pulmonary tuberculosis.

The Scientific Sessions were held in the University Lecture Hall. The programme included two symposia on 'National TB Control Programme' and 'Sarcoidosis' and a panel discussion on 'Smoking and Health'. Paper on 'Chemotherapy', 'TB Meningitis', 'Relapse in Pulmonary Tuberculosis' and on many other aspects of Tuberculosis and other diseases of Chest were also presented.

Delegates showed keen interest in the deliberations of the Conference and all the sessions were well attended. Drs. P.K. Sen and K.V. Krishnaswami were unanimously elected as representatives of the Conference on the Central Committee. On the concluding day at the plenary session, Dr. R. Viswanathan, Emeritus Scientist, moved and the Conference unanimously adopted resolutions emphasising the need for a Second National Sample Survey, requesting Government to appoint a high-powered committee of eminent Tuberculosis experts, to review the working of the National Control Programme and emphasising that the Government of India should introduce legislation against smoking of tobacco.

The Technical Committee met after the Conference and reviewed the Conference proceedings. It endorsed the resolutions passed at the plenary sessions.

On behalf of the delegates and the Association we record our profound thanks to Prof. K. Anbazhagan and his officials for the excellent arrangements made for the Conference. We record our appreciation of the tireless efforts put in by Dr. P.R. Balkrishnan, Director of Health Services, Dr. K.V. Krishnaswami, Dr. (Mrs.) Krishnaswami, Dr. S.K. Sudersan Lal, Thiru A. Gopala Padayatchi and others to see that the delegates were looked after properly. By all standards, the Madras Conference was a great success.

Readers will recall that from last year the Association brings out the April issue of the Indian Journal of Tuberculosis as the Special Conference Number. This Number carries the summaries of all available papers presented at the conference and full texts of such papers as the Editorial Board considers to be of special interest. Others, if selected, will be published in the subsequent issues of the Journal.

### **LETTERS TO THE EDITOR**

**The Indian Journal of Tuberculosis is starting this new feature. Readers are welcome to send their comments, observation etc. on papers published in the Journal in the form of 'Letters to the Editor'. Letters must be brief and pertinent.**

## AWARD OF TAI GOLD MEDAL



Major (Dr.) Khushdeva Singh

The Tuberculosis Association of India has decided that the 1973 Gold Medal be awarded to Dr. Khushdeva Singh.

Dr. Khushdeva Singh is a veteran in the TB field. Born at Patiala in 1902, he passed his M.B.B.S. in 1926 from King Edward Medical College, Lahore. He joined the Patiala Medical Service and served as District Medical Officer, Epidemic Controller and for some time as member of the Personal Staff of the Maharaja of Patiala. He took keen interest in tuberculosis work and took his T.D.D. He was awarded the "Dr. B.S. Schriff Memorial Gold Medal" for his thesis on Tuberculosis. He worked as Medical Superintendent of the Hardinge Sanatorium, Dharampore and later as Medical Superintendent of the TB Centre, Patiala. He was Honorary Secretary of the Patiala TB Association and later of the PEPSU Association. He was TB Adviser to the Government of PEPSU. After the reorganisation of States he worked as Honorary Secretary of the Punjab Association. In 1950 he was awarded the Norwegian Fellowship under which he travelled in Europe studying anti-TB work. He is an Emeritus Fellow of the American College of Chest Physicians. He was awarded "Padma Shri" by the President of India in 1957. He has been a member of the Tuberculosis Association of India since its inception. He was a member of the Standing Technical Committee and as its Chairman he presided over the 22nd National Conference and Chest Diseases held at Hyderabad in 1967. In recognition of his services to the anti-TB movement, the Tuberculosis Association of India decided to award its Gold Medal to him.

# BACTERIOLOGICAL STUDY OF TUBERCULOSIS LYMPHADENITIS

K.G. KULKARNI

(From Organised Home Treatment Clinic, Bombay)

## Introduction

Tuberculosis of lymph nodes in neck, axilla and groin is known since the 5th century. This disease is widely prevalent in our country.

Today, the diagnosis of tuberculosis lymphadenitis is mostly based upon the clinical impression on examination of a patient. Whenever there are facilities for biopsy, diagnosis is based upon histopathological evidence rather than demonstration of causative organisms on the assumption that *M. tuberculosis* produces a specific reaction in human tissues. Mycobacteria other than *M. tuberculosis* give rise to histopathologic reactions like those given by *M. tuberculosis*. It is possible that some other agents also may give similar reaction. Under such circumstances it is necessary to isolate and identify the causative agent for the proper management of such cases. There are shortcomings and deficiencies for each technique especially because of problems of proper selection and method of collection of specimen, collection of specimen before patient had extensive therapy and the technique of handling the specimen for histopathology or bacteriological examination itself.

In India, the infection with tubercle bacilli of human type is still widespread. There is also a high prevalence of non-specific skin sensitivity to tuberculin associated with infections by atypical mycobacteria. With such epidemiological background bacteriological study of tuberculous lymphadenitis seems to be of significance.

## Review of Literature

### *Age & Sex*

Thompson (1940) studied 224 patients from Clare Hall Sanatorium during 1934 to 1936. He observed that the great majority of cases occurred between ages of 5 to 14 years and that females outnumbered the male patients.

Siddiqui (1949) in a study of 140 patients of lymphadenitis during 1945-46, observed high prevalence in age groups 6 to 15 and 16 to 25 years and in females.

Jones (1951) in a study of 51 Nigerian Africans of tuberculous lymphadenitis observed that the prevalence was about 53 percent in children of the age of 0—14 years. In his study the prevalence was higher in males than in females.

German, Black and Chapman (1956) in a study of 47 veterans suffering from tuberculous adenitis observed 50 percent cases in the age group of 20 to 29 and the rest in the higher age groups.

Wilmot, James and Reilly (1957) in a study of 81 patients of tuberculous cervical adenitis observed that 54 percent of patients were under the age of 15 years.

Schless and Weir (1957) in a study of 120 cases of TB lymphadenitis observed that about 75 percent of cases were in the age group of 21 to 30 years and that 85 percent were males.

It can be concluded from the above observations that tuberculous adenitis which was a disease of childhood during early years of the century, a shift in the recent years and has now shown more and more cases are seen in young adults. Regarding the prevalence in males and females there are conflicting reports.

### *Sites of lymphnodes involved :*

Miller (1934) in a series of 536 cases of tuberculous lymphadenitis observed 25 cases of axillary and 6 cases of inguinal tuberculosis lymphadenitis.

Thompson (1940) during 1934 to 1936 observed 29 cases of axillary adenitis and 11 of inguinal adenitis. Axillary lymphnodes were presenting symptoms in 12 of these 29 cases and inguinal disease was presenting symptom in 4 of 11 cases.

Isolated cases of inguinal adenitis of tuberculous origin have been reported by Ramond (1936) and Tisseuil (1946) and two cases of axillary adenitis by Hudgins (1943). Hinden, Nardell and Anabtawi (1951) reported 2 cases of axillary adenitis and 3 others of inguinal adenitis.

Jones (1951) in a study of tuberculous adenitis in Nigerian Africans observed 7 cases

---

\*This work was carried out at Madanapalle Tuberculosis Research Unit (A.P.) India.

of axillary and 3 of inguinal adenitis of primary nature.

German, Black and Chapman (1956) in a series of 47 cases of tuberculous lymphadenitis observed only 2 cases of primary involvement of inguinal lymph nodes.

Lester and Jones (1956) in a study of 66 cases of tuberculous lymphadenitis reported only one case of isolated inguinal lymphadenitis.

Schless and Weir (1957) observed 8 cases of axillary adenitis in a series of 120 cases of tuberculous lymphadenitis they studied.

Miller and Cashman (1958) in a study of 163 cases of tuberculous adenitis observed 4 cases of primary axillary adenitis and 15 cases of primary inguinal lymphadenitis. The number of cases with inguinal lymphadenitis was exceptionally high in their series.

Doctor (1964) from India reported very low incidence of tuberculous involvement of inguinal lymph nodes.

In summary, it can be said that axillary and inguinal lymph nodes are involved in a tuberculous process though quite infrequently in a large series of patients with lymphadenitis.

*Diagnosis :*

The definite proof of diagnosis of tuber-

culosis is mainly by demonstrations of mycobacteria by microscopy and or culture of the material removed by lymph node biopsy or demonstration of acid fast bacilli in the stained preparation of tissue section and by histopathological examination of the tissue section of the biopsy specimen of the lymph node.

*Demonstration of mycobacteria :* On reviewing the literature it is observed that there are three distinct phases as far as the type of the causative agent responsible for the lymphadenitis is concerned.

In the first phase, the bovine strain of *Mycobacterium tuberculosis* appeared to be responsible for majority of tuberculous lymphadenitis in Western countries, especially in children below the age of 15 years. Mitchell (1917) from Edinburgh, observed that 88 percent of cases of adenitis in children were due to bovine bacillus and he could demonstrate tubercle bacilli in 20 percent of the samples of local milk supply. Griffith (1937) found that tubercle bacilli isolated from patients with cervical adenitis were bovine type in about 50 percent of cases both in England and Scotland.

Paul F. de'Gara (1942) on reviewing the literature for incidence of bovine tuberculosis in cervical lymph node lesions in various countries made the following observations:

Country	Total Examined	Percentage of bovine tubercle bacilli
Scotland	93	51.6%
England	126	50.0%
Denmark	251	49.0%
Switzerland	8	37.5%
Germany	94	22.3%
Spain	18	16.6%
Hungary	64	6.2%
Italy	27	3.7%
Greece	70	0.0%
Poland	8	0.0%

The higher incidence in first few countries was probably due, at least in part, to the large amount of milk or milk products consumed. The author observed that of the 21 strains he isolated from lymphadenitis specimens, 5 or 23.8 percent were of bovine type.

Boyd (1944) observed that bacilli were usually of bovine type in case of lymphadenitis in children. Wissler (1954) reported that 80 percent of cases of cervical adenitis in Swiss children were caused by bovine bacillus but he provided very little bacteriological evidence for this statement.

In New York, Park (1910) reported 34 percent of all cases and 54 per cent in children of bovine type. Park and Krumwiede (1910) typed the infection in 54 cases of cervical adenitis. One third of these were of bovine type. The percentage of bovine infection of lymph nodes in New York city fell from 30 per cent to 16.6 per cent because of general adoption of pasteurisation of milk. There was a remarkable reduction in USA as a whole because of this measure and because of eradication of tuberculosis in cattle. Thus in USA as early as in 1910 cases of lymphadenitis due to human type of tubercle bacilli predominated except in children in the age group of less than 5 years. The reduction in incidence of bovine tuberculosis was observed at later stage in England.

Bovine infection is not responsible for

“human” type of *M. tuberculosis* and Lester (1951), Rich (1951) and members of American Trudeau Society’s Committee on therapy (1954) as well as Wilmot and associates (1957) were of the opinion that there was little reason to think that tuberculosis of cervical lymph nodes was frequently caused by infection with tubercle bacilli of bovine type and that the human type of tubercle bacillus was responsible for almost all cases of lymph node tuberculosis.

The third phase has mainly begun in USA where the disease caused by human tubercle bacilli is well under control and this phase may be termed as an era of “Unclassified Mycobacteria”. There are, nowadays, many reports of cervical lymph adenitis caused by mycobacteria other than *M. tuberculosis* (Weed and associates 1956, Prissick and Masson, 1956 and Chapman and Guy, 1959).

Davis and Comstock (1961) reported that in a community of south eastern United States, 70 per cent of cases of granulomatous cervical lymphadenitis in children were not caused by *M. tuberculosis* but by atypical mycobacteria.

Sinclair and Mittal (1972) from All India Institute of Medical Sciences, New Delhi, in a study of 31 strains of atypical mycobacteria isolated from various sources, observed two cases of cervical adenitis caused by such strains

The relative figures of isolation of atypical and tubercle bacilli reported by various authors are as follows:

Authors, year and country	Total Number of cultures done	Number of Positive cultures	Number of atypical mycobacterial strains
Jones & Campbell 1962 — Australia	76	27	15
Marsden & Hyde 1962 - England	91	11	10
Dajani & others 1963 - U.S.A.	34	2	1
Black & Chapman 1964 - U.S.A.	29	20	13
MacKellar & others 1967 — Australia	26	13	11
Reid & Wolinsky 1969 — U.S.A.	36	30	30
Kulkarni & Frimodt Moller 1969 — India	190	104	1

Scrofula in India where milk is generally boiled before consumption.

In the second phase the main agent responsible for this disease was thought to be the

The increased incidence of isolation of “Unclassified Mycobacteria” may be because of the fact that infection by *M. tuberculosis* has diminished a good deal in these countries, and so it has been possible to get more and

more cases of disease caused by unclassified mycobacteria. Davis and Comstock (1961) observed that as the infection with *M. tuberculosis* continues to diminish there will be increase in proportion of cases of chronic cervical adenitis-caused by "Unclassified Mycobacteria."

*Histopathology:* Diagnosis of tuberculosis is many a time based on histopathological evidence rather than on demonstration of causative organisms. This is because of the firm belief that *M. tuberculosis* produces specific changes in the human tissue. It may be possible to differentiate the granuloma of tuberculous nature from the granuloma caused by mycobacteria, but it will not be possible to differentiate the type of mycobacteria responsible for the tuberculous type of histopathological changes.

Jones (1968) laid down certain histopathological diagnostic features of tissue changes caused by atypical mycobacteria but many other workers like Nassau and Hamilton (1957), Marsden and Hyde (1962), Corpe and Stergus (1963), Reid and Wolinsky (1969) and Rajvanshi and Tyagi (1970) observed that the histopathological features of atypical mycobacterial lymphadenitis were not sufficiently characteristic to enable the separation of this disease from that caused by *M. tuberculosis* of human or bovine type.

This differentiation can be obtained only by isolation and identification of mycobacteria from the diseased lymph nodes removed at operation from patients diagnosed as suffering from tuberculous lymphadenitis. This procedure is also desirable for proper treatment of the patients suffering from such disease.

McDonald and Weed (1951) observed that because of some of the shortcomings of the histologic diagnosis of tuberculosis the cases diagnosed as Hodgkin's disease or chronic non-specific adenitis may prove to be tuberculous in nature on bacteriological examination and similar cases suspected to be tuberculous on histopathological examination may turn out to have been caused by micro-organisms other than mycobacteria.

### Material and Methods

The study was set up at Madanapalle Tuberculosis Research Unit in the year 1964 first in collaboration with various Mission Hospitals in South India as an attempt to isolate mycobacterial strains from biopsy specimens of lymph nodes from clinically

diagnosed cases of tuberculous lymphadenitis. Subsequently the scope of study was widened in collaboration with the Norman Institute of Pathology, Christian Medical College and Hospital, Vellore (1969), Indian Council of Medical Research (Co-operative study of Cervical Lymphadenitis) during 1969-1970, and Institute of Child Health and Hospital for Children, Madras, between 1965 and 1970. The additional feature of the extended study was that histopathological studies were carried out at Norman Institute of Pathology, Christian Medical College and Hospital, Vellore, at various participating centres in the I.C.M.R. study and at the Institute of Child Health and Hospital for Children, Madras, on the specimens, parts of which were sent to Madanapalle for bacteriological study.

The histopathological examinations and the bacteriological studies were done quite independently of each other and the persons concerned had no knowledge of the results of the other examination. Thus, the bias was completely excluded.

### Collection of Specimen

The biopsy specimen of lymph node for the bacteriological study was transferred aseptically to a sterile Universal container supplied by the Research Laboratory at Madanapalle. The aluminium screw cap was screwed on the bottle tightly. The container was then put in a cardboard box which was dispatched by post to Madanapalle. (The specimen was refrigerated if there was any delay in dispatching it).

### Procedure at the Research Laboratory

*Grinding:* The biopsy specimen was transferred to a sterile mortar and cut into small pieces and caseous material if present squeezed out. Then the specimen was ground with the help of a sterile pestle as thoroughly as possible. Following this, sterile distilled water was added to the mortar and suspension made. The suspension was allowed to stand and then supernate was transferred to a sterile universal container.

*Microscopy:* A smear was made on a fresh glass slide by transferring a loopful of the suspension and spreading it uniformly over it. The smear was stained by a fluorescent stain, auramine phenol and examined by fluorescence microscopy. The results of microscopy were reported as positive when acid fast bacilli (AFB) were seen and negative when AFB were not seen on a thorough search.

Most of the positive smears contained few AFB in countable number in the whole smear and hence no attempt was made to grade the smears.

**Culture :** To the suspension equal volume of sterile 4 percent sodium hydroxide was added and the container was shaken by hand to assure thorough homogenisation. Then it was incubated at 37° C for 20 minutes. Following this, the specimen was centrifuged at 4000 rpm for 20 minutes in MSE Supermultex Centrifuge. The supernate was discarded and the sediment was neutralised with sterile 8 percent hydrochloric acid and the neutralised sediment was inoculated on four slopes of Lowenstein Jensen medium. The inoculated slopes were incubated for a period of 8 weeks—these being examined every week for growth of mycobacteria.

Whenever the growth of mycobacteria was observed the number of colonies on each slope was counted and noted down. The culture bottles which did not show any growth for a period of 8 weeks were discarded and reported as negative. Similarly the slopes which were contaminated were reported accordingly and discarded.

A bacillary suspension was made for the growth of mycobacteria on primary culture and was examined by microscopy to confirm that AFB were seen.

**Drug sensitivity test :** Drug sensitivity tests for streptomycin, PAS, Isoniazid and Thiacetazone were performed routinely on all cultures by the procedure adopted by Medical Research Council (M.R.C.) of Great Britain. The drug concentrations used were as follows:—

Drug	Mcg/ml of medium			
Streptomycin	0	8	16	32
PAS	0	2	4	8
Isoniazid	0	0.2	1	5
Thiacetazone	0	2	1	8

The definitions of M.R.C. were followed to definite a strain either as 'sensitive', 'doubtfully resistant' or 'resistant' to a particular drug.

**Identification tests :** All primary cultures were routinely subjected to following identification tests :

- 1) *Incubation at different temperatures :*

100 fold dilution of the bacillary suspension used for the drug sensitivity test was inoculated on 3 slopes of Lowenstein Jensen medium and one slope was incubated at 45° C, second at 22°C and third at 37°C in darkness, this being placed in a cardboard container.

- 2) *Photochronogenicity test :* The slope incubated at 37°C in darkness was examined at the end of 4 weeks' incubation for pigmentation of the growth. If there was no pigmentation the growth was exposed to daylight for one day after loosening the screw cap a little and the pigment production if any was noted.

- 3) *Cattle test :* Catalase test was performed on a four week old growth by pouring the mixture of 10 percent between 80 and 10 percent of hydrogen peroxide solution and noting the evolution of bubbles.

- 4) *Niacin test :* Niacin test was performed on a 4-week old sub-culture by extracting niacin by autoclaving the subcultures.

The niacin negative strains were subjected to some more identification tests like:

- 1) Butt Catalase test
- 2) Catalase test at 68°C in pH<sub>7</sub> Phosphate buffer
- 3) Nitrate reduction test
- 4) Tween 80 hydrolysis test
- 5) Aryl sulphatase test
- 6) Production of opacity in Tween 80 agar medium.

## Results

A total of 879 Lymph node specimens—758 from cervical region, 84 from axillary region and 37 from inguinal region were examined in the laboratory for demonstration of Mycobacteria. Of these 28 specimens from cervical region and 4 from inguinal region have been excluded from present analysis because either there was no detailed information regarding the specimens (22) or the specimens were duplicates (10), leaving 730 specimens from cervical region, 84 from axillary region and 33 from inguinal region for the present analysis. Histopathology results were available for 566 specimens of which 477 were from cervical, 66 from axillary and 23 from inguinal region.

The specimens belonging to different studies are shown in table 1.

Total specimens analysed here are 847. The

TABLE 1

*Total specimens analysed according to the centre of study*

Participating centre	Cervical	Axillary	Inguinal	Total
Mission Hospitals (MTRU)	219 (Nil)	18 (Nil)	10 (Nil)	247 (Nil)
CMCH, Vellore	180 (180)	58 (58)	19 (19)	257 (257)
ICMR Study	286 (265)	—	—	286 (265)
ICH— Madras	45 (32)	8 (8)	4 (4)	57 (44)
Total	730 (477)	84 (66)	33 (23)	847 (566)

(Figures in brackets indicate specimens with histopathology results).

TABLE 2

*Distribution of patients according to sex in broad age groups*

Age groups (in years)	Males		Females		Total	
	No	Percent	No	Percent	No	Percent
0 — 14	145 (41)	58	105 (16)	42	250 (47)	100
15 — 29	129	36	230	64	359	100
30 — 44	67	43	88	57	155	100
45 +	41	57	31	43	72	100
Not mentioned	2	—	9	—	11	—
Total	384	45	463	55	847	100

(Figures in brackets indicate number of patients from Institute of Child Health and Hospital for Children, Madras).

microscopy and culture results were available for all of them and histopathology results for 566 of them.

*Sex and age* : The distribution of these patients according to their sex is shown in table 2.

It is seen that the females outnumbered males. Of 847 patients, 463 or 55 percent were females and 384 or 45 percent were males. The preponderance of females over males was much more marked in the age group of 15 to 29 years wherein of the total 359 patients 220 or 64 percent or 2/3rd were females and 129 or 36 percent or 1/3rd were males. Similarly in the age group 30 to 44 years also females predominated over males, they being 88 or

57 percent of 155 patients and the males 67 or 43 percent. The males predominated over females in the younger and in the older age groups. Thus of the total 250 patients in the 0 to 14 years age group 145 or 58 percent were males and 105 or 42 percent were females. This preponderance of males over females was very obvious in patients from the Children Hospital, Madras. Of the total 57 patients from here, 41 or 72 percent were males and only 16 or 28 percent were females. In the elderly age group i.e. the patients over 45 years of age, of the total 72 patients 41 or 57 percent were males and 31 or 43 percent females.

For considering the age distribution, the patients from the Institute of Child Health and Hospital for Children, Madras, have been

excluded since this was a selected group. The distributions of the remaining patients—males and females according to their age are shown in table 3. and Fig. 1.

It is observed from fig. 1 that the curve of frequency distribution for females shows a steep rise with a peak for the age group of 20 to 24 years and then a steep fall suggesting a modal distribution. The curve for the males shows a slow rise with peak for the age group of 20 to 24 years and then a steep fall, but it rises again showing tendency for bimodal distribution.

*Results of Bacteriological examinations :*  
These results are shown in table 4.

Of the total 847 specimens 359 or 42.5 per cent were positive bacteriologically, 68 or 8 per cent by both microscopy and culture per cent 270 or 32 per cent by culture only, and 21 or 2.5 per cent by microscopy only. The remaining 488 or 57.5 per cent specimens were negative by both.

On considering these results according to

site of lymph nodes affected, it was observed that of the 730 specimens from cervical region, 319 or 44 per cent were positive by microscopy and/or culture. Similarly 31 or 37 per cent of the 84 specimens from axillary region and 9 or 27 per cent of the 33 specimens from inguinal region were positive. Thus, the proportion of specimens yielding positive results was highest for the specimens from cervical region and lowest for those from the inguinal region.

The results of bacterial examination for specimens received from the different participating centres are shown in table 5.

Of the 247 specimens received in the M.T.R.U. study, 130 or 53 per cent were positive by culture and another 12 or 5 per cent by microscopy only. There were minor differences in frequency of positive results for the specimens from cervical, axillary and inguinal regions.

Of the 257 specimens received from C.M.C.H. Vellore, 96 or 37 per cent were positive by culture and another 6 or 2 per cent

TABLE 3

*Distribution of male and female patients according to age*

Age groups (in years)	MTRU, CMCH & ICMR studies				ICHM	
	Males		Females		Males	Females
	No.	Percent	No.	Percent		
0 — 4	26	7.6	12	2.8	18	5
5 — 9	40	11.7	33	7.4	14	6
10 — 14	38	11.0	44	9.8	9	5
15 — 19	45	13.1	70	15.6	—	—
20 — 24	48	14.0	84	18.8	—	—
25 — 29	36	10.4	76	17.0	—	—
30 — 34	26	7.6	46	10.2	—	—
35 — 39	14	4.1	20	4.5	—	—
40 — 44	27	7.9	22	4.9	—	—
45 — 49	9	2.7	14	3.1	—	—
50 —	32	9.3	17	3.8	—	—
Not mentioned	2	0.6	9	2.1	—	—
Total	343	100.0	447	100.0	41	16

FIGURE 1 (TABLE 3)

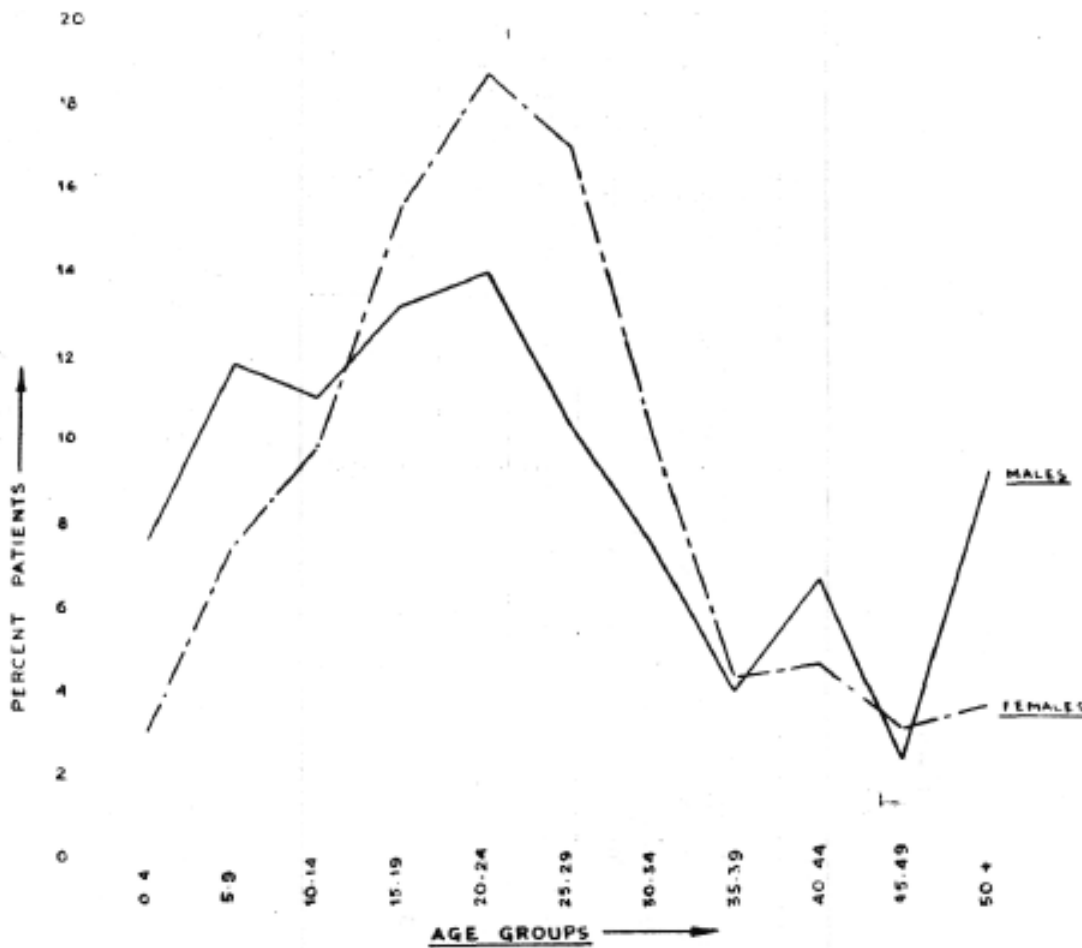


TABLE 4

Results of microscopy and culture for mycobacteria for all specimens according to the site of lymphnode biopsy

Results of Microscopy Culture	Site of lymph node biopsy						All No. Percent	
	Cervical		Axillary		Inguinal			
	No.	Percent	No.	Percent	No.	Percent	No.	Percent
+ +	60	8.2	8	9.5	—	—	68	8.0
— +	244	33.3	19	22.6	7	21.2	270	32.0
+ —	15	2.5	4	4.8	2	6.1	21	2.5
— —	411	56.0	53	63.1	24	72.7	488	57.5
Total	730	100.0	84	100.0	33	100.0	847	100.0

TABLE 5  
Bacteriology results for different participating centres

Participating Centre	Site of lymph node involvement																			
	Cervical			Axillary			Inguinal			All										
	Total Cult. No.	+ Micro. %	+ %	Total Cult. No.	+ Micro. %	+ %	Total Cult. No.	+ Micro. %	+ %	Total Cult. No.	+ Micro. %	+ %								
MTRU	219	54.0	8	3.7	18	9	50.0	3	16.7	10	3	—	1	—	247	130	52.8	12	4.9	
CMCH	180	78	43.0	4	2.2	58	15	26.0	1	1.7	19	3	15.8	1	5.3	257	96	37.4	6	2.3
ICMR	286	99	34.6	3	1.4	—	—	—	—	—	—	—	—	—	—	286	99	34.6	3	1.4
ICHM	45	9	20.0	—	—	8	3	—	—	—	4	1	—	—	—	57	13	22.8	—	—
TOTAL	730	304	41.5	15	2.5	84	27	32.1	4	4.8	33	7	21.2	2	6.1	847	338	40.0	21	2.5

Cult. + = Positive by culture  
Micro.+ = Positive by microscopy

by microscopy only: Here the yield of positive results was highest for the specimens from the cervical region and lowest for those from the inguinal region (43 per cent and 2 per cent as against 16 per cent and 5 per cent by culture and microscopy respectively).

All the 286 specimens in the I.C.M.R. study were from cervical region and 99 or 35 per cent of these were positive by culture and another 3 or 1 per cent by microscopy only.

Specimens from the Institute of Child Health and Hospital for Children, Madras, were from patients in the age group of 0 to 14 years and only 23 per cent of the total 57 were positive by culture.

Proportion of positive specimens was highest for those in the M.T.R.U. series and lowest for those from the Institute of Child Health and Hospital for Children, Madras.

#### **Histopathology and Bacteriology**

Results of histopathology examination were available for 566 specimens (257 C.M.C.H., 265 of 286 I.C.M.R. and 44 of 57 I.C.H.M. specimens). 341 or 60 per cent of these specimens showed changes suggestive of tuberculosis while the changes in others were suggestive of either chronic non-specific inflammation or new growth—benign or malignant including some of Hodgkin's disease.

The correlation between the results of histopathology and bacteriology examinations is shown in table 6.

Considering all the specimens together, it was observed that of the 341 specimens with histopathological changes suggestive of tuberculosis 196 or 58 per cent yielded positive results by bacteriology, 192 on culture and another 4 by microscopy only. On analysing these results centre-wise it was observed that there were differences in terms of yield of positive results among the centres.

Of the 128 specimens from C.M.C.H., Vellore, with histopathology results suggestive of tuberculosis, 97 or 76 per cent were positive, 95 by culture and another 2 by microscopy only. On splitting up the results according to the site of lymphnode involvement, it was observed that 80 or 78 per cent of the 102 specimens from cervical region, 14 or 67 per cent of the 21 specimens from axillary region and 3 of the 5 specimens from inguinal region were bacteriologically positive indicating that the specimens from cervical region yielded maximum number of positives.

Of the 193 specimens from I.C.M.R. study with histopathology results suggestive of tuberculosis, only 88 or 46 per cent were positive by bacteriology, 86 by culture and another 2 by microscopy only. All the specimens in the I.C.M.R. study were from cervical region.

Of the 20 specimens from I.C.H. Madras, with histopathology results suggestive of tuberculosis, 11 or 55 per cent were positive on bacteriological examination—all by culture.

Thus, in terms of yield of bacteriologically positive results in the specimens proved to be tuberculous on histopathology, it was observed that maximum number of positive results were from the specimens from C.M.C.H. Vellore, the specimens from I.C.H.M. were next in order the specimens from I.C.M.R. study giving the lowest number of positive results.

The difference between the bacteriological results of the histologically proved tuberculous lymphnode specimens from the two—C.M.C.H. and I.C.M.R. studies, appears to be of significance. (80 or 78 per cent of the 102 cervical lymphnode specimens from C.M.C.H., Vellore yielded positive results as against only 88 or 46 per cent of the 193 specimens from I.C.M.R. study).

Of the 281 specimens with no histopathology reports 152 or 54 per cent yielded positive results, 139 by culture and another 13 by microscopy only.

The histopathology results for 225 lymphnode specimens were indicative of non tuberculous diseases, 163 of chronic nonspecific adenitis and 62 of new growths (including lymphosarcoma, Hodgkin's disease and secondaries). 11 of these 225 specimens were positive bacteriologically, 7 by culture and another 4 by microscopy only. Of the 7 specimens which yielded growth of mycobacteria, 6 showed histopathological changes suggestive of chronic non-specific adenitis and one of new growth. Of the 4 specimens which were positive by microscopy only, 2 from cervical region showed histopathology results suggestive of anaplastic carcinoma and could be considered as false positives. The third was an axillary lymphnode. The smear obtained plenty of acid fast bacilli and the histopathology report was suggestive of leprosy. The fourth specimen was from inguinal region and the histopathology report was suggestive of chronic non-specific adenitis and this also could be a false positive.

TABLE 6  
Results of bacteriology in relation to results of histopathology

Centre	Histopathology Results	Bacteriology Results											
		Cervical		Axillary		Inguinal		All					
		No.	Positive %	No.	Positive %	No.	Positive %	No.	Positive %				
MTRU	No Histopathology	219	126(8)	58	18	12(3)	67	10	4(1)	40	247	142(12)	58
	Tuberculous Non Tuberculous	102 78	80(2) 2(2)	78 —	21 37	14 2(1)	67 —	5 14	3 1(1)	— —	128 129	97(2) 5(4)	76 —
ICMR	Tuberculous Non Tuberculous No Histopathology	193 72 21	88(2) 6 8(1)	46 — 38	— — —	— — —	— — —	— — —	— — —	— — —	193 72 21	88(2) 6 8(1)	46 — 38
	Tuberculous Non Tuberculous No Histopathology	14 18 13	7 — 2	50 — 15	4 4 —	3 — —	— — —	2 2 —	1 — —	— — —	20 24 13	11 — 2	55 — 15
ALL	Tuberculous Non Tuberculous No Histopathology	309 168 253	175(4) 8(2) 136(9)	57 — 54	25 41 18	17 2(1) 12(3)	68 — 67	7 16 10	4 1(1) 4(1)	— — —	341 225 281	196(4) 11(4) 152(13)	58 — 54

Figures in brackets indicate specimens positive by microscopy only.

*Age and Sex*

Relationship between the bacteriological positive results and age and sex of patients is shown in table 7 and Fig. 2.

Of the 384 males, 121 or 32 per cent were positive either by microscopy and/or culture while of the 463 females, 238 or 51 per cent were positive indicating that a higher proportion of bacteriologically positive results was seen among specimens collected from females than those from males. This difference between males and females was seen in all age groups (Fig. 2).

*Males:* On considering these findings in different age groups it was observed that 42 or 29 per cent of the total 145 specimens from patients in the age group of 0 to 14 years yielded positive results. This proportion of positive results was 54 or 42 per cent of the 129 specimens from patients in the age group of 15 to 29 years. In the latter age groups it was 18 or 27 per cent of 67 specimens and 6 or 15 per cent of 41 specimens respectively. Thus, the curve of frequency distribution of the positive results for specimens received from male patients showed rise and fall (Fig. 2).

*Females:* 40 or 42 per cent of the 105 specimen from patients in the age group of 0 to 14 years yielded positive results and the results were quite similar in the later age groups viz. 56 per cent, 52 per cent and 55 per cent of the 230, 88 and 31 specimens respectively

from patients in the age groups of 15 to 29, 30 to 44 and 45 years above being positive. Thus, after an initial rise, the proportion of specimens with positive result was constant for the later age groups (Fig. 2).

Relationship between the age and sex and the results of histopathology is shown in table 8 and Fig. 2. The histopathology results were available for specimens from 566 patients.

131 or 48 per cent of the 275 specimens from male patients showed histopathological changes consistent with tuberculosis as against 210 or 72 per cent of the 291 specimens from female patients, the proportion of positive results being significantly higher for females than that for males. This difference between the frequency distributions of histopathological changes suggestive of tuberculosis in males and females was seen in all the age groups.

*Males:* It was observed that 38 or 41 per cent of the 93 specimens from patients in the age group of 0 to 14 years showed tuberculous changes. This proportion of histopathologically positive results was 66 or 67 per cent of the 98 specimens from patients in the age group of 15 to 29 years, 19 or 38 per cent of 50 specimens from patients in the age group of 30 to 44 and 8 or 24 per cent of the 34 specimens from patients in the age group of 45 years and above (Fig. 2).

*Females:* 28 or 45 per cent of the 62 specimens from patients in the age group of

TABLE 7

*Relationship between age and sex and the bacteriological results*

Age Groups (in years)	Males			Females		
	Total †	Positives		Total	Positives	
		No.	Per cent		No.	Per cent
0—14	145*	42	29	105*	42	40
15—29	129	54	42	230	128	56
30—44	67	18	27	88	46	52
45— and above	41	6	15	31	17	55
Not mentioned	2	1	—	9	5	—
Total	384	121	32	463	238	51

†Including patients from I.G.H, Madras

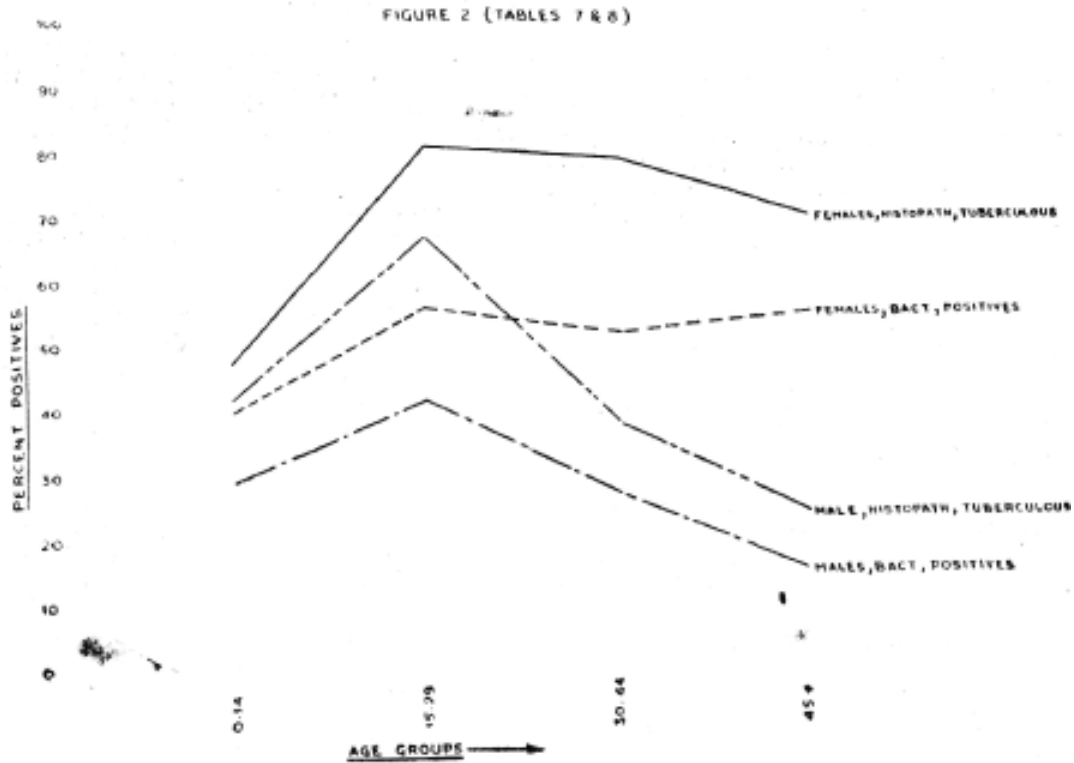


TABLE 8

*Relationship between age one sex and the Histopathological results*

Age Groups (in years)	Males			Females		
	Total	No.	Positives Percent	Total	No.	Positives Percent
0-14	93*	38	41	62*	28	45
15-29	98	66	67	144	117	81
30-44	50	19	38	61	48	79
45 and above	34	8	24	23	16	70
Not mentioned	-	—	—	1	1	—
Total	275	131	48	291	210	72

\*Including patients from ICH-Madras.

0 to 14 years showed tuberculous changes and then this proportion increased to 117 or 81 per cent of the 144 specimens from patients in the age group of 15 to 29 years, 48 or 70 per cent of the 61 specimens and 16 or 79 per cent of the 23 specimens from patients in the age group of 30 to 44 and 45 years and above respectively (Fig. 2).

The frequency distributions according to age and sex of all patients in the study, those showing positive results by bacteriology and those showing tuberculous changes on histopathology are shown in table 9 and Fig. 3. The patients in the age group of 0 to 14 years from I.C.H. Madras have been excluded from this analysis, since it formed a selected group of patients.

It is observed from Fig. 3 that the frequency distributions in different age groups were practically similar, for all patients, as well as for thQSe with bacteriologically and histopathologically positive results both in males and females. The maximum number of patients, seen in the ttge group of 15 to 29 years was; so also were the patients with results positive by bacteriology or by histopathology in that age group both in males and females. This observation suggests that the prevalence of tuberculous lymphadenitis is highest in the age group of 15 to 29 years of age, it being higher in females than in males.

*Bacteriological results in the groups of specimens with or without histopathology results*

In the subsequent analysis the results have

TABLE 9

*Frequency distribution of males and females according to age of all patients, those positive by bacteriology and those by histopathology*

Sex	Age Groups (in years)	All Patients		Positive by bacteriology		Total subjected to Histopathology		Positive by Hirtopathology	
		No.	Percent	No.	Per cent	No.	Per cent	No.	Per cent
MALES	0-14	104	30.3	35	30.7	64	26.0	26	21.8
	15-29	129	37.5	54	47.3	98	39.9	66	55.5
	30-44	67	19.6	18	15.8	50	20.3	19	16.0
	45 and above	41	12.0	6	5.31	34	13.8	7	7.7
	Age not mentioned	2	0.6	1	0.9	—	—	—	—
	Total	343	100.0	114	100.0	246	100.0	119	100.0
	I.C.H.—M 0-14	41	—	7	—	29	—	12	—
FEMALES	0-14	89	20.0	36	15.5	47	17.0	20	9.9
	15-29	230	51.4	128	55.0	144	52.2	117	57.9
	30-44	88	19.6	46	19.9	61	22.1	48	23.8
	45 and above	31	6.9	17	7.4	23	8.3	16	7.9
	Age not mentioned	9	2.1	5	2.2	1	0.4	1	0.5
	Total	447	100.0	232	100.0	276	100.0	202	100.0
	I.C.H.—M 0-14	16	—	6	—	15	—	8	—

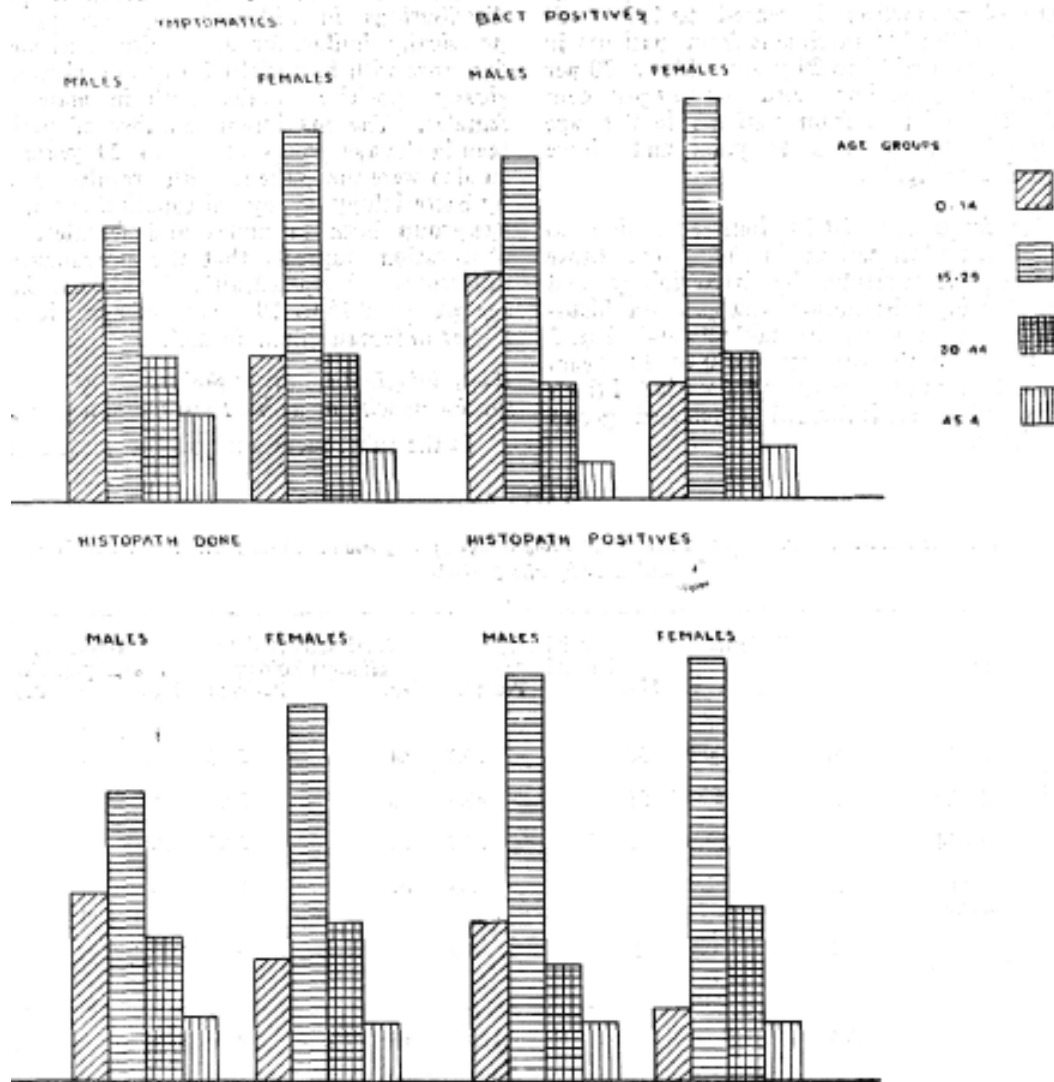


FIGURE 3 (TABLE 9)

been analysed separately for two major groups of specimens positive by microscopy only have been excluded from the figures of positive results.

The first group included the specimens with no histopathological results. There were in all 281 specimens—247 from M.T.R.U. study (219 cervical, 18 axillary and inguinal), 21 from I.C.M.R. study (all cervical) and 13 from the I.C.H. Madras (all cervical)

The second group included specimens, histopathological results of which were suggestive of tuberculosis. There were 341 such specimens, 128 from C.M.C.H. Vellore (102 cervical, 21 axillary and 5 inguinal), 193 from

I.C.M.R. study (all cervical) and 20 from the I.C.H. Madras (14 cervical, 4 axillary and 2 inguinal). In addition, 7 more specimens, the histopathological results of which were not tuberculous but the growth of mycobacterial strains was obtained (6 from I.C.M.R. study—all cervical—5 chronic adenitis, 1 malignancy and one from C.M.C.H. Vellore—axillary—chronic adenitis) have been included in this group. The specimens with histopathological results suggestive of changes other than tuberculosis have been excluded since there was no question of these specimens containing tubercle bacilli.

Table 10 shows relationship between the frequency of culture positive and the time (in

TABLE 10

*Frequency of culture positivity in relation to time required to receive the specimens*

No. of Days	Group I			Group II		
	Total	No.	Percent	Total	No.	Percent
4 or less	101	59	59	183	133	72
5 and 6	77	38	49	76	33	43
7 and more	74	30	40	64	21	33
No information	29	12	41	25	12	48
Total	281	139	49	348	199	57

days) required to receive the specimens in the central laboratory at Madanapalle from the participating centre.

Of the 281 specimens in the Group I the information regarding the time required for transit was not available for 29 specimens.

Of the 101 specimens received within 4 days from the time of biopsy 58 or 59 per cent were culture positive. Of the 77 specimens received on 5th or 6th day of the biopsy, 38 or 49 per cent were positive. Of the 74 specimens received on 7th day or afterwards only 30 or 40 per cent were positive. Thus there was a positive correlation between the time required to receive the specimens and culture positivity. Earlier the specimens were received more were the chances of isolating mycobacterial strains from them.

Of the 348 specimens in Group II the information regarding the time required, for transit was not available for 25 specimens.

Of the 183 specimens from this group received within 4 days from the time of biopsy 133 or 72 per cent were positive by culture. As against this, of the 76 specimens received on 5th or 6th day and 64 specimens received on 7th day or afterwards 33 or 43 per cent and 21 or 31 per cent respectively were positive. Thus in this group also there was a positive correlation between the culture positivity and the time required to receive the specimens.

These observations suggest that bacilli might become non-viable if the specimen was held up for longer time in the postal transit.

Results of relationship between the duration of lymph-node enlargement and the frequency of isolation of mycobacteria is shown in table 11.

It is observed that the proportion of positive results varied between 43 and 57 per cent for specimens in Group I and between 46 and 60 per cent for specimens in Group II. This shows that there was no relationship between the two factors under consideration.

Relationship between the frequency of isolation of mycobacteria and the duration of previous chemotherapy is shown in table 12.

It was observed that in the Group I series 97 or 50 per cent of the 193 specimens from patients with history of chemotherapy of less than 3 months duration yielded growth of mycobacteria as against only 8 or 38 per cent of the 21 specimens, from patients with history of previous chemotherapy of more than 12 months duration. Similarly in Group II series, 156 or 55 per cent of 282 specimens from patients with history of previous chemotherapy of less than 3 months duration yielded growth of mycobacteria as against only 5 of the 11 patients with history of previous chemotherapy of more than 12 months duration. But none of these differences appear to be of statistical significance.

*Some more observations in the I.C.M.R. study*

The relationship between the frequency of positive results by bacteriology and histopathology and the size of tuberculin reaction of the patients is shown in table 13.

TABLE 11

*Frequency of culture positivity and the duration of lymph-node enlargement*

Duration of lymph-node enlargement (in months)	Group I			Group II		
	Total	No.	Per cent	Total	No.	Per cent
Less than 3	70	30	43	94	50	53
3—6	77	38	50	79	47	60
7-12	54	27	50	46	21	46
More than 12	63	36	57	96	56	58
No information	17	8	47	33	25	76

TABLE 12

*frequency of culture positivity and the duration of previous treatment with anti-tuberculosis drugs*

Duration of Treatment	Group I			Group II		
	Total	No.	Per cent	Total	No.	Per cent
Less than 3	193	97	50	282	156	55
3-12	29	14	48	11	6	55
More than 12	21	8	38	11	5	45
No information	38	20	58	44	32	73

TABLE 13

*Relationship between the size of tuberculin reaction and positive results by bacteriology and histopathology*

Size of Tuberculin Reaction (in mm.)	Total	Bacteriologically Positive		Total	Histopathologically Positive	
		No.	Per cent		No.	Per cent
9 or less	37	4	10	37	14	38
10-14	63	23	37	63	51	81
15 or more	64	28	44	64	58	91
Not done	122	47	39	101	70	70
Total	286	102	36	265*	193	73

\*Excluding 21 specimens with no histopathology reports.

*Bacteriology* : 4 or 10 per cent of the 37 specimens from patients with reaction to tuberculin of the size of 9 mm or less, were bacteriologically positive as against 23 or 37 per cent of the 63 specimens and 28 or 44 per cent of the 64 specimens from patients with reaction of 10 to 14 mm and 15 mm or more respectively were positive.

*Histopathology* : 14 or 38 per cent of 37 specimens from patients with size of reaction of 9 mm or less proved to be tuberculous on histopathology, the others being either chronic non specific adenitis or new growths. On the contrary, 51 or 81 per cent of the 63 specimens from patients with size of reaction 10 to 14 mm and 58 or 91 per cent of the 64 specimens from patients with size of reaction of 15 mm or more turned out to be tuberculous.

These observations are very important from the point of view of differentiating tuberculous adenitis from non-tuberculous one and tuberculous lymphadenitis from other causes of enlargement of lymphnodes.

The relationship between the size of the enlarged lymphnodes and the bacteriological

and histological positivity is shown in table 14,

*Bacteriology*: 5 or 14 per cent of 35 specimens of the size of lymph-node enlargement of less than one cm. were bacteriologically positive as against 43 or 42 per cent of 103 specimens of size of 1-2 cm. and 54 or 36 per cent of 148 lymphnodes of the size of more than 2 cm. were positive indicating that the chances of yielding bacteriologically positive results were 2-3 times higher for lymphnodes of the size of 1 cm. or more than that for lymphnodes of the size of less than 1 cm.

*Histopathology*: 16 or 37 per cent of the 34 specimens of the size of lymphnode enlargement, of less than 1 cm. were tuberculous in nature as against 62 or 70 per cent and 115 or 80 per cent of the 88 specimens of the size of 1-2 cm. and 143 specimens of the size of more than 2 cm. respectively were tuberculous, indicating that bigger the lymphnodes more were the chances of these being tuberculous on histopathological examination.

The relationship between the number of lymphnodes involved and frequency of bacteriological and histological positivity is shown in table 15.

TABLE 14

*Size of lymph-node enlargement and positive results by bacteriology and histopathology*

Size of lymph-node enlargement (in cms.)	Total	Bacteriologically		Total	Histopathologically	
		No.	Per cent		No.	Per cent
Less than 1 cm.	35	5	14	34	16	47
1—2	103	43	42	88	62	70
2 or more	148	54	36	143	115	80

TABLE 15

*Number of lymph-nodes involved and bacteriology and histopathology results*

No. of lymph-nodes involved	No.	Bacteriologically		No.	Histopathologically	
		No.	Per cent		No.	Per cent
One only	19	7	37	19	13	73
2-3	103	38	37	91	65	71
4-10	118	41	35	110	83	75
More than 10	46	16	35	46	32	70

35 to 37 per cent of the specimens were positive bacteriologically and 70 to 75 per cent by histopathology irrespective of number of lymphnodes enlarged in the disease process indicating that there was no relationship between the number of lymphnodes involved in the disease process and the frequency of positive results by bacteriology or histopathology.

#### *Drug Resistance*

Of the total 338 strains subjected to drug susceptibility tests for streptomycin, isoniazid, and PAS, 23 or 7 per cent were resistant to streptomycin, 18 or 5 per cent to isoniazid and 50 or 15 per cent to PAS. Of the 243 strains tested for thiacetazone sensitivity test 20 or 8 per cent were resistant to it. On considering the relationship of prevalence of drug resistance to the previous chemotherapy, there were not any significant differences in the proportions of resistant strains whether the patients were previously treated or not.

#### *Isolation of unclassified or anonymous strains of Mycobacteria :*

In all 338 strains of mycobacteria were isolated, 304 from cervical lymphnodes, 27 from axillary lymphnodes and 7 from inguinal lymphnodes. In addition 21 specimens were positive by microscopy only, the culture report of these specimens being either negative or contaminated.

333 of these 338 strains isolated were Niacin Positive and so were classified as human type of tubercle bacilli. The remaining 5 strains proved to be those of unclassified mycobacteria. 2 of the 5 strains of unclassified mycobacteria showed growth on more than one of the four slopes inoculated for primary isolation and number of colonies on each slope was 50-60 in one case and 3-5 in second case. These two strains appeared to be definitely responsible for the lymphnode enlargement in the two patients on whom the biopsy was performed. The remaining three strains were isolated as single colony on one of the four slopes inoculated for primary isolation and could be considered only as probable etiologic agents for the lymphnode enlargement in those patients. Details of these five strains are given in table 16. The case histories of these five patients are given below.

*Case No. 1 (LN 91) :* Male, aged 16 years (M.T.R.U. study). History of fever and generalised lymphnode enlargement of the duration of 12 days, The condition was diagnosed as tuberculous adenitis and cervical

lymphnode biopsy was done for bacteriological studies. Microscopic examination did not reveal A.F.B. but growth was observed between 3rd and 4th week of incubation on all the four slopes inoculated for primary isolation (For details see table 16).

Some more tests carried out on this strain were :

- (1) Semi quantitative catalase test : 60 mm column of froth.
- (2) Tween 80 hydrolysis: Negative.
- (3) Aryl Sulphatase test at 3 days :  
Negative  
at 2 weeks :  
Negative
- (4) Production of opacity in Tween 80 agar medium: Positive.
- (5) Serological typing: "Watson" type.
- (6) Antigenic type: Like "Cause" strain.

*Provisional classification :* Scotochromogenic strain of "Cause" type. Definitely of causative organism of the disease.

*Case No. 2 (LN 360) :* Female, aged 16 years (C.M.C.H. Vellore) History of enlargement of cervical and axillary lymphnodes on right side of duration about one month. Cervical lymphnode biopsy was done.

*Histopathology:* Suggestive of tuberculosis. Section showed A.F.B.

*Bacteriological studies :* Microscopic examination did not show A.F.B. but growth of a single colony was observed during the 7th week of incubation (Details in table 16).

*Provisional classification :* Non-chromogenic strain of "Battey" type. This may have been responsible for the disease process.

*Case No 3 (LN 611) :* Male, aged 40 years (C.M.C.H. Vellore) History of enlargement of inguinal lymphnodes, duration not known. Inguinal lymph-node biopsy was done.

*Histopathology :* Necrotic granulomatous lymphadenitis.

*Bacteriology:* Microscopic examination did not reveal A.F.B. Growth was obtained in the 6th week as single colony on one of the four slopes inoculated (for details see table 16).

*Provisional Classification :* "Battey" type.

TABLE 16  
Morphological characters of the strains of unclassified bacilli isolated and results of a few identifications

Strain No.	Growth on primary culture and time required	Morphology and pigmentation	Ziehl-Neelson staining	Incubation at 37°C 22°C 45°C	Photochromogenicity test	Drug Sensitivity SM PAS INH TB-I	Biochemical tests	
							Catalase at RT	Nitrate Reduction test
91 rival	50-60 colonies on all 4 slopes during 4th week	Moist, smooth, spherical & yellow	Short AFB	+ + -	Yellow in dark & light	S R R R	++ +	- -
360 rival	Single colony on one slope during 7th week	Moist, smooth, buff to faint yellow	Short AFB	+ + -	Negative	S R R R	+ +	- -
611 ginal	Single colony on one slope during 6th week	Moist, smooth, buff to faint yellow	Short AFB AF Cocci	+ + -	Negative	S R R R	+ +	- -
721 rival	Single colony on one slope during 7th week	Moist, smooth, & buff	Short AFB	+ + -	Negative	R R R R	+ +	- -
885 ginal	3-4 colonies on 3 of the 4 slopes in 4th week	Dry, smooth buff-yellow	AFB Pleomorphic	+ + -	Positive	R R R S	+++ +	- + + + + Strong Positive

RT—Room temperature  
68°C—after inactivation at 68°C for 20 min, in pH 7 phosphate buffer.

This strain may have been responsible for the disease.

*Case No. 4* (LN 721) : Male, aged 30 years (I.C.M.R. study). History of swelling in left cervical region of 3-4 months duration. Cervical lymphnode biopsy was done.

*Histopathology* : Tuberculous lymphadenitis.

*Bacteriology* : Microscopic examination did not reveal A.F.B. but on culture one colony was grown on one of the 4 slopes inoculated in the 6th week of incubation (for details see table 16).

*Provisional Classification* : "Battey" type. This strain may have been responsible for the disease.

*Case No. 5* (LN 885) : Male, aged 7 years (I.C.H. Madras). History of swelling of lymphnodes in neck, axilla and inguinal region of about 1 to 2 years duration (1968).

Previous history : During 1964-65 (i.e. at the age of one year) the boy attended the I.C.H. Madras, with history of cough, fever and throat pain. Tuberculin test at that time was positive. X-ray chest showed hilar adenitis. He was treated with injections of streptomycin for one month along with isoniazid which was continued for further 11 months.

Clinical examination (in 1968): Cervical, axillary and inguinal lymphnode enlarged. Lymphnodes were discrete and firm—not much tender. Chest X-ray showed hilar adenitis. He reacted to tuberculin PPD—RT 23, 1 TU with 12 mm reaction. He was put on anti-tuberculosis line of treatment and inguinal lymphnode biopsy was done.

*Histopathology* : Tuberculous adenitis.

*Bacteriology* : Smear was negative for A.F.B. but a growth of 4, 3, 5 colonies respectively was observed on three of the four slopes inoculated for primary isolation during the 4th week of incubation. Initially the growth was dry, smooth and buff but on exposure to daylight it turned yellow the next day—suggesting that the strain was of Photochromogenic type, (for details see table 16).

*Tuberculin test on this patient with various antigens* :

Tuberculin	Dose	Diameter of induration
PPD—5	5T.U	6 mm
PPD Gause	"	20mm

PPD Avian	"	10mm
PPD Battey	"	6mm
PPD Kansasii	"	10mm

*Provisional Classification* : Photochromogenic strain of *M. kansasii* type. This strain must have been definitely responsible for the disease in this boy.

### Discussion

Patients with enlarged lymphnodes—cervical, axillary and rarely inguinal—are commonly met in the clinical practice in India. Such patients are usually treated as tuberculous on the basis of clinical diagnosis. It was, therefore, important to study this problem from bacteriological and also histopathological point of view.

There is a widespread prevalence of non-specific tuberculin allergy associated with infections of unclassified mycobacteria and hence the second objective of this study was to see if it would be possible to isolate mycobacteria other than *M. tuberculosis* from the diseased lymphnodes.

Of the 847 specimens examined by bacteriology, 359 or 42 per cent were positive, 338 (40 per cent) by culture and another 21 by microscopy alone. This is quite a high proportion of positives as compared with findings of others on this subject. In an investigation of cervical lymphnodes, by Medical Research Council (1949) it was possible to recover tubercle bacilli by culture or animal inoculation in only 19 per cent of specimens. Wilmot and others (1957), though were able to demonstrate acid fast bacilli by microscopy in 76 per cent of 54 specimens examined, could obtain growth on culture in 4 specimens only.

In the present study 86 to 90 per cent of the total specimens, and of those proved tuberculous by bacteriology or histopathology were from cervical region indicating that the cervical lymphnodes are most commonly involved in tuberculous process. Axillary lymphnodes were in proportion of 7 to 10 per cent and inguinal 2 to 4 per cent indicating that the lymphnodes at these two sites are very infrequently involved in tuberculous process.

On histopathological examination 2/3rd of the 477 cervical lymphnode specimens were tuberculous as against approximately 1/3rd of 66 axillary and 23 inguinal specimens were tuberculous. Of course, proportion of bacteriologically positive specimens was similar in histologically tuberculous specimens from all three sites.

These observations suggest that involvement of axillary lymphnodes is rare in tuberculosis and of the inguinal lymphnode is still rarer and are very much similar to those made by Miller (1934), Jones (1951), German and associates (1956), Lester and Jones (1956), Schless and Wier (1957), Miller and Cashman (1958) and Doctor (1964X).

Lymphnode enlargement was observed more often in females than in males especially in the age group of 15 to 29 and 30 to 44 years. Similarly, cases proved to be tuberculous by bacteriology or histopathology were about one and half times more frequent in females than in males and this difference in males and females was seen in all age groups inspite of the fact that the proportion of enlarged lymphnodes was higher in males than in females in the age groups of 0 to 14 years and 45 years and above. These observations suggest that tuberculosis lymphadenitis is more a disease of females than of males. In literature there are conflicting reports regarding prevalence of this disease in males and females. Thompson (1940), Siddiqui (1949) observed higher prevalence in females while Jones (1951) and Schless & Wier (1957) made the contrary observations.

It has been observed in the present study that the disease was more common in the age group of 15 to 29 years, the maximum number of patients of lymphnode enlargement being seen in the age group of 20 to 24 years both in males and females. The histopathologically and bacteriologically confirmed tuberculous lymphadenitis was also more frequent in the age group of 15 to 29 years both in males and females indicating that tuberculous lymphadenitis is no more a disease of children now at least in our country.

On considering the results according to participating centres it has been observed that maximum number as positive results, 58 per cent, were seen in specimens from M.T.R.U. study and least positives in specimens from I.C.H. Madras study. The possible explanation for higher number of positives for specimens in M.T.R.U. study may be that there might have been a selection of tuberculous cases, while the other centres may have carried out lymphnode biopsies on all cases presented at their centres—tuberculous or otherwise.

Of the total 847 specimens, 566 were examined by histopathology and 341 or 60 per cent of them were tuberculous in nature. Considering the results for specimens from different centres, 46 per cent of 44 specimens from I.C.H. Madras, 50 per cent of the 257 speci-

mens from C.M.C.H., Vellore and 73 per cent of 265 specimens from I.C.M.R. study were found to be tuberculous — proportion being significantly higher for I.C.M.R. specimens than that for either C.M.C.H. Vellore specimens or I.C.H., less Madras specimens.

58 per cent of the 341 specimens proved to be tuberculous on histopathology were bacteriologically positive. In spite of the fact that number of histologically proved tuberculous specimens was higher among I.C.M.R. specimens than that among C.M.C.H., Vellore specimens, the number of bacteriologically positive specimens was comparatively small in I.C.M.R. study. 88 or 46 per cent of 193 specimens tuberculous on histopathology from I.C.M.R. study were bacteriologically positive as against 97 or 76 per cent of the 128 tuberculous specimens from C.M.C.H., Vellore. This is a very significant difference especially when the specimens were tuberculous on histopathology.

There were seven specimens which were culture positive but the histopathology reports were suggestive of chronic adenitis in 6 and secondary carcinoma in another. It was possible that the histopathological results of chronic lymphadenitis may not be correct for these 6 specimens and that tuberculosis and carcinoma both may have affected one lymphnode under consideration though such occurrence is rare. Four more specimens showed acid fast bacilli on microscopy, though the histopathological changes in two were suggestive of anaplastic carcinoma and in one of chronic non-specific lymphatic carcinoma and in one of chronic non-specific lymphadenitis. These 3 specimens could be considered as false positives. The smear from the fourth specimen showed plenty of acid fast bacilli, and the histopathology report on this specimen was suggestive of leprosy.

To find out the reason for the difference in the bacteriologically positive specimens among the histopathologically proved tuberculous lymphnode specimens from C.M.C.H. Vellore study and I.C.M.R. study, the culture positive results were analysed according to time required to receive the specimens from the centre to the bacteriology laboratory. All the specimens from C.M.C.H. Vellore were received in the bacteriology laboratory usually within 8-10 hours — these being sent by a special courier. On the contrary, the time required for I.C.M.R. specimens varied anything between 3 to 12 days. It has been observed that earlier the specimens were received more were the chances of obtaining growth on culture — 59 per cent

of 101 specimens in Group I and 72 per cent of 183 specimens in Group II received within first 4 days being culture positive as against 40 per cent of 76 specimens in Group I and 31 per cent of 64 specimens in Group II received on 7th day or afterwards. Thus, there is a suggestion that some of the tuberculous lymphnode specimens might be harbouring a few viable bacilli and delay in transit might have been responsible for these few viable units becoming non-viable in many of the I.C.M.R. specimens as well as from Group I.

Two more observations have been made in the I.C.M.R. study. The first one is regarding the results of tuberculin test in relation to bacteriologically or histopathologically proved cases of tuberculous lymphadenitis. The tuberculin test appeared to be an important tool to differentiate the tuberculous or non-tuberculous adenitis. Chances of the lymphnode under consideration to be tuberculous were very small in patients who reached to tuberculin either negative or with small size of reaction (9 mm or less). 4 or 7 per cent of the 55 patients whose specimens were positive bacteriologically and 14 or 11 per cent of 123 patients whose specimens were tuberculous on histopathology, had 9 mm or less reactions to tuberculin, others having stronger reaction. This observation confirms the role of tuberculin test in differential diagnosis.

Another observation is in relation to the size of lymphnode enlargement. 5 or 5 per cent of the total 102 specimens bacteriologically positive and 16 or 8 per cent of the 193 specimens proved to be tuberculous on histopathology, were of the size less than 1 cm., others being 1 cm. or bigger in size indicating that smaller the palpable lymphnodes less were the chances of these being tuberculous by bacteriology or histopathology.

Of the total 338 strains of mycobacteria grown from the same number of specimens, 5 were classified as those of "unclassified" mycobacteria, the others being those of *M. tuberculosis* of human type. On the basis of these findings the prevalence of lymphadenitis caused by "unclassified" mycobacteria could be estimated as about one per cent. This is very low prevalence as compared to the findings of other workers in Western countries (Davis and Comstock, 1961; Jones and Campbell, 1962; Black and Chapman, 1964; MacKeller and others, 1967 and Reid and Wolinsky, (1969). Similar observations were made by Kulkarni and Frimodt-Moller (1971) in a study of pulmonary disease caused by "unclassified" mycobacteria wherein authors presented 4 cases of

pulmonary disease caused by "Battey" type of mycobacteria and prevalence of these cases was about one per cent among the cases caused by *M. tuberculosis* of human type. The rarity of disease caused by "unclassified" mycobacteria in our country is puzzling especially when there is widespread prevalence of skin sensitivity to the tuberculin PPD-Gause derived from one of the strains of "unclassified" mycobacteria indicating that these organisms are infecting Indian population from an early age. The reason for this may be that the infection and disease by human tubercle bacilli is still more prevalent and unless there is reduction in number of patients we may not get more cases of disease caused by "unclassified" mycobacteria.

Of the 5 strains isolated in the present study, 2 appeared to have been definitely responsible for the disease process by the fact that number of colonies isolated in one case was quite large and on further studies this strain was typed as one similar to the original "Cause" strain isolated from cervical lymphnodes from one child in U.S.A. The number of colonies grown in case of second strain, though were not many, were not few to be ignored as saprophytes. The spectrum of reaction to tuberculin test in this patient showed larger reaction to tuberculin derived from "unclassified" mycobacteria than that to tuberculin derived from tubercle bacilli of human type.

The other three strains were grown as single colony. It may not be correct to say that these were casual isolates or saprophytes since the isolation were from sterile specimens preserved aseptically and chances of contamination with saprophytes were remote. At the same time there is no ample evidence to say that disease was caused by these mycobacterial strains, except that histopathological reports on the specimens were suggestive of tuberculosis and that human bacilli were not isolated from these specimens. Skin tests with different tuberculin would have helped to come to some conclusion but this was not possible. In view of all these facts these strains have been labelled as "probable agents" responsible for the lymphadenitis in respective cases. All these were provisionally classified as "Battey" type.

### Summary

1. Of the 847 lymphnode specimens examined bacteriologically, 359 or 42 per cent were positive, 49 per cent by culture and 2 per cent by microscopy only. The proportion of positive results was highest for specimens from

inguinal region (44 per cent), and lowest for those from inguinal region (27 per cent), axillary specimens being in between (37 per cent). Considering these results according to the participating centres highest proportion of positive results was seen among specimens in M.T.R.U. study (58 per cent of 247 specimens). The proportions of positive results were similar for the specimens from C.M.C.H. Vellore and for I.C.M.R. study—these being 40 per cent of 257 C.M.C.H. specimens and 36 per cent of 286 I.C.M.R. specimens. The specimens from I.C.H. Madras centre yielded least number of positive results—23 per cent of 57 specimens.

2. Of the 566 specimens examined by histopathology, 341 or 60 per cent were tuberculous. According to the site of lymphnode involvement these proportions were 65 per cent of 477 cervical, 38 per cent of 66 axillary and 30 per cent of 23 inguinal lymphnode specimens.

196 or 58 per cent of the 341 specimens proved tuberculous on histopathology were positive for mycobacteria on microscopy and/or culture. 76 per cent of 128 specimens from C.M.C.H. Vellore proved tuberculous on histopathology, were positive by bacteriology as against only 46 per cent of 193 specimens from I.C.M.R. study of the same kind.

3. The prevalence of the disease as seen clinically, or proved by bacteriology and histopathology was higher in females than in males.

4. Disease was more common in young adults of the age between 15 to 29 years both in males and females.

5. There was a relationship between the proportion of isolation of mycobacteria on culture and the number of days required to receive the specimens, the yield of culture positive results being highest in specimens received on or before 4th day of dispatch. This fact may explain the difference in the bacteriologically positive results among histologically proved tuberculous specimens from C.M.C.H. Vellore study and the I.C.M.R. study. C.M.C.H. Vellore specimens were received within one day as against I.C.M.R. specimens anything between 3 to 12 days to reach to central laboratory.

6. Tuberculin test appeared to be important to differentiate the tuberculous and non tuberculous lymphadenitis. The proportions of positive results by bacteriology and histo-

pathology were very small—10 per cent and 38 per cent respectively of the 37 specimens from patients with size of reaction of 9 mm. or less. Stronger the reaction more were the chance of getting positive results by both the technique.

7. Size of enlarged lymphnodes also was important factor, smaller the size of lymphnodes (less than 1 cm.) less were the chances of these lymphnodes being tuberculous either by bacteriology or by histopathology.

8. 333 of the 338 strains were of M. tuberculosis human type and 5 strains were of the "unclassified" type. 2 of these 5 strains were definitely responsible for the disease and 3 others may have been responsible for the disease of those patients. The prevalence of isolation of "unclassified" mycobacterial strains in present study was about one per cent.

#### ACKNOWLEDGEMENTS

This study was carried out at Madanapalle Tuberculosis Research Unit as a part of larger investigation into classification of India Mycobacteria, carried out under the auspices of Indian Council of Medical Research, Union Mission Tuberculosis Sanatorium and the Tuberculosis Programme, Communicable Diseases Centre, Washington Office, United States Public Health Services and World Health Organisation, and was supported by the PL 480 funds.

I am most grateful to Dr. J. Frimodt Moller, Director of Union Mission Sanatorium, Aroyavaram (A.P.) for allowing me to use the present material for this purpose.

I am also grateful to the Superintendents of various Mission Hospitals in South India. Dr. C.K. Job, Professor and Head of the Dept. of Pathology and Dr. (Miss) H. Krishnaswamy of the Norman Institute of Pathology, C.M.C.H. Vellore, Dr. V. Balagopal Raju, Director & Superintendent and Dr. (Miss) Narmada of the Institute of Child Health and Hospital for Children, Madras and Dr. S.P. Pamra Director of New Delhi Tuberculosis Centre and Co-ordinator of the I.C.M.R. Cervical Lymphadenitis Study for sending me the lymphnode specimens for bacteriological study and for supplying me all the necessary information regarding the patients whose specimens were sent for bacteriological studies.

## REFERENCES

- 1 American Trudeau Society, (1954). *American Review of Tuberculosis*, 70, 949.
2. Boyd, W. (1944). *Pathology of Internal Diseases*, London.
3. Black, B.C. and Chapman, J.S. (1964). *Paediatrics*, 33, 887,
4. Chapman, J.S. and Guy, L.R. (1959). *Paediatrics*, 23, 323.
5. Corpe, R.F. and Stergus, I. (1963) *American Review of Respiratory Diseases*, 87, 289.
6. Dajani, A.S., Garcia, R.E. and Wolinsky, E. (1963). *New England Journal of Medicine*, 268, 1329.
7. Davis, S.D. and Comstock, G.W. (1961). *Journal of Paediatrics*, 58, 771.
8. Doctor, H.G. (1964). *Indian Journal of Medical Sciences*, 18, 411.
9. German, J.L., Black, T.C. and Chapman, J.H. (1956). *Diseases of Chest*, 30, 326.
10. Griffith, A.S. (1937). *Tubercle*, 18, 529.
11. Hinden, E., Nardell, S.G. and Anabtawi, S. (1952). *Tubercle*, 32, 2.
12. Hudgins, A.P. (1943). *Medical Times*, 51, 75.
13. Jones, B.S. (1951). *British Medical Journal*, 1 1056.
14. Jones, P.G. (1968). *Medical Journal of Australia*, 2, 949.
15. Jones, P.G. and Campbell, P.E. (1962). *British Journal of Surgery*, 50, 302.
16. Kulkarni, K.G. and Frimodt-Moller, J. (1969). Proceedings of the 24th Tuberculosis and Chest Diseases Workers' Conference, Trivandrum, January 1969, 391.
- 17 Kulkarni, K.G. and Frimodt-Moller, J. (1971). Proceedings of the 26th Tuberculosis and Chest Diseases Workers' Conference, Bangalore, January 1971, 352.
18. Lester, C.W. (1951). *American Review of Tuberculosis*, 64, 691.
19. Lester, C.W. and Jones J.M. (1956). *American Review of Tuberculosis and Pulmonary Diseases*, 73, 329.
20. MacKellar, A., Hilston, H.B. and Masters P.L. (1967). *Archives of Diseases of Childhood*; 42, 70.
21. Marsden, H.B. and Hyde, W.A. (1962). *Lancet*, I, 249.
22. McDonald, J.R. and Weed, L.A. (1951) *American Journal of Clinical Pathology*, 21, 323.
23. Medical Research Council, (1949). *Journal of Hygiene, Cambridge*, 47, 337.
24. Miller R.H. (1934). *Tuberculosis of Lymphatic System*, MacMillan and Co., New York, 192.
25. Miller, J.F.W. and Cashman, J.M. (1958), *Lancet*, 1, 286.
26. Mitchell, A.P. (1917). *Journal of Pathology and Bacteriology*, 21, 248.
27. Nassau, E. and Hamilton, G.M. (1957). *Tubercle*, 38, 387.
28. Park, W.H. (1910). *Bulletin of John Napkin's Hospital*, 21, 122.
29. Park, W.H. and Krumwicde, C.L., Jr. (1910). *Journal of Medical Research*, 23, 205.
30. Paul, F. de' Gara (1942). *American Review of Tuberculosis*, 42, 576.
31. Prissick, F.H. and Masson, A.M. (1956). *Canadian Medical Association Journal*, 75, 798.
32. Rajwanshi, V.S. and Tyagi, O.K. (1970). *Indian Journal of Pathology and Bacteriology*, 13, 21.
33. Ramond, L. (1936). *Presse Med.*, 44, 1475.
34. Reid, J.D. and Wolinsky, E. (1969). *American Review of Respiratory Diseases*, 99, 8.
35. Rich, A.R. (1951). *Pathogenesis of Tuberculosis*, Oxford.
36. Schless, J.M. and Wier, J.A. (1957). *American Review of Tuberculosis*, 76, 811.
37. Siddiqui, M.A.H. (1949). *Journal of Indian Medical Association*, 19, 9.
38. Sinclare, S. and Mittal, S.K. (1972). *The Indian Journal of Tuberculosis*, 19, 85.
39. Thompson, B.C. (1940). *Tubercle*, 21, 217.
40. Tisseuil, J. (1946). *Bull. Soc. Path. Exot.*, 49, 343.
41. Weed, L.A. Haddow, M.K. and Needhan, G.N. (1956). Proceedings of the Mayo Clinic, 31, 259.
42. Wilmot, T.J., James, E.F. and Reilly, L.V. (1957). *Lancet*, 2, 1184.
43. Wissler, H. (1954). *Acta Tuberc. Belg.*, 45 302.

## RELAPSE IN PULMONARY TUBERCULOSIS AFTER MEDICAL TREATMENT

S.P. PAMRA, GOVIND PRASAD AND G.P. MATHUR

*(From New Delhi Tuberculosis Centre)*

### Introduction

Yardsticks for measuring success of treatment in tuberculosis have been changing over the years and they have become more stringent with availability of potent specific drugs. At one time quiescence was considered a sufficiently satisfactory achievement even though it, was well known that a large number of such cases would relapse sooner or later. With the discovery of highly effective antimicrobial drugs, immediate results improved considerably. However, bacteriological cure in the strict sense of the word being neither possible nor capable of being demonstrated even if achieved, relapse rates, or late results are usually accepted as an important criterion of successful treatment. An earlier paper from the Centre (Sikand, Pamra and Mathur, 1959) had shown that relapse rates among patients treated in 1954 with the then treatment policies were still very high, although considerably lower than those obtaining in the pre-antimicrobial era. With increasing knowledge and understanding of the action and rationale of chemotherapy, more judicious combinations and prolonged administration, immediate results have improved considerably since 1954. The objects of the study being reported were to find out if relapse rates too have come down in recent years and to find out if any factor can be said to predispose to relapse.

### Material and Method

Freshly diagnosed patients of pulmonary tuberculosis reporting at the New Delhi Tuberculosis Centre in 1965 and 1966 from the domiciliary service area were included in the study. Only such of these patients who completed treatment successfully were considered eligible for the study. In other words, exacerbation occurring during the course of treatment has not been considered as relapse. X-rays of all patients at the start of treatment and at the time of completion of treatment were re-read by an independent assessor in respect of extent of disease and cavitory status.

Treatment policy of the Centre at this time was, briefly, to start treatment in previously untreated cases with at least two drugs (INH with any one of the three other standard drugs) till the 'Target Point' was reached. Those who

had had some treatment prior to reporting at the Centre and were still sputum positive were started on three drugs of which INH was one. Target point has been defined as a stage when no cavity is seen in the plain skiagram, lesions are stationary radiologically and sputum/laryngeal swab cultures have been negative for at least six months. INH is continued for one year thereafter as 'maintenance' therapy. All patients completing the treatment satisfactorily are followed up for five years. Follow-up included both radiological and bacteriological assessment every year. There were some patients who did not report for annual check up regularly. For purposes of this analysis a patient reporting after, say, two years whose lesions were judged as inactive at this examination was assumed to have remained inactive throughout this period.

Relapse has been defined as radiological exacerbation of pulmonary disease and/or bacteriological reversion of sputum and/or non-pulmonary tuberculous disease in any other organ of the body.

Of the freshly diagnosed cases first registering in 1965 and 1966, 530 successfully completed treatment and have been included in the present study. Of these, 367 were bacteriologically confirmed cases but in the remaining 163, diagnosis was based on clinical and radiological findings and subsequent response to anti-tuberculosis drugs.

### Results

In all, 34 of the 530 persons included in the study relapsed during follow up, 28 among the initially bacillary and 6 among the abacillary patients. These included 24 which showed both radiological and bacteriological deterioration, one with only bacteriological relapse and 7 which showed radiological worsening unaccompanied by bacteriological relapse. The remaining 2 cases were non-pulmonary, one of cervical lymphadenitis and the other of tuberculous empyema.

Since the number of patients available for examination varied from year to year, annual relapse rates have been calculated on the basis of those available for examination. An analysis of the 295 persons who have not completed 5 years', follow up out of the original 530 shows

that migration accounted for the largest number viz. 209 (71 per cent). Another 72 (24 per cent) had not yet completed the stipulated five years' follow up. Non-tuberculous deaths accounted for 4 patients and non-cooperation for the remaining 10.

Relapse rates in the two groups of patients viz. initially bacillary and initially abacillary have been calculated separately for each year following completion of treatment and are shown in tables 1 and 2 respectively. The last column of these tables shows the cumulative relapse rates calculated by the modified life table method. It has been assumed that patients continuing under observation in any

year were representative of the total patients, and drop out was not related to the incidence of relapse. Theoretically, this assumption may not be entirely justified in as much as patients who did not relapse and consequently did not have any symptoms are more likely to be non-cooperative in follow up than those who did. This is corroborated by the fact that out of the 151 ex-patients who had been defaulting in follow up and were specially examined for this study, only one was found to have relapsed. It can therefore be argued that the actual cumulative relapse rates may be somewhat lower than the ones shown here but there is no convincing method of proving or disproving this statement.

TABLE 1

*Relapses in successive years in initially bacillary patients' group*

	Patients at start of year	Patients withdrawing during year	Average no. of patients during year	Relapses during year	Relapse rate %	Cumulative relapse rate %
1st year	367	59	337.5	5	1.48	1.48
2nd year	303	30	288.0	2	0.69	2.16
3rd year	271	46	248.0	8	3.22	5.31
4th year	217	36	199.0	10	5.02	10.06
5th year	171	46	148.0	3	2.03	11.89

Standard Error of the 5 year cumulative relapse rate (approx.) = 1.91

TABLE 2

*Relapses in successive years in initially abacillary patients' group*

	Patients at start of year	Patients withdrawing during year	Average no. of patients during year	Relapses during year	Relapse rate %	Cumulative relapse rate %
1st year	163	28	149.0	1	0.67	0.67
2nd year	134	24	122.0	1	0.82	1.48
3rd year	109	12	103.0	1	0.97	2.44
4th year	96	11	90.5	—	0.00	2.44
5th year	85	20	75.0	3	4.00	6.34

Standard Error of the 5 year cumulative relapse rate (approx.) = 1.39

A comparison of the 5-year cumulative relapse rates among initially bacillary and initially abacillary patients shows that the rate in the former (11.89 per cent) is considerably

higher than that in the latter (6.34 per cent), the difference being statistically significant. The relapse rates were low in the first two years of follow up in both groups.

Since the results in bacillary and abacillary patients are so widely disparate, the subsequent analysis to evaluate the prognostic significance of several factors in relation to relapse are based only on 367 sputum positive patients. The cumulative relapse rates for the various sub-groups shown in table 3 have been calculated in exactly the same manner as that indicated in tables 1 & 2, but to simplify presentation, intermediate steps have been omitted and only the cumulative relapse rates and the standard errors thereof have been shown.

Table 3 shows the relationship between relapse rates and several factors. It can be seen that 15.28 per cent of patients below 25 years of age relapsed in 5 years as against 11.30 per cent in the age group 28 to 44 years, a difference which fails to attain statistical significance. Persons above 44 years may be ignored because of very small numbers. Similarly, the higher relapse rate (12.77 per cent) among males compared to females (10.46 per cent) is not statistically significant.

TABLE 3

*Five year cumulative relapse rates among initially bacillary cases according to various factors*

		Number of cases at start	Cumulative Relapse Rate (%)±S.E.
Age	Under 25 years	151	11.30 ± 3.27
	25—44 years	175	15.28 ± 3.38
	Over 44 years	41	*
Sex	Males	233	12.77 ± 2.36
	Females	134	10.64 * 3.19
Extent of initial disease	1 zone	39	11.74 ± 3.63
	2 zones	144	14.11 ± 3.39
	3 or more zones	134	9.54 ± 2.84
Initial Cavitation	Present	197	12.55 ± 2.86
	Not present	170	11.20 ± 2.52
Length of treatment	24 months or less	64	6.14 ± 3.61
	25 to 30 months	128	13.77 ± 3.02
	Over 30 months	175	12.29 ± 3.15
Regularity** during treatment	Regular	321	8.73 ± 2.02
	Irregular	46	13.40 ± 6.44*
Drug resistance during treatment	Res. to one or more drugs	47	10.77 ± 6.30*
	Sens. to all drugs	320	11.98 ± 2.01
Extent of residual lesion	Almost complete clearing	54	6.00 ± 3.96
	1 zone	253	13.05 ± 2.29
	2 or more zones	60	12.82 ± 5.50*

\* Based on small numbers

\*\* for definition, see text

Initial extent of disease and cavitory status also do not appear to materially influence the incidence of relapse. The rate varied from 9.54 per cent to 14.11 per cent in relation to extent of disease and from 11.20 per cent in non-cavitory to 12.55 per cent in cavitory cases.

Patients whose entire treatment lasted less than 24 months had a lower relapse rate (6.14 per cent) whereas the rates were 13.77 per cent among those treated for 25 to 30 months and 12.30 per cent among those with over 30 months' treatment. The difference between the first two-groups, although it falls short of statistical significance, is again highly suggestive.

The relapse rate over five years among 47 patients who were known to excrete bacilli resistant to one or more drugs before or at any time during treatment was 10.77 per cent compared to 11.98 per cent among those whose bacilli were sensitive. The difference once again is not significant.

It is also interesting to mention that excluding relapses in initially abacillary group, there were 20 patients with bacteriological relapse. Of these, 15 were sensitive to all drugs before and during the course of treatment but 9 of these were found resistant to at least one drug at the time of relapse. Three were resistant both during treatment and at time of relapse. Pre-treatment sensitivity results were not available for the remaining two. Of these, one was sensitive to all drugs at time of relapse and the other resistant to INH and streptomycin.

Since regularity of treatment may also be a possible factor in the causation of relapse, data were also analysed from this point of view. For this analysis regularity during any period was defined as

$$\frac{\text{Drugs collected during the entire treatment period}}{\text{Drugs which should have been taken during the period}} \times 100$$

The patients were labelled as regular where this percentage worked out to 80 per cent or more. All others were classified as 'irregular'. The five year relapse rates in the regular and irregular patients were found to be 8.73 per cent and 13.40 per cent respectively, a difference which is not statistically significant.

The incidence of relapse was also analysed in relation to the extent of residual lesion. Where lesions cleared almost completely, the relapse rate over a period of 5 years was 6.0

per cent compared to 13.05 per cent where the residual lesion extended over one zone and 12.82 per cent among those where it occupied more than one zone. Although the difference between the first two falls short of statistical significance, it is highly suggestive.

Information was also collected about the incidence of relapse among patients whose residual lesions included what is commonly called 'cystic cavity' when treatment was completed. There were only 17 patients falling in this category and 3 of them relapsed within 5 years. It is not possible, however, to assess the prognostic significance of this factor with any confidence because of small numbers.

#### Discussion

When this analysis was taken in hand, all pulmonary tuberculosis patients irrespective of their original bacteriological status were included in the study. On the basis of an earlier study undertaken in 1954, it appeared that relapse rates among initially sputum positive and sputum negative cases were not significantly different. However, the present study has revealed considerable differences in the relapse rates in these two groups of patients. For evaluation of various factors possibly connected with relapse it would, therefore, be clearly untenable to combine two groups which have now been found to be so widely disparate. Further analysis has, therefore, been confined to bacteriologically proved cases. The total number of cases available for study was thus considerably reduced. One consequence of this was that some differences which are apparently important fail to attain statistical significance.

In the 1954 series comprising both bacillary and abacillary cases the cumulative relapse rate was 18.9 per cent over a 3 year period, whereas in the present study the cumulative rates up

to 3rd year are only 5.3 per cent for the initially bacillary cases and 2.4 per cent for the initially abacillary cases. It is natural to assume that this considerable fall is the result of more efficient treatment regimens than those in vogue 10 years back.

Among factors which do not seem to influence the frequency of relapse are age, sex, initial extent of disease and cavitation. Certain other studies (Segarra et al 1967), Phillips S.

(1964), S.E.M. Regional Thoracic Society 1973 have shown a higher risk of relapse in older age groups and among males. However, our earlier study (Sikand et al, 1959) had also not revealed any significant differences in relation to age, sex, initial extent of disease and cavitary status.

One factor which appears to have some relationship with the incidence of relapse is the extent of residual lesion at the time of stopping treatment. Where lesions cleared almost completely, the relapse rate over 5 years period were found to be 6.0 per cent compared to 13.05 per cent where the residual lesion extended over one zone and 11.82 per cent among those where it occupied more than one zone. Although the difference between the first two falls short of statistical significance, it is highly suggestive and if a larger number of patients were available for analysis, it may well be that this difference would become significant. This feeling is reinforced by the fact that our earlier study (Sikand et al, 1959) had also revealed that this factor had a significant effect on subsequent relapse. On the other hand a report from Research Committee of the South East Metropolitan Regional Thoracic Society of Great Britain (1973) states that no differences in relapse rates were found among patients with varying degrees of residual lesions.

An apparently anomalous finding was that

patients who had longer treatment had a higher relapse rate (13.77 per cent in 5 years) than those who had a shorter treatment (6.14 per cent). Although this difference is not statistically significant it is again highly suggestive. Obviously patients whose initial disease was minimal had in general a shorter length of chemotherapy. However, the lower relapse rates among patients with shorter treatment is not reflected in patients with initially minimal disease, as one would have expected.

To summarise, it has not been possible to prove conclusively that any of the factors studied has any definite association with relapse, though there is a strong suggestion that the extent of residual lesion at the conclusion of treatment and the total length of treatment may have some bearing on relapse rates.

#### REFERENCES

1. Phillips. S. (1964) *Amer. Rev. of Resp. Dis.* **90**, (1), 120.
2. Segarra F. et al. (1967) *Dis. of Chest*; **51** (1), 59.
3. Sikand, B.K., Pamra SP., and Mathur G P. (1959) "Proceedings of the Fifteenth International Tuberculosis Conference", Istanbul; **XXIX**, **4**, 728.
4. South-East Metropolitan Regional Thoracic Society, *Brit. J. Dis. Chest*, (1973), 67, 73.

# INTERPRETATION OF PHOTOFLUOROGRAMS OF ACTIVE PULMONARY TUBERCULOSIS PATIENTS FOUND IN EPIDEMIOLOGICAL SURVEY AND THEIR FIVE YEAR FATE

G.D. GOTH, A.K. CHAKRABORTY AND G.C. BANERJEE  
(From National Tuberculosis Institute, Bangalore)

## Introduction

The limitations of interpretation of radiological abnormalities on single photofluorograms without any other information are well known<sup>1,2,3</sup>. Moreover the assessment of abnormalities on single film as active or inactive pulmonary tuberculosis, cannot be done with any certainty. Accordingly, the estimates of prevalence of active abacillary pulmonary tuberculosis<sup>4,5</sup> in India, which are based on the interpretation of single photofluorograms, taken during mass surveys of sample population, may not be precise.

For accurate estimation of prevalence of active abacillary tuberculosis precise interpretation of radiological abnormalities is required. Study of future course of lesion on serial X-rays could be one of the methods of improving their interpretations. Springett<sup>6</sup> has also suggested that comparison of two or more chest radiographs of an individual taken at intervals of one to three months can provide more useful information than a single X-ray film. This procedure, if found useful, will provide more accurate epidemiological indices of abacillary tuberculosis in the community and reduce the errors in diagnosis and avoid wrong treatment. To find out whether the interpretation of abnormal shadows could be improved by comparing X-ray films of individuals taken at different intervals, the material from "Five Year Study of Epidemiology of Tuberculosis"<sup>7</sup> undertaken by National Tuberculosis Institute (NTI) has been analysed.

## Objectives

1. To study the proportion of abacillary patients of pulmonary tuberculosis (suspect cases) diagnosed on single miniature X-ray in the survey that could still be classified suspects on the basis of comparison of two or more serial X-rays taken at intervals of 1- to 2 years and results of tuberculin test and sputum examination.
2. To study the bacteriological status and death rates of suspects classified on the basis of comparison of two or more

X-rays and with knowledge of results of follow up examination.

## Material and Methods

The population of a random sample of 119 villages from three taluks of Bangalore district, South India was surveyed four times from May 1961 to July 1968. The three subsequent surveys were conducted at intervals of one and half years, three years and five years from the initial survey. The entire population was registered on individual cards and offered Mantoux test with 1 TU RT 23 with Tween 80. Persons aged five years and above were offered a 70 mm chest photofluorograms in the villages. The photofluorograms were initially read by two readers independently without the knowledge of results of any other examination. Persons whose X-rays were read abnormal by any of the two readers or technically inadequate and having physical inability to come for X-ray were eligible for sputum examination. Two samples, one spot and the other overnight, were collected from each eligible person. The survey techniques for all the four surveys remained the same. No organised anti-tuberculosis treatment was available to this population during the study period and also patients diagnosed during surveys were not offered specific anti-tuberculosis chemotherapy.

### *X-ray reading*

The X-ray readers interpreted the photofluorograms as per the following code:

### *Normal*

N=No pathological abnormality.

*Abnormal pulmonary shadows considered to be of:*

A=non-tuberculous etiology

B=tuberculous etiology but judged inactive

C=tuberculous etiology possibly active

D=tuberculous etiology probably active

Disagreements on C and D readings between the two initial readers were referred to a third

reader who gave his interpretation after taking into consideration both the earlier readings (Umpire Reading).

*Joint Parallel Reading (JPR)*

All photofluorograms classified as C and D by two of the three readers were later on reviewed jointly by a panel of three X-ray readers. They compared the first survey X-rays with those taken on subsequent surveys. While reviewing these X-rays, the results of sputum examinations and tuberculin tests from all surveys, personal data of the individuals like age, sex and subsequent status e.g. dead or alive were also taken into account for interpreting the abnormal shadows. The interpretation of X-ray abnormalities by this method is termed as Joint Parallel Reading (JPR). Majority opinion was considered as final interpretation.

*Joint Umpire Reading (JUR)*

The photofluorogram of persons with C and D abnormalities interpreted by two readers at the first survey who were not followed up at subsequent surveys, were also read by the same panel of readers jointly among with full knowledge of results of initial examinations and personal data and subsequent status. Such an interpretation of single film of the first survey X-rays is termed as Joint Umpire Reading (JUR).

*Sputum examination*

All sputum specimens were examined by direct microscopy techniques and culture. Positive cultures were subjected to drug sensitivity and other identification tests. A culture satisfying all the criteria of human strain was considered positive for Mycobacterium tuberculosis. Sputa positive on direct smear but not confirmed by culture have been considered negative.

*Study population and coverages for various examinations*

The data from the 61,663 persons of first survey have been analysed for the purpose of this report. Excluding population in the 0-4 year age group, 52,355 persons aged five years or more were eligible for X-ray examination (Table 1).

Of these, 45,434 (86.8 per cent) were X-rayed. Out of 52,355 persons 5,989 were eligible for sputum examination, but sputa of 5,284 (88.2 per cent) could be examined. X-ray and sputum examination coverages in different age groups in both sexes varied from 81 per cent to 91 per cent. Out of 45,434 persons, 43,903 were without BCG scars. Among them, on the interpretation of single film, X-rays of 590 persons were judged to have active tuberculosis abnormalities (initial CD) and 4,521 other abnormalities (AB). Sputum specimens of 128 of the initial CD, (21.7 per cent), and 50 of AB, were positive on culture for Mycobacteria (tuberculosis cases). The remaining 462 CD (initial suspects) and 4,471 ABs were culture negative. Of the 590 initial CD the follow up X-rays of 118 (20.0 per cent) persons, 43 sputum positive cases and 75 initial suspects were not available for comparison for reasons not examined or dead and X-rays of two more persons could not be traced. In all, one or more follow up photofluorogram of 470 persons with initial CD abnormalities were available for JPR.

**Results**

*Joint parallel reading of radiologically active cases of tuberculosis (CD) at first survey by two readers independently (initial readers)*

X-rays of 470 persons, 85 sputum positive cases and 385 initial suspects, were reviewed by the JPR method. X-rays of all sputum positive cases were confirmed as CD. Of the 385 initial suspects, JPR classified 85 (22.1 per cent) as CD (JPR suspect), 246 (63.9 per cent) as AB

TABLE I

*Eligible for X-ray and sputum examination and coverages at first survey*

	Eligible	Examined	Coverage
X-ray examination	52,355	45,434	86.8
Sputum examination	5,989	5,284	88.2

TABLE II

*Initial radiologically active cases of pulmonary tuberculosis\* by sputum status at first survey and by subsequent examination*

Subsequent follow up examinations	Total	Culture positive	Culture negative
Note done	118 (20.0)	43	75
Done	472** (80.0)	85	387**
Total	590** (100.0)	128	462

\*Initial CD abnormalities on single photofluorogram interpreted by two independent readers.

\*\*Follow up X-rays of 2 persons not traced. Figures in parenthesis are percentages.

TABLE III

*JPR and JUR interpretation (joint reading) of initial suspects of first survey*

Interpretations procedure	O	AB	CD	Total
JPR	54 (14.0)	246 (63.9)	85 (22.1)	335 (100.0)
JUR	10 (13.3)	40 (53.3)	25 (33.4)	75 (100.0)
Total	64 (13.9)	286 (62.2)	110 (23.9)	460 (100.0)

and 54 (14 per cent) as normal (Table 111). Thus, in all out of 470 initial CD X-rays that could be reviewed by JPR only 170 (36.2 per cent) were confirmed as CD.

Of the 25 initial suspects with cavity, JPR classified only eight as suspects, five of them with cavity (Table IV).

Out of 246 initial suspects which were classified AB by JPR, there was agreement between initial reader and JPR in 233 (94.7 per cent) with regard to presence or absence of cavity; for the 85 JPR suspects such agreement was in 78 (91.8 per cent).

Among the 30 initial suspects with lesion extending over more than three zones, JPR classified only nine as suspects, eight of them with more than three zone involvement (Table V). Among 246 initial suspects classified AB by JPR, the agreement was in 231 (93.9 per cent), and out of 85 JPR suspects in 82 (96.5

per cent). Thus agreement with regard to presence of cavity and extent of lesion was good between initial reader and JPR, but not with regard to etiology.

*Joint umpire reading for X-rays of initial CD of first survey*

There were 118 persons who could not be examined after the first survey. They were classified as CD by the Initial Readers on single picture interpretation (Table II). Of these 43 were sputum positive and 75 sputum negative. Their initial X-rays were reviewed by JUR method. Of the 75 sputum negative persons, X-rays of 25 (33.4 per cent) were confirmed as CD by JUR (Table III).

*Fourth survey status of JPR suspects as compared to that of the initial suspects*

*Sputum status and crude mortality*

Out of the 85 JPR suspects, 20 (23.5 per

TABLE IV

*Correlation between initial reading and JPR on cavity status among initial suspects of first survey*

Interpretation by JPR		Initial CD interpretation		
		No cavity	Cavity	Total
Normal	No lesions	54	—	54
AB	No cavity	224	8	232
	Cavity	5	9	14
	Total	229	17	246
CD	No cavity	73	3	76
	Cavity	4	5	9
	Total	77	8	85
Grand total		360	25	385

TABLE V

*Correlation between initial reading and JPR of extent of lesions among initial suspects of first survey*

Interpretation by JPR		Initial CD interpretation		
		1—3 zones	More than 3 zones	Total
Normal	No lesions	54	—	54
AB	1—3 zones	221	11	232
	> 3 zones	4	10	14
	Total	225	21	246
CD	1—3 zones	74	1	75
	>3 zones	2	8	10
	Total	76	9	85
Grand total		355	30	385

cent) were dead and 65 (76.5 per cent) were alive for 5 years. Sputa of 55 persons could be examined at the fourth survey; 14 (25.5 per cent) of them were positive (Table VI).

Out of 385 initial suspects followed up, 54 (14 per cent) had died and 331 (86 per cent) were alive for 5 years. Sputa of 264 persons were examined at fourth survey; 19 (7.2 per cent) were positive.

*X-ray status of the initial suspects by JPR at IV survey*

Out of 85 JPR suspects, by the fourth survey, 44 were either dead or sputum positive or sputum not examined. Of the remaining 41 sputum negative JPR suspect cases 37 were X-rayed at IV survey, X-rays of 6 of these were read as normal, 13 as AB and 18(48.7 per cent) as CD by JPR (Table VII).

TABLE VI

*Suspects of first survey by mortality and sputum status at 5th year*

Status at 5th Year		JPR confirmed suspects	Initial suspects
Death		20 (23.5)*	54(14)*
Sputum examination not done		10	67
Sputum examined	Positive	14 (25.5)**	19 (7.2)**
	Negative	41 (74.5)*	245 (92.8)**
Total		85	385

\*Percent out of total suspects

\*\*Percentage of the total sputa examined

TABLE VII

*Fourth survey X-ray status of suspects of the first survey remaining abacillary at 5th year*

X-ray status at IV survey (by JPR)	JPR confirmed suspects (CD)	Initial suspects (CD)
Normal	6 (16.2)	70 (32.3)
AB	13 (35.1)	125 (57.6)
CD	18 (48.7)	22 (10.1)
Total X-rayed	37 (100)	217(100)
Not X-rayed	4	28
Total sputum negative	41	245

Of the total 385 initial suspects of the I survey, sputa from 264 persons were examined at the fourth survey; 245 of them were negative. Of these sputum negative persons 217 were X-rayed at IV survey, 70 of them (32.3 per cent) were classified as normals, 125 (57.6 per cent) as AB and 22 (10.1 per cent) as CDs on JPR. Thus, X-rays of 48.7 per cent of the JPR suspects remained JPR suspects even at the end of 5 years while among the initial suspects 10 per cent were classified as suspects at IV survey.

*Incidence of culture positive cases among initial suspects of I survey during 5 years follow up*

The incidence rate of bacillary disease among 85 JPR suspects during 5 years period was 112.1 per thousand person years (Table VIII); during the initial 1½ years it was 210.5 per thousand person years. For the total 385 initial suspects, incidence rate of abacillary disease in 5 years was 29.9 per thousand person years and during the initial 1½ years it was 48.6 per thousand person years. The incidence rate was higher during initial one and a half year among both JPR and initial suspects. The ratio of incidence of bacillary disease between initial and JPR suspects at one and half period of observation as well as at 5 years remained same.

### Discussion

Review of miniature photofluorograms classified to have active or probably active

abacillary tuberculosis on the basis of single film taken during initial survey and their comparison with those taken during repeat survey has once again underlined the limitations of interpretations of single photofluorograms. It has also indicated the probable extent of error in the estimates of prevalence rates of abacillary pulmonary tuberculosis when these are based on the interpretation of miniature films without other information or follow up.

Out of 460 sputum negative patients classified to have active tuberculous lesion on initial single photofluorogram, only 110 were confirmed by the joint reading procedure. Agreement between initial and joint readings was high with regard to cavitory status and the extent of lesion, but was very low with regard to etiology and activity of the lesion (Tables IV and V). Thus even diagnosis of tuberculosis with cavitory or extensive disease, on single picture, is often unreliable.

Comparison of fate of persons classified as suspect cases on the basis of initial X-ray alone with that on JPR is an additional evidence of over reading of abnormal X-ray shadows on single film. Among 460 initial suspect cases of 1st survey 97 (20.7 per cent), and of the 110 suspect cases of joint reading 34 (31 per cent), (Table not presented) were dead in five years. The crude mortality among suspect cases confirmed by joint reading was about one and a half times that of the total initial suspects. Secondly, the proportion of JPR suspects whose sputum had become positive at the

TABLE VIII

*JPR and initial suspects of first survey by incidence of culture positive cases over five years*

		No. of initial suspects	Period of observation (in person years)	No. of incidence cases	Rate per 1000 p.y.
Based on 1st 1½ year follow up	JPR suspects	85	114.0	24	210.5
	Total initial suspects	385	514.5	25	48.6
Based on 5 years follow up	JPR suspects	85	330.0	37	112.1
	Total initial suspects	385	1507.25	45	29.9

fourth survey was about three times that among the total initial suspects. Further, at the fourth survey, as compared to 49 per cent of the JPR suspect cases, only 10 per cent of the total initial suspect cases were classified as suspect cases. It could be inferred that many of the initial suspect cases were not active abacillary cases of pulmonary tuberculosis, while those classified on JPR were mostly active abacillary cases. The comparative reading of X-ray with the other information did help in assessment of activity and etiology of the lesions. Thus the classification of active abacillary pulmonary tuberculosis is best made with the knowledge of the results of available initial and follow up investigations. It may be argued that the comparison between initial and JPR interpretation is biased in favour of JPR method. Among 50 sputum positive persons with X-ray abnormality classified as AB by two independent readers initially, only 29 were judged to have CD abnormality and 19 were still classified normal (tables not presented) despite the fact that they were all sputum positive. However, for a proper comparison of the two methods it may be necessary to have an independent follow up examination after initially establishing the diagnosis by the two methods separately.

The estimates of prevalence of abacillary pulmonary tuberculosis on the basis of single photofluorogram without any follow up are likely to be over gross estimates. At the initial survey, on the basis of interpretation of single film, photofluorograms of 460 persons in a total population of 43,903 aged five years and above were judged to have active abacillary pulmonary tuberculosis. Out of these, only 110 were confirmed to have suspect disease by joint reading. In addition to these, if films of 4,471 persons judged to have non-tuberculous or inactive tuberculous abnormalities, but sputum negative, were also reviewed by JPR method, then the lesions in some of them might have been assessed as active abacillary tuberculosis. The incidence of bacillary cases among persons with AB abnormalities was reported to be 0.3 per cent per year<sup>7</sup>. At this rate, the total number of new cases, that can arise among 4,471 persons with AB abnormality, would be about 67, in five years. Even if it is considered that these 67 cases would have been classified as CD at the first survey on the basis of JPR then too, the total number of abacillary cases would be at the most 177 (110+67) i.e., about one third of the prevalence of 460 on the basis of single films. Thus, the prevalence rates of active abacillary pulmonary tuberculosis in India which are widely used appear to be about 3 times the actual estimates.

In the "District Tuberculosis Programme in India where mass miniature radiography is used, the procedure of diagnosis of pulmonary tuberculosis on single film read by one medical officer is in vogue. In the light of the material reported here it is hypothesised that there may be considerable over-diagnosis of active pulmonary tuberculosis leading to the over-treatment of inactive tuberculous shadows and wrong diagnosis of other radiological abnormalities and their improper treatment. However, this hypothesis has to be carefully investigated. How far follow up investigation, at what intervals and for how long, can improve the diagnostic efficiency of the X-ray active abacillary tuberculosis in the district tuberculosis programme, and what are the operational problems of following this procedure may be the topic of another study.

### Summary

Photofluorograms of persons with active pulmonary tuberculous lesions at the first survey of a "Five Year Study of Epidemiology of Tuberculosis" were reviewed along with photofluorograms of subsequent survey and results of other initial and follow up examinations.

On the basis of interpretation of single miniature film taken at initial survey, the lesions in 590 were read as tuberculous and active and the sputa of 128 persons were positive and that of remaining were negative.

Of the 460 abacillary cases reviewed, 110 (24 per cent) were confirmed. The remaining miniature films were assessed as normals, non-tuberculous or inactive tuberculous. The prevalence estimates based on the review was one third of that based on the interpretation of single photofluorogram.

Of the 460 persons, 385 were re-examined at subsequent surveys. The abnormalities in 85 were confirmed as active tuberculosis. The rates of incidence of bacillary disease, mortality and those continuing to remain active abacillary were higher among the 85 persons as compared to those among the total 385.

The interpretation of the radiological abnormalities on the basis of comparison with the follow up miniature film, along with the knowledge of results of other examination seems to be more reliable.

This review shows that diagnosis of pulmonary tuberculosis on the basis of a single X-ray as practiced widely in India leads to considerable over diagnosis. This is so even for those

sputum negative patients who are considered to have abacillary disease with cavity and extensive lung involvement.

#### ACKNOWLEDGEMENTS

The authors are grateful to the Technical Co-ordination Committee of the National Tuberculosis Institute, for helpful suggestions and valuable comments and particularly to Mr. S.S. Nair, Senior Statistical Officer for his guidance, to the staff of X-ray and Statistical Sections and to Miss Indira Bai for secretarial help.

#### REFERENCES

1. Yerushalmy, J., Harkness, J.T., Cope, J.H. and Kennedy, B.R. (1950). *Amer. Rev. Tuberc.* 61, 443.
2. Raj Narain and Subramanian, M. (1962). Proceedings of the XIX Tuberculosis and Chest Diseases Workers' Conference, Bangalore, 64-76.
3. Growth-Peterson, E., Knudsen, J. and Wilback, E. (1959). *Bull. Wld. Hlth. Org.* 21, 5.
4. Indian Council of Medical Research (1955-58). *Tuberculosis in India* : I.C.M.R. Special Report Series No. 34.
5. Raj Narain, Geser, A., Jambunathan, M.V. and Subramanian, M. (1963). *Ind. J. Tub.*, X, 85.
6. Springett, V.H. (1968). *Bull. Int. Un. Tuberc.* Vol. XLI, 125-129.
7. National Tuberculosis Institute, Bangalore. Five Year Study of Epidemiology of Tuberculosis in a Rural Population of South India - sent for publication.
8. Nagpaul, D.R. (1967). *Ind. J. Tub.* Vol. XIV, 186-198.

## TUBERCULOSIS AND DIABETES

D.C. LAHIRI AND P.K. SEN  
(From B.C Roy Research Institute, Calcutta)

It is well known that diabetic patients suffer more from tuberculosis than the non-diabetic population in a community. It is also known that diabetes is mainly a disease of the older age group. From the National Sample Survey (1) and a number of other studies it has also been recognised that pulmonary tuberculosis is more frequent in the older age groups.

Tables I & II are presented here-under showing the prevalence of diabetes and tuberculosis in relation to age (2, 3, 1).

As both the diseases are more frequent in older age group, it can be reasonably assumed that there may be a concentration of both the diseases in the older persons.

TABLE I

*Prevalence of diabetes in India and abroad in general population*

Place	Year	Author	Age group	Prevalence o/o
<i>India</i>				
Delhi	1966	Anuja et al	Of all age groups	7.6
Chandigarh	1966	Beny et al	” ”	1.53
Pondicherry	1966	Dalton et al	5 years and above	0.7
Lucknow	1964	Ganguly et al	Of all age groups	2.3
Calcutta	1973	Mukherjee et al	Of all age groups	12.7
Bombay	1963	Patel et al	20 years and above	2.36
Hyderabad	1966	Rao et al	10 years and above	1.5
Cuttack	1970	Tripathy et al	Of all age groups	12.67
Ahmedabad	1970	Gupta et al	5 years and above	2.84
<i>Abroad</i>				
Argentine Republic	1967	Cordnet et al	Of all age groups	12.5
New Zealand	1967	Bearen et al	” ”	10.5
Ottawa, Michigan				
U.S.A.	1947-48	W.H.O. Survey	Adults	0.4
Oxford, Mass, U.S.A.	1947	” ”	Adults	1.99
Ontario, Canada	1951	” ”	Of all age groups	1.22
Destock, U.K.	1957-58	” ”	” ”	2.39
New Castle, U.K.	1960	” ”	” ”	0.95
Fowfar, Scotland, U.K.	1962	” ”	” ”	0.96
Habstead, Essex, U.K.	1961	” ”	” ”	1.25

TABLE II

*Prevalence of pulmonary tuberculosis in relation to age in Calcutta area (per 100)**Age in years*

	5-14	15-25	25-34	35-44	45-54	55 and above
Male—	0.622	1.172	1.911	2.052	3.110	4.457
Female—	0.707	1.069	1.821	2.331	3.906	5.919

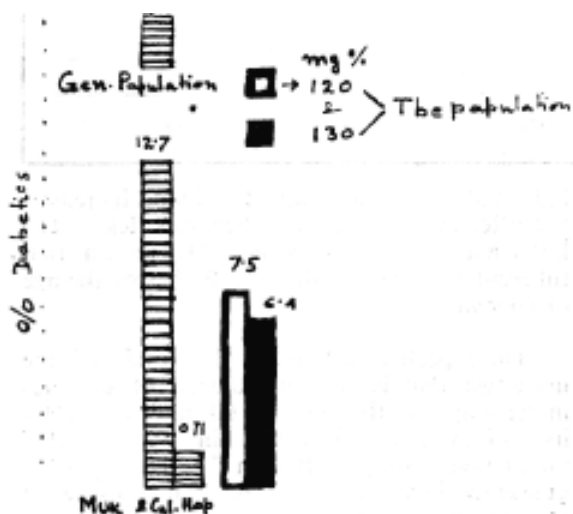


FIG. I

The object of this study is to determine the prevalence of diabetes in a tuberculous population and to compare this rate with that in general population.

### Material and Method

All the 875 patients admitted serially into K.S. Ray T.B. Hospital, Jadavpur, Calcutta, during the period from 18th June, 1971 to 30th April, 1972, were accepted for this study. Among them males were 769 or 88 percent and females were 106 or 12 percent. The diagnosis of Tuberculosis was made by sputum tests, x-ray and clinical examination.

Sputum tests were made by collecting 24 hours' sample in all cases. Microscopy of direct smear and that of concentrated materials obtained both by acid and alkali methods was made, Ziehl-Neelson's method of staining was used. A sample was cultured for TB on Lowenstein-Jensen media and observations of growth were made from 7th day till 2 months.

X-ray study was made by using large films in all cases.

A board of specialists considered all the findings in regular weekly conference and made the final diagnosis.

The diagnosis of Diabetes was made by post prandial blood sugar estimation and test of sugar in urine.

A sample of venous blood in each case was collected exactly two hours after normal lunch consisting of Rice, Potatoe, Dal, Vegetables, Fish, Chatneys and Sweets etc. amounting to an average of : Carbohydrates 230 grams., Protein 40 grams, and Fat 37.5 grams, total Caloric value was 1600 approximately. Blood sugar was estimated by Folin and Wu method (4) with Photo-electric Colorimeter.

The Urine was also collected 2 hours after lunch and qualitative test by Benedict's solution was made. A rough estimate of the percentage of sugar present in the urine was also made as 'low', "moderate" and "high" from the extent of changes in the colour of the precipitate from blue to green, yellow and brick red.

It may be seen that comparatively the number of females is much less than that of the males; males 769 and females 106. This is due to the fact that the number of beds in the hospital for females are much less than those of the males.

The data show that the males suffered, more from diabetes than the females—8 per cent and 5 percent respectively. A peculiar finding is that the females suffered less during younger ages but more after the age of 60 years.

In our study there was no case of diabetes in 14 to 19 years age group. The frequency of diabetes increased along with the advancing

TABLE III

*Age-wise distribution of Diabetes (121 mg% and more of sugar in blood) in Males and Females*

Age groups	Male			Female			Total	
	Total	Diabetes	%	Total	Diabetes	%	Diabetes	%
14—39	296	10	3.5	51	1	1.9	11	3.1
40—59	418	46	11	40	2	5	48	10.4
60 & above	65	5	8	15	2	13	7	8
	769	61	8	106	5	5	66	7.5

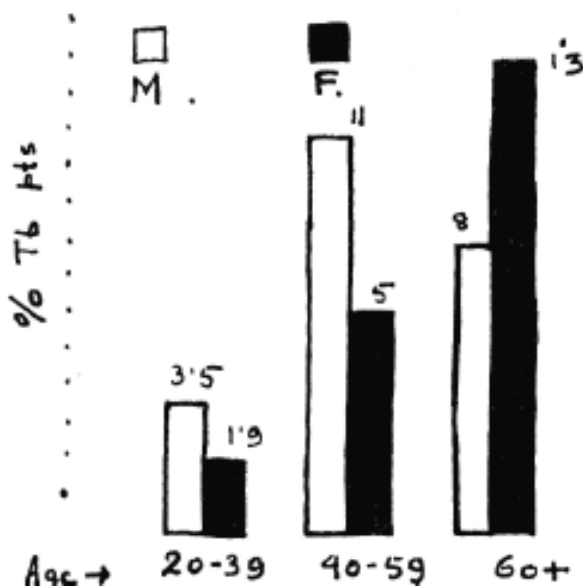


FIG. 2

age till 59 years. Thereafter there has been a drop in the case of males but not so in the females.

As there may be some differences of opinion in the criteria of diagnosis of diabetes on blood sugar levels, Table IV and Fig. III are given here-under showing the distribution of diabetic cases according to blood sugar among tuberculous patients. This may help the readers in accepting diabetes according to their own interpretations.

The data also show that with increasing age the rates and the severity of diabetes as

indicated by sugar content of blood increases, but after 60 years the rate becomes less. The latter may be due to a possible reason that tubercular diabetics die mostly before the age of 60 years.

The expected pattern of the result of the urine test, that is, the prevalence of diabetes increasing upto the age of 60 and thereafter its diminution is found in "low" and "moderate" groups. But, in the "high group" gradually increasing rate is maintained even after the age of 60 years.

It should be interesting to note the comparative value of blood and urine sugar tests in the diagnosis of diabetes in this tubercular population. For this purpose Table V and Fig. IV are presented below.

There is no case where urine test proved positive but blood test was less than 121 mg percent. Most interesting finding, however, is that in the higher age group of 40 years and above 24 out of 55 or 43.6 percent cases and in the lower age group than 40 years, 3 out of 11 or 27.2 percent cases will be missed if the diagnosis of diabetes is dependent on urine test alone.

### Discussion

It is common knowledge that diabetes predisposes to tuberculosis. It is, therefore, expected that the prevalence of diabetes in a group of tubercular patients will also be higher than that in non-tubercular group. This study was undertaken to determine how much this difference is. For this purpose post-prandial blood sugar and urine sugar were estimated

TABLE IV

*Age-wise distribution of diabetics according to blood sugar level among tuberculosis patients*

	Age in years	20-29	30-39	40-49	50-59	60 & above	Total
	Total No. of TB cases	122	191	261	197	80	851
Potential Diabetes	Blood sugar (mg%) 110-120	2(1.6%)	2(1%)	5(1.9%)	7(3.5%)	2(2.5%)	18
	121-130	Nil (-)	1(0.5%)	4(1.5%)	5(2.5%)	Nil (-)	10
	131-140	Nil (-)	Nil (-)	Nil (-)	2(1.0%)	Nil (-)	2
Diabetes	141-160	1(0.8%)	1(0.5%)	3(1.1%)	4(2.0%)	2(2.5%)	11
	161-180	Nil (-)	1(0.5%)	3(1.1%)	2(1.0%)	1(1.2%)	7
	180 & above	1(0.8%)	6(3.1%)	14(5.3%)	11(5.5%)	4(5.0%)	36
	Total	2(1.6%)	9(4.6%)	24(9.0%)	24(12.0%)	7(8.7%)	84

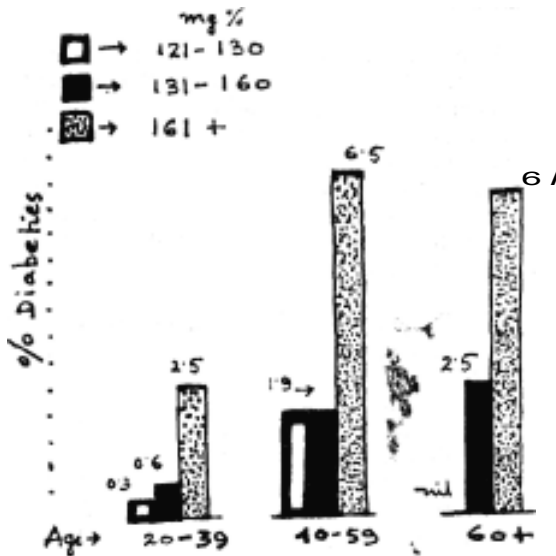


FIG. 3

in 875 serially admitted tubercular patients hospitalised during 1971-72, and the rates were compared with those in normal population as determined by others.

In presenting such a comparative finding the authors met with two important difficulties

viz. the level of blood sugar indicating diabetes and great differences in the rates of diabetes determined by other workers even in the same area. Some regarded more than 121 mg per cent, but WHO (5) recommended 130 mg per cent as indicative of diabetes. In the general population the rates recorded differed from 0.71 percent (6) to 12.0 percent (7) as shown in Table IV.

In many such studies age-groups were not quite well recorded which is obviously important for any comparative study. We have accepted the diagnosis of diabetes when post-prandial blood sugar level is 121 mg percent or more mainly to facilitate comparative study. To minimise these difficulties and to let the readers accept any criterion for his interpretation, we have also classified the tubercular patients in groups according to several blood sugar levels and ages.

Accepting all age-groups together and 121 mg percent and more blood sugar level as indicative of diabetes, the prevalence of the disease is 7.5 percent in this tubercular population. Accepting 130 mg percent and more as indicative of diabetes, this rate proved to be 6.4 per cent. This rate appears to be both higher and lower than that found in normal

TABLE V

*Distribution of patients according to urine positiveness in different age groups*

Range of age	Total No. of T.B. cases (blood sugar—121 mg%+)	Number of diabetics	Number of urine positive cases
20—39	313	11 (3.5%)	8 (2.5%)
40-59	458	48 (10.4%)	26 (5.6%)
60 and above	80	7 (8.7%)	5 (6.2%)

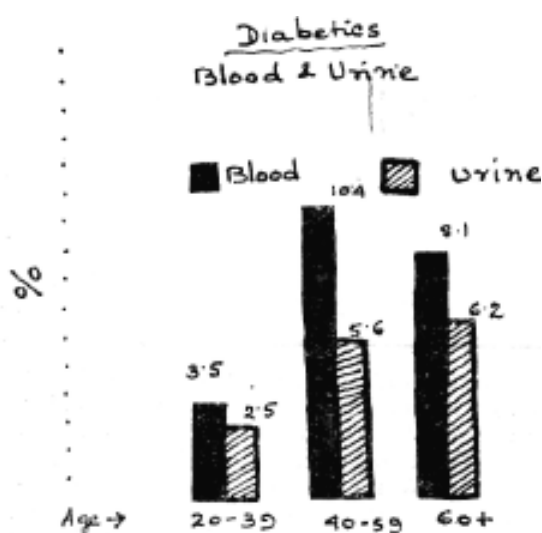


FIG. 4

population as shown previously in Table (I) and somewhat higher than 4.25 percent detected by Deshmukh (8) in Bombay.

Our findings generally tallied with the expectation that the rate of diabetes will increase with increasing age. But after the age of 60 years this trend was reversed. This was also found in normal population by Mukherjee and others (7). It may be reasonable to assume that persons suffering from both the diseases die earlier and will be less after the age of 60 years. Urine sugar tests also showed the same trend of increasing incidence with age till 60 years and then a fall in the "low" and "moderate" sugar level groups, but among those with "high" level such a fall after 60 years was not noticed.

It should also be important to note that with urine test alone 43.6 percent cases of

diabetics were missed in the older and only 27.2 percent in the younger age-groups.

Though the prevalence rate of diabetes in this group could not be compared well under conditions stated earlier, a rate of 6.4 percent or 7.5 percent appears to us quite high. As the prevalence rate of tuberculosis according to National Sample Survey in the age groups of 45-54 years is 3.1 percent, and in 55 years and more is 4.5 percent there will be a concentration of both these consuming diseases in the community in the older age group.

### Summary

With the object of finding the rate of prevalence of diabetics in tubercular patients, 875 such patients serially admitted in a hospital were investigated by post-prandial blood sugar estimation on their admission. Sixty-six or 7.5 percent cases among them had blood sugar level more than 120 mg percent, but only 15 or 1.7 percent gave history of diabetes at the time of admission.

*Distribution of 875 tubercular patients in accordance with blood sugar content is given below:*

Less than 120 mg%	809	(92.4%)
More than 120 mg%	66	(7.5%)
More than 130 mg%	56	(6.4%)
More than 140 mg%	54	(6.2%)
More than 160 mg%	43	(4.9%)

According to WHO criterion of 130mg percent and more, 6.5 percent should be regarded as the prevalence rate. Potential diabetics of 1 percent may be added to this if more than 120 mg percent is accepted.

Age-wise distribution of the diabetes showed that with the increase of age not only the frequency of diabetes increased, but there

was a definite shift towards more severe disease. The findings were as follows:—

*Distribution of diabetes in accordance with*

20—39 years.....	1.2%
40-59 ,, .....	5.4%
60 years and above	0.8%

Comparative study of diabetes in this tubercular community with that of the general population in the same area was not found feasible as results of studies made on general population by different workers in the same area varied greatly from 0.7 percent (Cal. Hospitals) to 12.7 percent (Mukherjee).

Comparative study of blood and urine sugar examination showed that there was no case where urine sugar proved positive but blood sugar level is below 121 mg percent. In fact, there was no case with urine sugar finding in the group whose blood sugar level ranged from 121 mg percent to 130 mg per cent. Amongst the tubercular patients having 121 mg percent and more content of blood sugar, urine sugar proved negative in 3 or 27.2 percent in the age group below 40 year and 24 or 43.6 percent in age group above 40 years. This appears to show that more cases of

diabetes will be missed in the older age group than the younger if only urine is tested for sugar.

REFERENCES

1. National Tuberculosis Sample Survey (1955 to 1958), *I.C.M.R.* Report.
2. Sathi, R.V.; Problems of Diabetes mellitus in India *Journal of I.M.A.* July, 1973, page No. 12.
3. WHO Technical Report series 1965 No. 310 (Diabetes mellitus) page 39.
4. Hawk's Physiological Chemistry, Edited by Bernard Loser, Fourteenth Edition—Published McGRAW—HILL BOOK COM-PANY—INC. New York 1965, page No. 1052.
5. WHO Technical Report Series 1965, No. 310, page 12.
6. Editorial; *Indian Journal of Tuberculosis*—1971 Vol. XVIII page No. 2.
7. Mukherjee A.B. et al—Epidemiological Survey of Diabetes Mellitus in a mixed population of Calcutta—*J.I.M.A.* Vol. 61 No. 1, July 1973 page No. 21.
8. Deshmukh, M.D. Pulmonary Tuberculosis & Diabetes, Proceedings of Eighteenth Tuberculosis & Chest Diseases—Workers' Conference, January, 1962, page No. 314.

# A STUDY TO EVALUATE THE CONTRIBUTION OF AN ADDITIONAL THIRD DRUG AS AN INITIAL SUPPLEMENT IN THE TREATMENT OF PULMONARY TUBERCULOSIS

S.P. PAMRA, B.B. SURPAL AND G.P. MATHUR  
(From New Delhi Tuberculosis Centre)

## Introduction

It is usually recommended that in previously untreated sputum positive cases, 3-drug regimens in initial stages of the treatment give better results than 2-drug regimens. There are other studies which tend to show that the advantage of the former over the latter is marginal.

In practically all trials where 3-drugs are compared with 2-drugs, the usual 2-drug combination is INH with thiacetazone or PAS and the third drug is streptomycin. Since streptomycin and INH are known to be a somewhat superior combination at least in the initial stages of the treatment, it is possible that in these trials the so-called superiority of the 3-drug regimen over the 2-drug regimen may virtually be the superiority of INH and streptomycin over the other regimens where INH is combined with PAS or thiacetazone.

In order to obviate this flaw, a study was planned to compare INH and streptomycin with a 3-drug combination, the third drug being thiacetazone. Thus streptomycin and INH were common to the two regimens.

## Material and Methods

All new patients reporting at the New Delhi Tuberculosis Centre from the domiciliary treatment area having radiographic evidence of pulmonary tuberculosis were considered eligible for inclusion in the study provided they fulfilled the following criteria :—

1. Age 15 years or more but not over 45 years.
2. No or less than two weeks' anti-TB chemotherapy before reporting at the Centre. To make sure that patients ineligible on this score were not inadvertently included in the study, inquiry regarding previous treatment was made twice, once before the intake and again 4 weeks after the start of treatment.
3. Sputum positive by direct smear.
4. Willing to accept tablets and injections.

5. Likely to remain in the area for at least one year, as ascertained by the area health visitor.

The presence of any of the following conditions made the patients ineligible for the study,

1. Patient moribund or too ill for domiciliary treatment.
2. Body weight less than 32 kg.
3. Pleural effusion obscuring more than one third of one lung field.
4. Patient known to be pregnant.
5. Non-respiratory tuberculosis, diabetes, leprosy or any other condition which was likely to lead to difficulty in domiciliary management.

To reduce the chance of inadvertent omission of any patient, a register was maintained in which the reason or reasons for exclusion were entered.

The intake of the patients was started on June 15, 1971. Patients were allocated either to the two-drug Regimen or to the Three-drug Regimen, by opening sealed envelopes in serial order.

The detail of the drug regimens are as follows:-

### 1. Two-drug regimen

Streptomycin one gram daily, 6 days in a week with INH 300 mg once daily for 7 days in the week for the first 12 weeks; thereafter INH 300 mg and thiacetazone 150 mg once daily till the 'target point'\* was achieved. INH alone was to be continued for 52 weeks after attainment of the 'target point'.

### 2. Three-drug Regimen

It differed from the Two-drug regimen only

---

\*The target point is defined as a stage when no cavity is seen in the pLain skiagram, lesions are stationary radiologically and sputum/laryngeal swain cultures have been negative for at least six months.

to the extent that for the first 12 weeks thiacetazone 150 mg daily was prescribed in addition to streptomycin and INH.

The entire treatment was carried out in the patients' homes. They were required to visit the Centre every 4 weeks to collect the drugs. Apart from routine defaulter action, health visitors paid two surprise visits to the patients' homes in every 4 weeks for pill counting and general supervision. For purposes of this study drug collection has been taken as an evidence of drug consumption. Facilities for streptomycin injection were provided at subsidiary injection centres within easy walking distance of all patients.

### Routine Investigations

#### (a) Radiographic Examinations

P.A. conventional size skiagrams were taken every 4 weeks till the 'target point' was reached. After attainment of the 'target point', a skiagram was taken on the completion of a further period of 12, 24, 40 and 52 weeks. Where deterioration was suspected, skiagram was repeated immediately.

All radiological assessments were made by an independent assessor who was not aware of the treatment regimen of any patient.

#### (b) Bacteriological Examinations

(i) Sputum was examined by direct smear and culture every 4 weeks till the 'target point' was reached and thereafter after a further lapse of 12, 24, 40 and 52 weeks. In case of deterioration or reversion of sputum, further examinations were carried out every 4 weeks. When a patient had no sputum, laryngeal swab was taken.

(ii) Sensitivity tests for streptomycin, INH and thiacetazone were carried out on all positive cultures before the start of treatment and at 24, 44, 48 and 52 Weeks as well as for any positive cultures thereafter.

(c) Weight was recorded at the start and at the end of every 4 weeks till 'target point' was reached.

(d) Examination of urine, routine and for urobilinogen.

(e) Haemoglobin, red cell, white cell differential counts of blood,

### Change of Chemotherapy

Treatment regimen could be changed only under the following circumstances :—

- (i) Major toxicity or serious intolerance that could not be controlled by temporary alteration of dosage or administration or anti-histamines.
- (ii) Radiographic deterioration but only if it was accompanied by positive sputum.
- (iii) Non-conversion of sputum upto 24 weeks. Sputum was considered as converted if two consecutive cultures at interval of at least 4 weeks were negative.

### Results

All the treatment was carried out in the patients' homes. Regularity of drug collection was uniformly high in both groups and was of the order of about 95 per cent. Regularity has been denied as 'drugs actually collected as a percentage of the amount that should have been consumed in any period'.

$$\frac{\text{Drugs Collected} \times 100}{\text{Drugs Prescribed}}$$

Drugs Prescribed

Of the 148 patients included in the study, 6 were found on later scrutiny to be ineligible for inclusion in the study in terms of the protocol. For another 19, the pre-treatment cultures were subsequently found to be resistant to one or more of the three drugs used in the study.

As all patients have not yet completed, twelve months' treatment, the results being presented are based on 24 weeks' treatment. Of the 123 patients included in the analysis, 59 were in the 2-drug regimen and 64 in the 3-drug regimen.

Table 1 shows the distribution of the patients in the two regimens in respect of age, sex, initial extent of disease and cavitation. As will be seen, patients in the two groups are almost similar in all respects except that the extent of disease in the 3-drug group was somewhat more than in the 2-drug group. This difference, however, was not significant and no standardization was done for presenting the results set forth in further tables. Nearly eighty per cent of the patients were males. In more than half of the patients disease extended to more than two lung zones and only about one sixth were non-cavitary. Nearly one-third of the patients had multiple cavities;

TABLE I

*Background information on cases included in the main analysis*

		Two-drug regimen		Three-drug regimen	
		No.	%	No.	%
Sex	Males	50	84.7	51	79.7
	Females	9	15.3	13	20.3
Age	15-24 years	27	45.8	29	45.3
	25-34 years	20	33.9	21	32.8
	35-45 years	12	20.3	14	21.9
Extent of disease at start	1 & 2 zones	31	52.5	27	42.2
	3 & 4 zones	26	44.1	30	46.9
	5 & 6 zones	2	3.4	7	10.9
Cavitation at start	None	10	16.9	12	18.8
	Single cavity	28	47.4	30	46.9
	Multiple cavity	21	35.6	22	34.4
Total Patients		59	100.0	64	100.0

Although patients were carefully questioned at the start regarding likelihood of their continued stay in the domiciliary treatment area, 22 patients, 12 in the 2-drug group and 10 in the 3-drug group, left the area before completion of 24 weeks, mainly for socio-economic reasons. Another 4 patients (1 and 3 in the two regimens respectively) became non-cooperative and stopped treatment.

Table 2 shows that the drug regimen had to be changed for 12 patients due to intractable toxicity. It is interesting to note that ten cases in the 3-drug group developed major drug toxicity as compared to two in the 2-drug group. Both patients in 2-drug group developed dizziness due to streptomycin within 4 weeks. In the 3-drug group, 8 patients developed dizziness due to streptomycin, five in the first four weeks, one in

4-8 weeks and remaining two in 8-12 weeks period. Two patients in 3-drug group developed toxic reaction to thiacetazone, one developing rashes within 4 weeks and the other nausea and vomiting during 4-8 weeks' period. High streptomycin toxicity seen in the 3-drug regimen involving concurrent administration of thiacetazone has been reported by other workers too.

Table 3 shows the results of bacteriological examination of successive stages during 24 weeks' treatment. It can be seen that at no stage does the 3-drug regimen show any advantage over the 2-drug regimen. The sputum conversion rates at 24 weeks are of the order of about 80 per cent to 85 per cent in either group and the observed speed of conversion too does not differ significantly in the two regimens. During the period of 24

TABLE 2

*Patients whose treatment had to be changed due to drug toxicity*

	Number of patients	Patients removed due to drug toxicity		
		Thiacetazone	Streptomycin	Total
Two-drug Regimen	59	—	2	2 3.4%
Three-drug Regimen	64	2	8	10 15.6%

TABLE 3

*Sputum conversion rates at successive examinations among initially drug sensitive patients*

		4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	
Two-drug Regimen	No. exmd.	53	51	48	47	45	44	
	Sputum Negative	No.	27	38	40	40	39	38
		%	50.9	74.5	83.3	85.1	86.7	86.4
	No. exmd.	55	52	50	44	43	41	
Three-drug Regimen	Sputum Negative	No.	26	32	36	34	35	34
		%	47.3	61.5	72.0	77.3	81.4	82.9

weeks, there was one reversion in each of the two regimens after sputum conversion.

There were 3 deaths during 24 weeks' treatment, all in 3-drug group. For purposes of table 3, these patients have been counted as if they had completed 6 months' treatment and remained unconverted.

Of the 6 patients in the 2-drug group who were still sputum positive at 24 weeks, 4 were still sensitive to all 3 drugs, one was resistant to streptomycin, and another to all 3 drugs. Of the 7 shown unconverted at 24 weeks in the 3-drug group, 2 were sensitive to all drugs and one was resistant to INH alone and the other one to both streptomycin and thiacetazone. The other three had died.

It must be mentioned that sputum conversion rates shown in table 3 have been calculated

after excluding patients whose treatment regimen had been changed due to intractable toxicity. This would not have mattered much if the number of such cases was nearly the same in both groups. However, since toxicity was more common in the 3-drug group, the actual results achieved show up the 3-drug group in an even worse light, if cases excluded because of toxicity are also taken into account.

Radiological assessment at 24 weeks is shown in table 4. Three cases in the 3-drug group had to be excluded from this table as their radiological assessment at 24 weeks could not be completed. It can be seen that radiological changes in the two groups run more or less parallel and no statistically significant differences are discernible.

There were 2 patients in the 2-drug group in whom radiological worsening was noticed

TABLE 4

*Radiological Assessment at 24 weeks*

	+3	+2	+1	No change	Worse	Dead	Total
Two-drug Regimen	7 15.9%	24 54.5%	11 25.0%	— —	2 4.5%	— —	44 100.0%
Three-drug Regimen	7 18.4%	23 60.5%	4 10.5%	1 2.6%	— —	3 7.9%	38 100.0%

during the 24 weeks period and 3 patients in the 3-drug group died during the same period. Under the terms of protocol, changes in drug regimen were not permissible for the first 24 weeks and hence all patients were continued on the original drug regimen.

It has been mentioned earlier that the pre-treatment cultures of 12 patients in 3-drug 1 regimen, and 7 in the 2-drug regimen were found resistant to one or more of the three drugs used. In the 3-drug group, eight patients had their pre-treatment cultures resistant to INH and 4 to INH as well as streptomycin, whereas in the 2-drug group, five were resistant to INH, one to streptomycin. Their treatment too was continued as per protocol and at the end of 24 weeks, no clear cut difference in the

behaviour of these cases was seen, though the number of cases is too small to draw any conclusions.

In conclusion, it can be said that interim results of 24 weeks' treatment in respect of speed and quantum of sputum conversion and emergent drug resistance in this study have failed to show any advantage in adding thiacetazone as third drug to INH and streptomycin in the initial stages of treatment in patients with bacilli initially sensitive to all three drugs. Indeed, if the slightly higher incidence of toxicity in 3-drug regimen also is taken into account, the observed results appear to be somewhat poorer than those in the 2-drug regimen.

## SOCIAL AND PSYCHOLOGICAL ASPECTS OF TUBERCULOSIS CONTROL PROGRAMME

TAHIK MIRZA

(From J & K TB Association, Srinagar)

Within a social process and ecological situation there are only two factors which determine the problem of tuberculosis and its control. These are:—

- (1) The attitude and the behaviour of the aggregate of infectious individuals.
- (2) The reaction of the community to this attitude and behaviour.

The former determines the quality and the quantity of tuberculosis, its level of transmission and thereby the nature of its morbid dynamics. This also determines the attitude of the patients towards a given tuberculosis control programme. The latter determines the nature of public reaction to the prevalence of the disease leading to intensification of efforts, leading to research, leading to formulation of the programme for the control of the disease. In other words, a programme to be effective has to be adaptable, to the changing social structures and -cultural mores of the community without losing its primary objectives. But it's not as easy in practice as it sounds because when a programme is introduced into a community which is not a part of the self of the community the latter tends to mould the contents of the programme in such a manner as to suit its characteristic bio-social personality. But when it finds the programme too rigid, the frustration of goal achievement leads to a variety of adaptive and mal-adaptive behaviours. The adaptive behaviours are being interpreted as indifference of the community, and mal-adaptive behaviours as the so called 'drug defaults.'

In fact in most of our studies social psychology of the symptomatics has not been sufficiently studied to understand the behavioural pattern of the individuals or the aggregate of individuals with infectious pathology of tuberculosis. Biologists "often use a term, the directionality of behaviour in the sense that most animal species have an in-built capacity "to approach an object which is relevant to its survival and avoid the object or stimuli which threatens. The former is approach behaviour and the latter avoidance behaviour. While the approach behaviour has been studied at the NTI while formulating the DTP, the avoidance behaviour has not been so

well considered. A study of this behaviour which is an in-built instinct of many creatures including humans may lead to a better understanding of the phenomenon of default and drift in the patients.

there is another aspect of this directionality of behaviour, and this is *community default*. In order to understand this aspect of default one either has to be a villager or one should be in a position to identify oneself with the village community. Sentimentally speaking, when you identify yourself with the rural community you also identify yourself with real India. India has about 80 per cent of its population and the villager is its real citizen. The experience is highly satisfying.

In a village community one has to be more careful in the sense that one wrong step on the part of the DTO or his associates may 'fix' the entire cluster of village community against the programme. Many people do not realise the amount of consultation which goes on in these communities, and every government office including the DTO and his staff is dissected to core. This is what happens in Kashmir,

Now with the present state of disparities between one treatment centre and another between the PHC and the DTC and between one PHC and other there is plenty of scope to fix the village community more against rather than for the programme.

The village communities today are becoming increasingly aware of their rights to check the efficacy of one treatment centre against another. With the present state of disparities between them there are enough opportunities for the cases to drift from one place to another.

In our health care system there is a large variety of organisations; some are popular strong and prestigious, others not so. This state is, as it appears, directly related to their case holding capacity, but it does not seem to be related to their capacity to convert a sputum positive case to sputum negative, because the strong organisations such as large hospitals and even chest institutes are more geared to the clinical and academic aspect of the problem of tuberculosis rather than the control of tuberculosis. These

two aspects are quite different and must not be confused with each other.

A strong organisation is one to which people report directly as well as are referred to by other smaller and weaker organisations. The DTC is stronger in this sense than the PHC because a large number of patients are referred to it by the PHCs and by general practitioners as well. One observes that patients tend to stick to the place where their diagnosis was made and treatment was initiated. In many areas neither the distance nor the cost of drugs is of prime importance; what is important is relief of their immediate suffering, and if properly motivated, long term goal achievement as well. This explains the phenomenon of siphoning off a large number of cases from the weaker to the stronger organisations, thus neutralising the concept of decentralised and integrated DTP. The directionality of our behaviour dictates that the DTC is recognised as a small specialised unit and the DTO more a specialist than a supervisor of the programme; only we do not recognise the fact. A developed DTC is better equipped than the PHC—better supplies of drugs, better diagnosis and treatment facilities. What is not being realised is the fact that the greater the social value of these institutions greater is the individual need for these centres. This explains the expansion of TB Hospitals and TB beds. For these reasons public demands motivate the governments in matters of allocation of funds with the result that large sums are allocated for smaller number of hospitalised patients and smaller sums at State level for very large number of domiciliary patients. Of the limited resources, if a large chunk is spent on the sentimentally valued objects, the natural result is thinning out of the facilities as we proceed from the centre to the periphery. And thus thinning out of their case finding capacities as well. Now since we cannot channelise the movements of the patients dictated by their directionality of behaviour as referred above, we will have to rechannelise the procedural aspect of the DTP to synochronise with the behaviour of the patients.

Lastly, there is the problem of tuberculosis itself. It is said that the perception of a problem is directly related to the amount of resentment and intolerance which the people express against it and it is also inversely related to the amount of tolerance in the community for the problem. Tuberculosis began to be perceived as a problem by the people when the National Sample Survey for the first time revealed in precise arithmetic terms its extent and its

prevalence in rural and in urban areas. Subsequently so much was done in the field of TB control programme that the like of which was never seen before or even after. It was envisaged then that what was available and what would be available in the course of future phased development schemes would be sufficient to attract a large number of symptomatics under the free-flow system and thus a large number of infectious cases would be detected by microscopy alone. Later several unexpected events and unprecedented population growth tended to deflect the content of collective thinking of our planners to other activities for the well being of the people. This perhaps explains the slow expansion and growth of the DTP and other health care facilities in the country. The most disturbing fact is that the patient-holding capacity of such centres began to deteriorate. Increasing default rates began to encourage the process of osmosis between the visible and the submerged portion of the iceberg and vicious circle was thus created. The multi-purpose workers at the multi-purpose PHCs are at present not effective enough to influence the faith-belief systems of the patients in favour of National Programme for the control of tuberculosis. The decision of the patient not to report for subsequent collection of drugs appears non-conformist and illogical to the doctor while the behaviour of the doctor and his efforts to retain the patient for the required duration appears equally illogical, inhuman and perhaps an encroachment of his rights.

The fact which is not being generally realised is that so long as a patient receives his treatment on correct lines he cannot be considered a defaulter from the public health point of view, regardless of the fact where he is being treated and by whom. Therefore unless the motivation techniques of the motivator are improved and all these centres of treatment in private as well as in public sector in the Indian as well as the Western system of medicines are involved in the entire programme there cannot be any progress in the DTP.

The important point is that the motivator must be accepted as a part of the 'self of the community. For, in the rural communities no one is considered more "alien" than a representative of the Government, quite often he is being taken as one of the huge variety of persons who periodically descend upon them and try to influence their decisions.

The motivators must maintain an explicit psychological relationship with the problems of

tuberculosis, the tuberculosis and the cultural mores of the community. To solve the situation like this there are only two ways.

- (i) Either the centre of attraction of the DTC i.e. its clinic is removed and the centre functions entirely as a supervisory body. But in this case a very large number of patients are likely to become submerged and thus get lost, or
- (ii) Put a portion of this nucleus at each PHC in the form of a multi-purpose worker who should not only look after the interests of the TB patients at the periphery and other treatment centres but also should help to maintain a liaison between the DTC on the one hand and the private practitioners on the other.

It is therefore absolutely necessary for these reasons that in addition to the usual Government officials there has to be one from the community, for the community and chosen by the Community.

### Conclusions

1. A degree of resentment against the problem of tuberculosis is necessary for the intensification of efforts on the part of the Government and the involvement of the whole community in these efforts. This can only be brought about when a state of awareness is created once again as it was done following the

last National Sample Survey. This is only possible by plotting date of incidence and prevalence of the disease repeating this procedure over points in time to establish a trend. The infector 'pool' must not appear as a stagnant pool.

2. The public interest in the programme is related to its goal achievement capacity. If this is not so then a variety of adaptive and maladaptive behaviours begin to operate which are social and psychological in nature rather than administrative or managerial.

3. The solution of the problem lies in:—

- (i) A representative of the community as multi-purpose worker would be placed at each PHC.
- (ii) Widening the scope of the DTP to such an extent as to involve as many practitioners as possible. Since it may not be possible at the Government level, the TB Associations should step in order to fill the gap.
- (iii) Improve the diagnostic and treatment facilities at the peripheral centre in remote areas rather than in capital town in order to synchronize the PHC and DTC activities.
- (iv) Periodic surveys so as to create a sense of awareness and to motivate the community to intensify its efforts.

## TWENTY-EIGHTH NATIONAL CONFERENCE ON TB & CHEST DISEASES

***The following are the Summaries of papers (except those published in full) read at 28th National Conference of TB and Chest Diseases held at Madras in January 1974.***

### Symposium on "National Tuberculosis Programme"

In the absence of Dr. N.L. Bordia, Dr. Viswanathan took the Chair in this symposium. Dr. Barua, the acting Tuberculosis Adviser to the Government of India, gave a review of the objectives of National TB control programme and some of the achievements upto December, 1973. He also referred to the tentative provision of the 5th Five Year Plan under which supply of anti-TB drugs and BCG vaccine would be centrally sponsored whereas the rest of the expenditure would be incurred by the states.

Dr. Gothi from N.T.I, reviewed the average achievements from District TB Control Programmes. Programme efficiency is currently working at 30 per cent. The main hurdles in the successful implementation of the programme were administrative and organisational problems, inadequate supervision and motivation and lack of interest on the part of P.H.I. personnel.

Dr. S.D. Maqbool analysed the causes of failure of District TB control programme in Punjab, Haryana & Rajasthan. The conclusions were that the state administration, district authorities and PHC staff were not taking requisite interest and DTC staff failed to elicit the necessary co-operation and help from the various authorities.

Dr. Deshmukh also referred to the shortfalls in achievements of the N.T.P. and reasons thereof. He emphasised the necessity of proper communication between workers at various levels. He gave a review of the work of 50 shibirs held in Bombay and Maharashtra and showed that such shibirs could add a lot to the achievements of the district control programme.

Dr. Mehrotra gave the Agra Demonstration Centre's achievements in rural tuberculosis control programme. Instead of leaving the work to PHC staff, he (at Agra) sends his unit and workers to each PHC once a week on fixed days. The yield is very high and the defaults very low. This method creates confidence in medical profession and the patients from rural areas.

Dr. Mirza suggested that a multi-purpose tuberculosis worker should be posted at each PHC and the general practitioners should be involved in the working of D.T.P. He also raised the question of suitable incentives for TB workers.

Mr. Menon from Nagpur Centre gave a review of D.T.P. work from 98 sub-centres and showed that inspite of best efforts the performance had been poor.

Dr. Visweswaraiah from Tumkur gave reasons for failure of D.T.P. in that district, the main cause being failure of P.H.I. to avail of the facilities offered by D.T.C. and to take proper and prompt action to check drug default by patients.

Dr. Vishwanathan thanked the various speakers and referred to the overall impression of the participants in the symposium that the national tuberculosis control programme may be theoretically ideally conceived but it had failed to deliver the goods so far.

If tangible and satisfactory results are to be achieved, it is essential to modify it in the light of the experience so far and for this purpose a high powered committee of experts should be set up by the Government of India, which should go into the causes of failure and suggest ways and means to improve the programme.

## PREVALENCE OF BACTERIOLOGICALLY CONFIRMED TUBERCULOUS MENINGITIS IN CHILDREN—A COOPERATIVE STUDY

BY

H.B. DINGLEY

Bacteriological confirmation of diagnosis of tubercular meningitis is very difficult in a large majority of patients and cytological and biochemical determinations are the two principal criteria of diagnosis. AFB could be demonstrated by direct smear in three specimens.

Of the 209 specimens of C.S.F. Cultures were contaminated in 74 or 35.4 per cent. Of the remaining 135, acid fast bacilli could be demonstrated in 31. Of the 31 positive cultures, 24 or 77.4 per cent were positive in Krischner's medium, 7 or 22.6 per cent with the Lowenstein Jensen medium and 5 specimens were positive both in the Krischner and the Lowenstein Jensen medium. Biochemical and cytological evidence was in favour of TBM in 112 or 80.7 per cent.

Five patients had a known familial source and two of these were excreting resistant bacilli. In spite of this, the bacilli isolated from C.S.F. of all the 31 cases were sensitive to standard drugs.

There was obvious correlation between positive bacteriology and total leucocytic and lymphocytic count and sugar content of CSF. The protein and chloride content apparently had no correlation.

## SOME OBSERVATIONS ON TUBERCULOUS MENINGITIS

BY

M. PRASAD

An analysis of 44 cases of tuberculosis meningitis from amongst 2,066 admissions (2.1 per cent) in 1973 was presented. Most of the cases were in 0-10 years age group. Signs of meningeal irritation were present in  $\frac{3}{4}$  of the cases. Other common symptoms were fever, convulsions and vomiting. Only 25 cases gave a tuberculin reaction of 10 mm or more. Tubercle bacilli were isolated from 5 cases only. No pyogenic micro-organisms were isolated from any case. Diagnosis was based on examination of CSF. Lymphocytosis with increased protein and decreased sugar contents were considered diagnostic.

## TUBERCULOUS MENINGITIS IN ADULTS AND ADOLESCENTS

BY

C.C. MUKHOPADHYA

Data relating to 63 cases of TBM (0.2 per cent of total hospital admissions) in the age group of 15-61 years were presented. In nearly half of the patients duration of symptoms was less than 21 days. Fever was absent in 11 cases. Presenting symptoms were bizarre and atypical signs of meningeal irritation were absent in 9 cases. Sixth cranial nerve involvement was seen in 7 cases. Other cranial nerves were involved much less frequently. In 2 cases spinal merrings alone were involved. In 31 cases, tuberculosis of some other organ was present concomitantly. Six of the 25 female cases were pregnant. TB were isolated from CSF in 7 cases only, the basis of diagnosis in the remaining being changes in CSF. There was no correlation between the degree of changes in CSF and clinical severity of the disease. Results of treatment were not satisfactory. Only 27 cases could be followed for 6.22 months and in five of these, there was a recurrence,

BY

S. MUTHUSWAMY

The paper dealt with 50 cases of TB meningitis treated in the Ramalingam Sanatorium from 1940 to 1970. Thirty of these pertain to the period 1940-50. Nearly  $\frac{3}{4}$  th had pulmonary disease including miliary lesions as well. TB were isolated from CSF in 40 per cent of the cases. Value of corticosteroids in addition to anti-microbial drugs in the treatment of TB meningitis was stressed. Whereas the mortality was only 3.5 per cent among those without neurological signs, it was 60 per cent when these signs were present.

#### **RESULTS OF TESTING WITH RT XXIII PPD-S AND PPD-B IN PERSONS HAVING SYMPTOMS SUGGESTIVE OF PULMONARY TUBERCULOSIS**

BY

M.L. MEHROTRA

A study was carried out to determine the value of multiple antigen testing in patients attending the Agra Training and Demonstration Centre.

Dual skin testing was found to be of little diagnostic value in typical as well as atypical mycobacterial infections

While multiple antigen testing was of marginal benefit in separating infected from the non-infected in children and young adults, it was not of much utility in adults who constituted a highly selected group.

For reasons of sensitivity and biological accuracy, the stabilized solution of one T.U. R.T. XXIII with tween 80 should be the method of choice for tuberculin skin sensitivity for identifying human type of mycobacterial infections, but the dividing line between positive and negative may be raised to 16 mm to one T.U tuberculin.

#### **RELAPSE AFTER SURGERY OF PULMONARY TUBERCULOSIS**

BY

H.B. DINGBEY and K.L. SEHGAL

1,335 patients had surgical treatment in TB Hospital, Mehrauli from 1953 to 1972. Of these 1,223 could be followed (the remaining 112 died within one year of surgery) and 101 (8.2 per cent) relapsed. Nearly f of the patients who had a relapse were below 35 years in age. Most of relapsed cases were males and those whose post surgical stay was relatively short. Site, type and extent of the disease had an unfavourable influence on the frequency of relapse. Most of them had positive sputum at the time of surgery. Most of the relapses (63 out of 101) occurred in the first two years and thereafter the frequency declined steadily.

#### **THE INFLUENCE OF SOCIO-ECONOMIC CONDITION AND PHYSICAL ACTIVITY ON RELAPSE IN REHABILITATED PULMONARY TB PATIENTS**

BY

B. RAY

Five years follow up results of 585 arrested cases rehabilitated from 1958 to 1963 were presented. Relapse rate was 8.4 per cent in heavy manual workers and 7.6 per cent in those engaged in light work. Of a total of 48 relapses, 8 were in the first year of follow up, 18 in the second and 16 in the third year. Relapse rates were higher in patients with poor socio-economic status and unsatisfactory housing condition and in illiterates.

**TUBERCULOSIS PROVED ANEW TO BE DISEASE ON THE FAT METABOLISM  
WITH THE INFECTIVITY OF H 37 RV STRAIN OF TUBERCLE BACILLI ETC.**

BY

K.P. MALLICK

It was suggested that tuberculosis was associated with defect in fat metabolism. Treatment and prophylaxis by means of a lipoclastic enzyme was advocated.

**ANTIBODIES TO ASPERGILLUS FUMIGATUS IN SERA FROM HEALTHY  
INDIVIDUALS AND PATIENTS WITH CYSTIC FIBROSIS**

BY

K.L. SOBTI and BARDANA

Serum samples from 52 confirmed cases of cystic fibrosis and 67 controls were tested with labelled antigens isolated from *Aspergillus Fumigatus* and other frequently present lung pathogens i.e. *P. Aerugenose*; *H. Influenzae*; *Staphylococcus aureus*; *Canada Albicans*. Since exposure to *Aspergillus* is ubiquitous, all areas were found to contain antibodies against this fungus; however sera from patients with cystic fibrosis demonstrated significantly increased level of anti-bodies. This is probably due to impaired mucociliary mechanism and poor alveolar phagocytic activity in cases of cystic fibrosis.

The antigen binding observed was specifically inhibited by homologous aspergillus components but not by the other lung pathogens in cystic fibrosis. Precipitating antibodies were demonstrated in 22 of 52 (or 42 per cent) of the cystic fibrosis cases and 4 of the 67 controls.

**VALUES OF ABRAHAM AND MENGHINI NEEDLES IN PLEURO-PULMONARY  
BIOPSY**

BY

O.P. MITAL ET AL

Abraham's needle was used for pleural biopsy and Menghini's needle for pulmonary biopsy. Of the 122 cases of pleuro-pulmonary disease, 56 had pleural and 66 pulmonary biopsy. Of the 56 pleural, 49 had pleural effusion and 7 had pleural thickening. There were three failures in patients with effusion and in two with thickened pleural. Among 66 cases of pulmonary biopsy, 42 had solid lesions and 24 diffuse lesions. There were 8 failures, 6 in diffuse and 2 in solid lesions. In pleural biopsies, specific pathology was confirmed in 60-85 per cent. In pulmonary biopsy confirmation was 95 per cent in solid lesion and 75 per cent in diffuse lesions.

Complications occurred in 8 or (14.3 per cent) after pleural biopsy and in 17 or 25.7 per cent after pulmonary biopsy. All complications were mild, self-limiting and required no special treatment except one case of severe haemoptysis following lung biopsy in a case with diffuse lesions.

**THERAPEUTIC RESULTS OF A CLINICAL TRIAL WITH MATRONIDOZLE AND  
DIETHYL CARBAMAZINE IN 24 CASES OF TROPICAL PULMONARY  
EOSINOPHILIA**

BY

H.K. SINGH AND R.K. SINHA

Clinical trial with metronidazole (flagyl) and diethyl-carbamazine (D.E.C.) in a group of 25 patients of pulmonary eosinophilia showed no clinical cure with metronidazole, whereas 20 had complete cure and 4 marked improvement with diethyl carbamazine. 45 per cent of those treated with metronidazole revealed deterioration in all parameters, but they subsequently improved with diethyl carbamazine.

## **RADIOLOGICAL APPEARANCE OF INTRATHORACIC SARCOIDOSIS**

BY

O.P. MITAL AND A.S. SACHAN

Radiologically, intra thoracic sarcoidosis may lead to enlargement of hilar/mediastinal glands, pulmonary infiltration, a combination of both glandular and pulmonary lesions, post sarcoid fibrosis, clarification and cardiovascular changes. Glandular enlargement is the commonest, considerable, obvious and normally bilateral. It has to be differentiated from lymphoblastoma, lymphatic leukaemia, tuberculosis, fungal disease, protozoan infections, infectious mononucleosis, disseminated lupus erythematosus and polyarteritis nodosa. Unilateral enlargement is rare in sarcoidosis. A visible mass of paratracheal and bifurcation glands without bronchopulmonary glandular involvement is unlikely in sarcoidosis. Pulmonary lesions usually follow or accompany glandular enlargement and may be either miliary infiltration involving the whole of both lungs and individual nodule being about 0.5 mm in size or there may be wide spread nodulation in both lungs with individual foci not very sharply defined and average 2 to 3 mm in size. Occasionally pulmonary lesions may present an increased linear pattern with B lines.

In about 50 per cent cases both glandular and pulmonary lesions are present. There is enlargement of the bronchopulmonary glands with the larger, rather ill-defined nodules and increased linear striations.

Post sarcoid fibrosis is usually interstitial and bilateral but not linear-nodular as in the collagen type fibrosis. It is coarse fibrosis with thick striae and large and small bullae. Hila are pulled outwards and intrapulmonary vessels are straightened out. Pleural fibrosis is rare because sarcoid seldom attack the serous membrane.

Disturbance of calcium metabolism with hypercalcaemia and hypercalciuria may lead to Eggshell calcification of glands. Cardiovascular changes are rare and non-characteristic. Heart may be enlarged in size.

## **KVEIM TEST IN THE DIAGNOSIS OF SARCOIDOSIS IN INDIA**

BY

S.C. CHAKRAVARTY

27 patients suspected of having sarcoidosis were tested with Kveim antigen. The list was positive in 15 patients and negative in 12. Lung biopsy was positive in three of the 12 with negative Kveim test. The remaining 9 patients were diagnosed on the basis of clinical findings which were compatible with sarcoidosis, serum calcium, tuberculin negativity and therapeutic response to steroids. All the 15 Kveim test positive patients were negative to 1 : 100 dilution of O.T. The most important criterion of positive Kveim test is the presence of at least one epithelioid granulation in the biopsy material with or without giant cells.

Steroids depress the Kveim reaction and should therefore be stopped at least for 2 weeks before the test.

Kveim test gives false positive result in about 2 per cent. Similarly negative Kveim test does not rule out sarcoidosis. Recently affected patients have more chance of being Kveim positive.

## **SARCOIDOSIS**

BY

V.S. SELVAPATHY

Sarcoidosis is a rare disease of unknown etiology. The number of cases published are

**Ind. J- Tub., Vol. XXI, No. 2**

few. It is of importance in the differential diagnosis of chest diseases especially pulmonary tuberculosis.

X-ray chest shows enlarged hilar and paratracheal glands. It may also show miliary lesions or broncho-pneumonic patches in the lung fields or extensive fibrotic changes.

Clinical symptoms are comparatively less compared to the gross pathology as seen in the X-ray chest. Negative tuberculin test, positive epithelioid tubercle formation in the biopsy material either gland or Scalene nodule or Scalene pad of fat or lung or liver biopsy material, positive Kveim test, increased serum globulin and calcium and elevated serum alkaline-phosphatase help in diagnosis.

### **ETHAMBUTOL AND RIFAMPICIN IN THE TREATMENT OF RESISTANT CASES OF PULMONARY TUBERCULOSIS**

BY

O.P. MITAL ETAL

Twenty cases of chronic far advanced disease which had failed to respond to previous treatment with streptomycin, INH, PAS, thiacetazone, ethionamide, pyrazinamide and cycloserine were allocated to two drug regimens, Group A was given rifampicin, ethambutol and kanamycin while Group B was given rifampicin and ethambutol. They were all positive on direct smear and no sensitivity studies were carried out. Rate and percentage of sputum conversion by direct smear, similar in the two groups, were 50 to 60 per cent after two months, 80 to 90 per cent after three months and 100 per cent after four months, 10 per cent showed marked radiological improvement in both groups and cavity closure was obtained in 60 per cent and 50 per cent in groups A and B respectively.

No toxic reactions attributable to ethambutol were seen. Two cases developed liver toxicity due to rifampicin. One case of partial deafness due to kanamycin was also seen.

Bacterial reversion was seen in one case of Group A in the ninth month of treatment, 7 months after conversion. It was concluded that rifampicin and ethambutol are very effective in the treatment of pulmonary tuberculosis and addition of kanamycin did not influence the result.

### **COMPARATIVE STUDY OF EFFICACY OF BI-WEEKLY STREPTOMYCIN AND INAH REGIMEN AGAINST DAILY INAH, PAS THERAPY AFTER INTENSIVE CHEMOTHERAPY IN THE FORM OF STREPTOMYCIN, INAH AND PAS FOR FIRST TWO MONTHS**

BY

Y. RAJASEKHARA

100 patients of pulmonary tuberculosis were randomly allocated to two drug regimens : Biweekly streptomycin and high doses of INAH with pyridoxine hydrochloride (S.I.) and daily INAH and PAS (I.P.). All patients were given daily SM, INH and PAS for 2 months before allocation to the two regimens. Treatment for the first 4 months was indoors and domiciliary for the subsequent 8 months.

13 patients out of 48 in SI groups and 25 out of 52 in IP group were sputum negative to begin with. Results of 71 patients who completed 12 months treatment were presented. Regularity obtained was 78 per cent in the SI Group and 66 per cent in IP Group. 16 per cent in SI group and 27 per cent in IP group were highly irregular. The results of sputum conversion, gain in weight and radiological improvement were similar in both the groups. Two patients had to be withdrawn from SI group because of severe giddiness due to streptomycin.

## LUNG CYSTS

BY

O.A. SARMA

Ten typical cases of lung cysts were presented. Pathogenesis, symptomatology, radiological appearance, differential diagnosis and 4-5 years follow up were discussed. This condition considered rare previously is seen more frequently with increasing radiographic examinations of chest.

## CHEMOTHERAPY IN THE DISTRICT TUBERCULOSIS PROGRAMME

G.V.J. BAILY

In the routine chemotherapy of pulmonary tuberculosis, premature termination of treatment and irregularity of drug intake by patients are common. Though rarely documented, it is often expressed by treating physicians that regimens containing Streptomycin are more acceptable to patients. Acceptability of drug regimen by TB patients may mean different things to different persons but it can best be defined by the two most important criteria (besides regimen efficacy) for obtaining a favourable response, viz., adequate duration of treatment and a high regularity of drug intake. In the study reported, the acceptability of drug regimen under routine programme conditions was studied in terms of the duration for which the patients continued to remain on treatment and the level of drug collection achieved by them. The bacteriological response to treatment as assessed on the basis of four samples of sputa collected one each at the end of the 10th and the 11th months and 2 at the end of the 12th month of treatment was also studied.

474 bacillary patients were admitted to the study of which 232 were allotted to biweekly Streptomycin and Isoniazid regimen (SH) and 242 to self-administered daily oral regimen with Isoniazid and Thioacetazone (TH) on a random basis. The findings regarding acceptability and response to treatment are presented for 323 patients of which 134 were on the SHTW regimen and 189 were on the TH regimen. It was seen that drug acceptability with reference to duration as well as the level of drug collection was similar among both the groups of patients. While 63 per cent of the SHTW patients remained on treatment almost upto one year, 58 per cent of TH patients were on treatment upto one year. Considering the response to treatment, the sputum conversion and the development drug resistance were similar in both the groups while deaths were higher among patients treated with the TH regimen.

It is concluded that regimen characteristics do not influence acceptability. A four-year follow up of these patients is at present in progress.

## INTERMITTENT CHEMOTHERAPY IN PATIENTS OF PULMONARY TUBERCULOSIS ATTENDING A TUBERCULOSIS CLINIC IN BOMBAY

BY

M.D. DESHMUKH, K.G. KULKARNI And S.S. VIRDI

One hundred and thirty six consecutive sputum positive patients were treated on a domiciliary basis with bi-weekly streptomycin and INH supervised regimen. Thirty three of these had taken treatment for 2 weeks to one year already prior to reporting at the Organised Home Treatment Clinic, Bombay.

Three patients died within two weeks of starting treatment and 47 stopped treatment prematurely within the first 6 months. 87 per cent of the 68 previously untreated patients showed radiological improvement and sputum conversion as against 33 per cent of the 18 previously treated patients. Evidence of toxicity or intolerance was seen in 6 patients only.

## **ORAL INTERMITTENT CHEMOTHERAPY WITH THIAACETAZONE AND ISONIAZID: PRELIMINARY REPORT**

BY

K.V. KRISHNASWAMY

Eighty six patients were put on oral intermittent therapy (INH 650 rag and Thiacetazone 450 mg daily twice a week) after an intensive daily treatment with streptomycin, INH and thiacetazone for 4 weeks. During 44 weeks of intermittent oral chemotherapy 26 per cent of the patients complained of dizziness. 10 per cent complained of vomiting. All other side effects were mild and seen most often during the first 3 months of treatment and more so in males. Sputum conversion was 52 per cent in 6 months and 83-89 per cent after 12 months. Radiological improvement was seen in all cases.

## **FOLLOW UP OF PATIENTS TREATED UNDER THE URBAN DOMICILIARY TREATMENT PROGRAMME IN MADRAS**

BY J. FRIMODT-MOLLER, K.V. KRISHNASWAMI AND G.S. ACHARYULU

Nearly 1500 new patients from three big clinics in Madras, treated on domiciliary basis during the period 1966 to 1970, were followed up with a view to assess their subsequent status. Information was collected ordinarily on their visit to the clinics but in some cases sputum was collected even at the house of the patients if they did not attend for follow up. Only 25 per cent of the patients continued their treatment for 12 months or more. Sputum conversion could be studied only in the case of patients from one clinic and it was 55.3 percent. 21 per cent of the patients relapsed but most of them had incomplete treatment. It is possible that some more who had relapsed took treatment elsewhere. At the end of 6th year, 48 per cent of the patients from one clinic and 23 per cent of the patients from another clinic were known to have died. The marked difference between the death rate could have been due to under-reporting.

The authors conclude that the achievement of domiciliary treatment as available from these clinics is not significant, the patients who derived maximum benefit did not exceed 20 per cent of the total number of patients followed. The main cause for poor results has been default on the part of the patients.

## NEWS AND NOTES

### ANNUAL MEETINGS

The Thirty-fifth Annual General Meeting of the Tuberculosis Association of India was held on 30th April, 1974 in the conference hall of the Association. This was followed by a meeting of the Central Committee of the Association. Shri S. Ranganathan presided over both these meetings. A conference of Secretaries of State TB Associations and Seal Sale Committees was held on 29th April, 1974.

### KHUSHI RAM SHIELD

The Association has awarded the KHUSHI RAM SHIELD for outstanding work done during 1973 to the Bengal TB Association. The Shield is named as Khushi Ram Shield in recognition of Rai Sahib Khushi Ram's generous donation to the Association of Rs. 1,50,000 for an Endowment Fund out of which a sum of 1,00,000 has already been received from him. The Association has also awarded a Merit Certificate to the Delhi TB Association for its good work.

### SEAL SALE AWARDS

The Association's Seal Sale Trophy for the 23rd Campaign was awarded to the Tamil Nadu TB Association. This Association has bagged this coveted Shield for the seventh year in succession. The Tamil Nadu Association collected Rs. 6,26,621.10, the highest collection so far made by a State Association. The Runner-up-Gup was awarded to Kerala TB Association which collected Rs. 2,25,283.77.

The Cup offered for the best performance made by smaller States and Union Territories was won by the TB Association of Goa, Daman and Diu. This Association gets the Cup for the second time. This Association collected Rs. 13,061.40 for this Campaign. The Associations of Karnataka, Punjab and Tripura were given certificates of Merit for the best use of Seal Sale collections.

Shri S. Ranganathan, President, gave away awards at the 35 Annual General Meeting held on 30.4.1974.

### TWENTY-FIFTH TB SEAL

The Tuberculosis Association of India has selected the design depicting 'A DOVE IN FLIGHT', received from Shri Y.N. Verma, Asst. Professor of Arts and Crafts, Lucknow, for the

25th TB Seal Campaign which will commence from October 2, 1974. The design was adjudicated as the best out of 57 designs received from 28 artists and carries a cash prize of Rs. 1,000/-. It may be recalled that Shri Verma had won the last year's cash prize for his design 'BUTTERFLY'.

### HEALTH VISITORS' COURSE

The 1974-75 TB Health Visitors' course will commence in July 1974. The Course will be of 9 months duration of which five months will be spent in the New Delhi TB Centre, two weeks in LRS TB Hospital, Mehrauli, two weeks for examination (in December) and three months internship which will last from 1st January to 31st March (including two weeks in a rural centre). The minimum qualification for admission to this course is Higher Secondary/Pre-University with Science or Hygiene and Physiology in Matriculation.

### SEMINAR IN INDORE

The Madhya Pradesh TB Association held a Seminar on Tuberculosis on 2nd and 3rd May, 1974 at Indore. Leading specialists in TB attended the Seminar. Important subjects discussed in the Seminar were "National TB Control Programme", "Current problems in TB and their management", "Diagnosis of Tuberculosis" and "Results of surveys in India".

### ANTI-TB SHIBIRS

The 52nd Anti-TB Sibir of the Maharashtra State Anti-TB Association was held at Mhsala (Dist. Colaba) on 3rd February, 1974 in collaboration with the Gram Panchayat, Lions Club of Worli and Themis Pharmaceuticals. A team of Specialists and Technicians, led by Dr. M.D. Deshmukh, examined 86 persons and vaccinated 877 children with BCG. Thirteen cases of pulmonary Tuberculosis were detected in the Sibir and bacilli of TB were found in sputum of 6 of these 13 patients.

The Karnataka State TB Association organised a TB Health Education and Case Detection Camp at Badavara Balage, Cubbonpet, Bangalore, on 9th February, 1974. Hon'ble H. Siddaveerappa, State Health Minister, presided and the Camp was inaugurated by Hon'ble N. Rachaiiah, State Minister for Social Welfare and Community Develop-

ment. The Camp was addressed by Dr. K. Nagappa Alva, M.P. and Shri Y. Ramachandra, MLC.

#### **CHANCHAL SINGH MEMORIAL AWARD**

The Tuberculosis Association of India will award a cash prize of Rs. 500/- to a Tuberculosis worker, below 45 years of age, 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 Tuberculosis. Papers may be sent in quadruplicate to reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-1, on or before 31st August, 1974.

#### **ESSAY COMPETITION—1974**

The Tuberculosis Association of India will award a cash prize of Rs. 300/- to a final year medical student in India for an original essay on Tuberculosis. The subject selected for the 1974 competition is "Prevention of Tuberculosis". The article should not exceed 15 pages (approximately 3000 words) in foolscap size, double-spaced excluding diagrams etc. Four copies should reach the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-1 on or before 31st August, 1974.

#### **EASTERN REGION CONFERENCE**

The IXth Eastern Region Tuberculosis Conference of the International Union Against Tuberculosis will be held in New Delhi from 3rd to 8th November, 1974, combined with 29th National Conference on TB and Chest Diseases. The Conference will be organised by the Tuberculosis Association of India with the active participation of State TB Association. For registration forms and other details please contact the Secretary-General, Tuberculosis Association of India, 3, Red Cross Road, New Delhi-110001.

#### **BOGUS REGISTRATION BOARD**

The Secretary, Medical Council of India,

in a statement has warned that an organisation under the name of 'India Medical Council and Registration Board, Hyderabad' (Government of India) has been issuing certificates to persons who do not possess recognised Medical qualifications included in the Schedules to the Indian Medical Council Act 1956. That Association is also said to have shifted its organisation to Delhi. At present registration of doctors is being done by the State Medical Councils in India which have been constituted under the State Acts.

#### **DR. R. VISWANATHAN**

Dr. R. Viswanathan, Emeritus Scientist, Vallabhbhai Patel Chest Institute, has been awarded "Padma Bhusan" by the President of India on the Republic Day, 1974. Dr. Viswanathan is a member of the Central Executive and Technical Committee of the Association. He is also Chairman of the Research Committee of TAI.

#### **DR. B.C. ROY NATIONAL AWARD**

The Managing Committee of Dr. B.C. Roy National Award Fund invites nominations for their annual award to be given in recognition of the best talents in encouraging the development of Specialities in Medicine. For details write to the Secretary, c/o Medical Council of India, Temple Lane, Kotla Road, New Delhi.

#### **OBITUARY**

Dr. P.K. Doraiswami, an eminent Orthopaedic Surgeon and a former Director General of Health Services, passed away on 11.3.74. Dr. Doraiswami was Chairman of this Association (1968-70) and took keen interest in anti-TB work in general and in the activities of the Association in particular.

Dr. L.R. Dongrey, TB specialist, passed away on 21.2.74. Dr. Dongrey was Chairman of the Technical Committee of the Association (1963-65) and president of the XIXth National Conference of TB and Chest Diseases.